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STUDIES OF THE GEM-DIALKYL EFFECT IN
THE 2,2-DIALKYL-1,3-PROPANEDIAMINE CHELATES
OF COPPER (II) AND NICKEL (II)

DISSERTATION

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

By


* * * * * *

The Ohio State University
1968

Approved by

Melvin S. Hyman
Adviser
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I. INTRODUCTION

Studies in the formation of ring compounds from acyclic precursors show that the rates of cyclization and the equilibrium product distributions exhibit large substituent effects, especially when the alkyl substituents are geminal. The gem-dialkyl effect has been noted in a number of different systems, of which a few examples are given below.

a. Anhydrides. In a detailed study of the hydrolysis of substituted glutaric anhydrides it was found that the replacement of one \( \beta \)-hydrogen by a methyl group decreased the rate of hydrolysis of glutaric anhydride by 40\%. When two \( \beta \)-methyls were present the rate was decreased by a factor of 13. When ethyl or isopropyl groups were incorporated at the \( \beta \)-position, smaller decreases in the rates of hydrolysis were noted. (See Table 1).

\[
\begin{align*}
&\text{R} \quad \text{O} \\
&\text{R} \quad \text{O} \\
\end{align*}
\]

oh\(-\)/h\(_2\)o

\[
\begin{align*}
&\text{R} \quad \text{CO}_2\text{H} \\
&\text{R} \quad \text{CO}_2^- \\
\end{align*}
\]


TABLE 1
Rates of Hydrolysis of Substituted Glutaric Anhydrides

<table>
<thead>
<tr>
<th>R</th>
<th>R'</th>
<th>$k_{OH} \times 10^{10}$</th>
<th>$k_{unsub}/k_{subst}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>H</td>
<td>4.16</td>
<td>1.0</td>
</tr>
<tr>
<td>H</td>
<td>CH$_3$</td>
<td>2.58</td>
<td>1.61</td>
</tr>
<tr>
<td>CH$_3$</td>
<td>CH$_3$</td>
<td>0.316</td>
<td>13.2</td>
</tr>
<tr>
<td>C$_2$H$_5$</td>
<td>C$_2$H$_5$</td>
<td>0.228</td>
<td>18.2</td>
</tr>
<tr>
<td>i-C$_3$H$_7$</td>
<td>i-C$_3$H$_7$</td>
<td>0.125</td>
<td>33.3</td>
</tr>
</tbody>
</table>

b. Formation of epoxides. Another good example of the gem-dialkyl effect was reported in the formation of epoxides from chlorohydrins on treatment with aqueous base as shown in Table 2. A rate enhancement of from five- to twenty-fold per methyl group was found. It was not determined whether the rate being measured was for an internal Sn$_2$ ring closure or an Sn$_1$ hydrolysis of the chloride followed by ring closure.$^3$

TABLE 2  
Substituent Effects on Rate of Formation of Ethylene Oxide

<table>
<thead>
<tr>
<th>Substituent</th>
<th>Relative Rate $k_{\text{subst}}/k_{\text{unsubst}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{H} \ \ \text{H} \ \ \text{H} \ \ \text{H}$</td>
<td>$1.0$</td>
</tr>
<tr>
<td>$\text{CH}_3 \ \ \text{H} \ \ \text{H} \ \ \text{H}$</td>
<td>$21.5$</td>
</tr>
<tr>
<td>$\text{H} \ \ \text{H} \ \ \text{CH}_3 \ \ \text{H}$</td>
<td>$5.5$</td>
</tr>
<tr>
<td>$\text{CH}_3 \ \ \text{CH}_3 \ \ \text{H} \ \ \text{H}$</td>
<td>$252.5$</td>
</tr>
<tr>
<td>$\text{H} \ \ \text{H} \ \ \text{CH}_3 \ \ \text{CH}_3$</td>
<td>$248.8$</td>
</tr>
<tr>
<td>$\text{CH}_3 \ \ \text{CH}_3 \ \ \text{CH}_3 \ \ \text{H}$</td>
<td>$1370.0$</td>
</tr>
<tr>
<td>$\text{H} \ \ \text{CH}_3 \ \ \text{CH}_3 \ \ \text{CH}_3$</td>
<td>$2040.0$</td>
</tr>
<tr>
<td>$\text{CH}_3 \ \ \text{CH}_3 \ \ \text{CH}_3 \ \ \text{CH}_3$</td>
<td>$11600.0$</td>
</tr>
</tbody>
</table>
c. Cyclic amines. A study of the rate of cyclization of 4-bromobutylamine in a buffered aqueous acetic acid solution gives an excellent example of the gem-dialkyl effect.\(^4\) Gem-dimethyl groups in the 2 position caused an 158-fold rate enhancement and di-isopropyl groups a 9190-fold increase.

\[
\begin{align*}
\text{Br-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH}_3 & \quad \xrightleftharpoons{K} \quad \text{Br-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH}_2 \\
\text{Br-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH}_2 & \quad \xrightarrow{k} \quad \text{N} \\
\end{align*}
\]

**TABLE 3**
Substituent Effects on Rate of Formation of Pyrrolidine

<table>
<thead>
<tr>
<th>Substituents</th>
<th>(k_{\text{subst}}/k_{\text{unsubst}})</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,2 H</td>
<td>1.00</td>
</tr>
<tr>
<td>2,2 di-CH(_3)</td>
<td>158.</td>
</tr>
<tr>
<td>2,2 di-C(_2)H(_5)</td>
<td>594.</td>
</tr>
<tr>
<td>2,2 di-i-C(_3)H(_7)</td>
<td>9190.</td>
</tr>
<tr>
<td>2,2 diphenyl</td>
<td>5250.</td>
</tr>
</tbody>
</table>

\(k_{\text{unsubst}} = 2.66 \times 10^{-6} \text{ sec}^{-1}\)

d. Ketals. The rates of hydrolysis of cyclic ketals show a consistent trend of decreasing rate with increasing size of gem substituent. As with the hydrolysis of glutaric anhydrides mentioned above the largest change in rate occurs in going from the unsubstituted to the dimethyl ketal with additional but smaller changes when the methyl groups are replaced by ethyl or isopropyl groups.

**TABLE 4**

Relative Rates of Ketal Hydrolysis

<table>
<thead>
<tr>
<th>Glycols</th>
<th>Cyclohexanone</th>
<th>Cyclopentanone</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethylene glycol</td>
<td>1.0</td>
<td>13.0</td>
</tr>
<tr>
<td>1,3-propanediol</td>
<td>30.6</td>
<td>172.</td>
</tr>
<tr>
<td>2,2-dimethyl-1,3-propanediol</td>
<td>2.01</td>
<td>16.5</td>
</tr>
<tr>
<td>2,2-diethyl-1,3-propanediol</td>
<td>0.888</td>
<td>7.65</td>
</tr>
<tr>
<td>2,2-diisopropyl-1,3-propanediol</td>
<td>0.335</td>
<td>2.67</td>
</tr>
</tbody>
</table>

*aSolvent: 70-30 dioxane-water, 0.003 N. HCl, at 30°C.*

---

Newman and Smith\textsuperscript{6} have studied the relative rates of hydrolysis plus the equilibrium constants of steriod cyclic ketals to determine which of the diols would be the most selective blocking group in a diketo steriod.

Table 5 gives the equilibrium constants for ketalization of 5\(\alpha\)-androstane-3,17-dione.

\begin{center}
\begin{tabular}{|l|c|c|c|}
\hline
Glycol & \(K_3\) & \(K_{17}\) & \(K_3/K_{17}\) \\
\hline
ethylene glycol & 0.76 & 0.027 & 28 \\
1,3-propanediol & 0.03 & ---- & -- \\
2,2-dimethyl-1,3-propanediol & 0.45 & 0.004 & 113 \\
2,2-diethyl-1,3-propanediol & 0.57 & 0.002 & 285 \\
\hline
\end{tabular}
\end{center}

This data shows that the ketals derived from ethylene glycol are more stable than those derived from 1,3-propanediol, but that the introduction of 2,2-dialkyl substituents into 1,3-propanediol increased

the stability of the corresponding ketals, and the latter are almost as stable as those derived from ethylene glycol. The equilibrium constants also show that the reaction of the 3-keto group (K₃) was greater than those for the 17-keto group (K₁₇) with all diols studied. The largest value of the ratio K₃/K₁₇ occurred in the case of 2,2-diethyl-1,3-propanediol. The results above show also that the equilibrium method offers the greater selectivity in blocking the 3-position since only trace amounts of the 17 ketal are formed with even a 20-fold excess of glycol. In addition, the substituted propanediols showed greater selectivity than ethylene glycol, the usual glycol used to block ketones.

Newman and Dickson have studied the gem-dialkyl effect of small rings. The above studies showed that ketals prepared from 1,3-propanediols with substitution at the middle carbon are more stable the larger the substituent. Since the increased stability of the ketals with bulky substituents could be due to a compressed bond angle (\( \alpha \)), their study was to determine if the 3-, 4-, 5-, and 6-membered rings (\( R, R' = -(CH₂)_n^-, n = 2, 3, 4, \) and 5) would have a similar influence on the rates and equilibrium constants.

\[
\begin{align*}
&\text{CH}_2\text{O}L

\begin{array}{c}
\text{CH}_2\text{O}L
\end{array}
&\text{R}
\end{align*}
\]


8R. E. Dickson, Ph. D. Dissertation, The Ohio State University, 1968.
The kinetic and equilibrium data are given in Table 6. The equilibrium data show that the equilibrium constant is largest for cyclohexyl acetals and smallest for cyclopropyl ones. As expected, if the relief of angle strain is an important factor in the stability of the acetals, and the hydrolysis thereof, the most stable ones would be the spirocyclohexyl acetals and the least stable would be the cyclopropyl one. The greatest change in equilibrium constant between adjacent members of a series occurred between the cyclopropyl and cyclobutyl acetal with further but smaller changes between the other members of the series. However, the rate of formation calculated from K and k_{hyd} showed that the change in the carbocyclic ring has no systematic effect on the rate of acetal formation.

Thorpe\textsuperscript{9} and Ingold\textsuperscript{10} have attributed the so called gem,\textsuperscript{10} or gem-dialkyl effect to the spatial requirements of the atoms involved. They hypothesized that as the size of the alkyl groups increases, the angle alpha decreases, thereby facilitating ring closure.

Hammond\textsuperscript{11} and Allinger and Zalkow\textsuperscript{12} attributed the gem-dialkyl effect to entropy differences between the open chain and cyclic structures. A possible restriction of free rotation in substituted


\textsuperscript{10}E. K. Ingold, ibid., 119, 305 (1921); E. K. Ingold, ibid., 121, 2676 (1923).


<table>
<thead>
<tr>
<th>Diol</th>
<th>(k_{\text{hyd}}) (mole/l-min)</th>
<th>(K_{\text{eq}})</th>
<th>(k_{f} = K \times k_{\text{hyd}}) (moles/l-min)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACETAL of 1-naphthaldehyde</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)-cyclopropane</td>
<td>4.2</td>
<td>0.92</td>
<td>4.0</td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)-cyclobutane</td>
<td>0.28</td>
<td>11.0</td>
<td>3.1</td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)-cyclopentane</td>
<td>0.14</td>
<td>26.2</td>
<td>3.6</td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)-cyclohexane</td>
<td>0.09</td>
<td>61.</td>
<td>5.5</td>
</tr>
<tr>
<td><strong>ACETAL of 2-naphthaldehyde</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)-cyclopropane</td>
<td>4.3</td>
<td>1.27</td>
<td>5.5</td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)-cyclobutane</td>
<td>0.22</td>
<td>9.6</td>
<td>2.1</td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)-cyclopentane</td>
<td>0.14</td>
<td>26.6</td>
<td>3.7</td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)-cyclohexane</td>
<td>0.068</td>
<td>66.</td>
<td>4.5</td>
</tr>
</tbody>
</table>
acyclic molecules may occur and thereby if rotation about the bonds
of the alkylated carbon is restricted by the R groups, the entropy
of formation of a cyclic isomer would be less negative than with
the corresponding acyclic compound.

Similar studies of substituent effects have been made on the
formation and stability of metal complexes. The effect of steric
hindrance on the chelating tendencies of N-substituted ethylene
diamines has been reported. Studies of the chelating tendency
of propylene diamine to that of ethylene diamine show that one
methyl group on a carbon atom of ethylene diamine does not alter
greatly the coordinating ability of the diamine. Another study
of the effect of steric factors on the chelating tendencies of
diamines with copper (II) and nickel (II) ions is the use of
multi C-substituted ethylene diamines. The stepwise formation
constants of these two ions with \( \text{H}_2\text{N-} \text{CR}_2\text{CR}_2\text{-NH}_2 \) (R = H, Me, or
phenyl) have been determined. The formation constants for Cu (II)
and Ni (II) complexes are shown in Tables 7 and 8.

---

(1952); ibid., 76, 211 (1954).

14 Propylene diamine is \( \text{H}_2\text{N-CH}_2\text{CH(CH}_3\text{)NH}_2 \)

15 G. A. Carlson, J. P. McReynolds, and R. H. Verhoek, ibid.,
67, 1334 (1945).

16 F. Basolo, Y. T. Chen, and R. K. Murmann, ibid., 76, 956
(1954).
**TABLE 7**  
Formation Constants of Cu (II) with Substituted Ethylene Diamines  
25° C. in water

<table>
<thead>
<tr>
<th>Diamine</th>
<th>log $K_1$</th>
<th>log $K_2$</th>
<th>log $K_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethylene diamine</td>
<td>10.76</td>
<td>9.37</td>
<td>20.13</td>
</tr>
<tr>
<td>propylene diamine</td>
<td>10.78</td>
<td>9.28</td>
<td>20.06</td>
</tr>
<tr>
<td>dl-butylene diamine</td>
<td>11.39</td>
<td>9.82</td>
<td>21.21</td>
</tr>
<tr>
<td>meso-butylene diamine</td>
<td>10.72</td>
<td>9.34</td>
<td>20.06</td>
</tr>
<tr>
<td>isobutylene diamine</td>
<td>10.53</td>
<td>9.05</td>
<td>19.58</td>
</tr>
<tr>
<td>tetramethyl ethylene diamine</td>
<td>11.63</td>
<td>10.34</td>
<td>21.87</td>
</tr>
<tr>
<td>dl-stilbene diamine$^a$</td>
<td>10.07</td>
<td>9.11</td>
<td>19.18</td>
</tr>
<tr>
<td>meso-stilbene diamine$^a$</td>
<td>8.46</td>
<td>7.50</td>
<td>15.96</td>
</tr>
</tbody>
</table>

$^a$Insoluble in water, run in a 50-50 mixture of dioxane-water.

$(\text{Cuen(H}_2\text{O)}_4)^{2+}$ and $(\text{Cu(en)}_2(\text{H}_2\text{O})_2)^{+2}$ form readily, but $(\text{Cu(en)}_3)^{+2}$ forms only at extremely high concentrations of ethylene diamine (en). The addition of the third molecule of ethylene diamine is difficult because the Cu (II) ion does not bind the third ligand strongly due to the Jahn-Teller effect.
TABLE 8
Formation Constants of Ni (II) with Substituted Ethylene Diamines

25° C. in water

<table>
<thead>
<tr>
<th>Diamine</th>
<th>log $K_1$</th>
<th>log $K_2$</th>
<th>log $K_3$</th>
<th>log $K_t$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethylene diamine</td>
<td>7.60</td>
<td>6.48</td>
<td>5.03</td>
<td>19.11</td>
</tr>
<tr>
<td>propylene diamine</td>
<td>7.43</td>
<td>6.19</td>
<td>4.27</td>
<td>17.89</td>
</tr>
<tr>
<td>dl-butylene diamine</td>
<td>7.71</td>
<td>6.48</td>
<td>4.31</td>
<td>18.50</td>
</tr>
<tr>
<td>meso-butylene diamine</td>
<td>7.04</td>
<td>5.70</td>
<td>2.89</td>
<td>15.63</td>
</tr>
<tr>
<td>isobutylene diamine</td>
<td>6.77</td>
<td>5.40</td>
<td>2.25</td>
<td>14.42</td>
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<tr>
<td>dl-stilbene diaminea</td>
<td>7.37</td>
<td>6.09</td>
<td>4.38</td>
<td>17.84</td>
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<tr>
<td>meso-stilbene diaminea</td>
<td>4.70</td>
<td>3.52</td>
<td></td>
<td>8.22</td>
</tr>
</tbody>
</table>

*a insoluble in water, run in a 50-50 mixture of dioxane-water.*
The results of this study show that generally C-substitution on ethylene diamine has only a relatively small effect on its coordinating tendency toward Cu (II) and Ni (II) ions. However, this study also shows that the complexes of dl-butylene diamine are more stable than those of meso-butylene, which is also true for dl-stilbene diamine compared to meso-stilbene diamine. Models given below show that the five-membered chelate of the racemic bases are free of internal strain as the methyl or phenyl groups have ample room being on opposite sides of the ring.

These results show that strain within the chelate ring is playing a minor role.

The above chelating tendencies closely parallel the findings on the intramolecular hydrogen bonding in alcohols. Intramolecular hydrogen bonding in the alcohols involves the formation of a ring, which is somewhat analogous to the chelation which occurs during the coordination of diamine with metal ions. The extent of intramolecular

---

hydrogen bonding in dl-butane-2,3-diol (Av = 45 cm\(^{-1}\)) is greater than that in meso-butane-2,3-diol (Av = 38 cm\(^{-1}\)).

Another possible type of steric influence on chelating tendencies is the study of the stepwise stability constants of metal complexes of ethylene diamine and 1,3-diaminopropane.

The Cu (II) and Ni (II) complexes of 1,3-diaminopropane are significantly less stable than those of ethylene diamine.\(^\text{18}\)

Increased chain length by increasing ring size brings about a noticeable decrease in stability although the basicity of the ligand increases. An explanation advanced is the following.\(^\text{18}\)

Since the \(-\Delta H\) values for the chelation with 1,3-diaminopropane are larger in accord with the greater basicity of this diamine, the large difference in stability of the chelates of these two diamines arises from a less favorable entropy change in the formation of the six-membered ring. This is probably associated with an increase in strain in the ring and with a greater loss of freedom of the ligand when the 1,3-diaminopropane molecule is fixed in a ring system.

TABLE 9

Formation Constants of Cu (II) and Ni (II) with Ethylene Diamine and 1,3-Diaminopropane at 20°

<table>
<thead>
<tr>
<th></th>
<th>log $K_1$</th>
<th>log $K_2$</th>
<th>log $K_3$</th>
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</thead>
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<tr>
<td>$H^+$ Cu(II) Ni(II) H$^+$ Cu(II) Ni(II) Ni(II)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ethylene diamine</td>
<td>10.09</td>
<td>7.52</td>
<td>4.49</td>
</tr>
<tr>
<td>1,3-diamino propane</td>
<td>10.62</td>
<td>8.64</td>
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Thermodynamic Quantities$^a$

<table>
<thead>
<tr>
<th></th>
<th>$-\Delta H_1$</th>
<th>$-\Delta H_2$</th>
<th>$-\Delta H_3$</th>
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<tr>
<td>$H^+$ Cu(II) Ni(II) H$^+$ Cu(II) Ni(II) Ni(II)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ethylene diamine</td>
<td>11.5</td>
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<tr>
<td>1,3-diamino propane</td>
<td>13.3</td>
<td>13.9</td>
<td>8.2</td>
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<table>
<thead>
<tr>
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<th>$-\Delta S_1$</th>
<th>$-\Delta S_2$</th>
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</thead>
<tbody>
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<td>$H^+$ Cu(II) Ni(II) H$^+$ Cu(II) Ni(II) Ni(II)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ethylene diamine</td>
<td>7</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>1,3-diamino propane</td>
<td>-3</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

$^a -\Delta H$ in kcal/mole from 10-40°; $-\Delta S$ in cal/mol-deg at 20°
The above studies have shown that the chelating tendencies of ligands are not only a function of the basicity of the ligand but also of the steric requirements and the resulting ring strain.

Further studies of the relative stability of complex ions containing chelate rings of more than five members have been conducted. It was found in all cases studied that the 6-membered rings were considerably less stable than the corresponding 5-membered rings and no complexes were formed with those amines which might form 7-membered chelate rings.

In addition it was found that the copper and nickel complexes of 2,2-dimethyl-1,3-propanediamine were more stable than those of 1,3-propanediamine. It was suggested that the increased stability of the 2,2-dimethyl-1,3-propanediamine complexes could not be explained on the basis of inductive effects of the methyl groups because the basicity of the ligand toward the proton is actually less than that of 1,3-propanediamine. Therefore, other factors must be influencing chelation and causing an increase in stability of the complexes. The formation constants of these complexes are given in Table 10.

<table>
<thead>
<tr>
<th></th>
<th>log $K_1$</th>
<th></th>
<th>log $K_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$H^+$</td>
<td>Cu(II)</td>
<td>Ni(II)</td>
</tr>
<tr>
<td>1,3-Propanediamine</td>
<td>8.95</td>
<td>9.62</td>
<td>------</td>
</tr>
<tr>
<td>2,2-Dimethyl-1,3-propanediamine</td>
<td>8.18</td>
<td>9.94</td>
<td>6.59</td>
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</table>
The above chelating tendencies can also be compared with the findings on the intramolecular hydrogen bonding in 1,3-propanediols. Schleyer's results show that $\Delta \nu$ ($\Delta \nu = $ spectral shift to shorter wavelength in the infrared spectrum of the free and intramolecularly hydrogen bonded diol) increases with methyl and ethyl disubstitution at the 2 position. See Table 11.

For the 1,1-di(hydroxymethyl)cycloalkanes, the cyclobutyl compound showed a significantly decreased $\Delta \nu$, while the spectral shift for cyclopropane-1,1-dimethanol was the lowest for any compound studied. The other cyclic compounds had normal values.

These results are attributed to the OH...O distance which is a function of the HOCH$_2$-C-CH$_2$OH bond angle.

Therefore, a comparable substituent effect including the effect imposed by the small rings (cyclopropyl and cyclobutyl) may be operating in chelation with the corresponding substituted 1,3-propanediamines.

![Chemical structures](image)

2,2-dialkyl-1,3-propanediol
intramolecularly hydrogen bonded

2,2-dialkyl-1,3-diaminopropane
metal chelate

---

TABLE 11
Hydrogen Bonding in Propane-1,3-diols

<table>
<thead>
<tr>
<th>R</th>
<th>R</th>
<th>(v), free cm(^{-1})</th>
<th>(v), bonded cm(^{-1})</th>
<th>(\Delta v) cm(^{-1})</th>
</tr>
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<tbody>
<tr>
<td>H</td>
<td>H</td>
<td>3637.0</td>
<td>3559.8</td>
<td>77.7</td>
</tr>
<tr>
<td>(\text{CH}_3)</td>
<td>(\text{CH}_3)</td>
<td>3641.7</td>
<td>3553.7</td>
<td>88.0</td>
</tr>
<tr>
<td>(\text{C}_2\text{H}_5)</td>
<td>(\text{C}_2\text{H}_5)</td>
<td>3643.0</td>
<td>3553.0</td>
<td>90.0</td>
</tr>
<tr>
<td>cyclopropyl</td>
<td></td>
<td>3635.7</td>
<td>3566.9</td>
<td>68.8</td>
</tr>
<tr>
<td>cyclobutyl</td>
<td></td>
<td>3637.7</td>
<td>3552.7</td>
<td>85.0</td>
</tr>
<tr>
<td>cyclopentyl</td>
<td></td>
<td>3638.3</td>
<td>3550.2</td>
<td>88.1</td>
</tr>
<tr>
<td>cyclohexyl</td>
<td></td>
<td>3640.3</td>
<td>3550.8</td>
<td>89.5</td>
</tr>
</tbody>
</table>

\[
\text{RCH}_2-\text{O}\equiv\overset{\text{H}}{\text{H}}\equiv\overset{\text{H}}{\text{H}}
\]
The process of chelate formation involves a competition between the chelating agent and the solvent for the metal ion. The operative principle is that of the Lewis Acid-Base Theory whereby the metal ion may be regarded as an electron pair acceptor and the ligand, the base, or electron donor. Thus the combination of a molecule of the chelating agent with a hydrated metal ion involves the displacement of the weak base, water, by a stronger base, the ligand. This process usually occurs at a low pH for chelates with a high stability constant, whereas chelates with a low stability constant are usually formed in alkaline solution.21

To have a knowledge of the magnitude of the stability constant involves an understanding of the thermodynamic quantities being measured. Potentiometric titrations are based on the evaluation of the free energy change associated with the reaction being considered. The equilibrium constant is a measure of the standard free energy of the reaction, that is,

$$\Delta F^0 = -RT \ln K$$

There is also a relation between free energy and enthalpy and entropy which must be considered.

$$\Delta F^0 = \Delta H^0 - T\Delta S^0$$

21 J. Bjerrum, Metal Ammine Formation in Aqueous Solution, P. Haase and Son, Copenhagen, (1941).
Therefore, an increase in an equilibrium constant may arise either because $\Delta H^o$ becomes more negative, or because $\Delta S^o$ becomes more positive, or both. In the formation of a complex, the enthalpy component may be attributed to the difference in bond energies of the metal solvent bonds broken and the new metal ligand bonds formed. This enthalpy difference cannot usually account for the greater stability of metal chelates versus the corresponding nonchelated coordination compounds, and therefore, the chelate effect has been attributed mainly to an entropy effect. Increasing chelation corresponds to increasingly positive values of $\Delta S^o$ and is largely due to an increase in randomness of the system resulting from a release of water molecules during chelation. In a nonchelate system, each water molecule is displaced by one ligand molecule, and thus the total number of molecules in the system remains constant. But in chelation reactions, one ligand molecule displaces two or more water molecules, making the net number of independent molecules greater.

It is possible under rigidly controlled conditions and with some difficulty, to obtain enthalpy changes titrametrically. This is invaluable in revealing the chemistry of complex formation reactions, but due to the inherent experimental difficulties

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associated with enthalpy titrations, the measurement of free energy changes, i.e., the equilibrium constants, has been favored.

There are several methods by which the stability constant of a metal chelate may be evaluated. The most widely applicable being potentiometric, spectrophotometric, and polarographic techniques. The potentiometric titration technique of Calvin and Bjerrum is the one employed here. This method allows semi-quantitative determinations of the extent of complex formation.

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II. OBJECT OF RESEARCH

Newman and Harper\(^1\) and Smith\(^2\) have studied the formation and hydrolysis of the six-membered cyclic ketals and acetals (1,3-dioxanes) derived from 1,3-propanediols and ketones or aldehydes. They have found from their kinetic and equilibrium studies that 1) the cyclic ketals derived from ethylene glycol are more stable and are hydrolyzed less readily than are the ketals derived from 1,3-propanediol; 2) the introduction of 2,2-dialkyl substituents into 1,3-propanediol increases the stability of, and decreases the hydrolysis rates of, the corresponding ketals. The ketals derived from 2,2-dimethyl, 2,2-diethyl, and 2,2-diisopropyl-1,3-propanediol are almost as stable as those derived from ethylene glycol and exhibit hydrolysis rates comparable to those of the corresponding ethylene ketals.

The coordination complexes of a metal ion with 1,3-diaminopropane and its homologs, 2,2-dialkyl-1,3-diaminopropanes and the diamines

\[
\begin{array}{c}
\bigg \{ \\
\text{CH}_2 \bigg \}^n \\
\text{C(CH}_2\text{NH}_2 \bigg \}^2
\end{array}
\]

\(n = 2, 3, 4, \text{ and } 5\)

---


also involve the corresponding six-membered chelates. (These six-membered chelates would be similar to the six-membered cyclic ketals (1,3-dioxanes) of 1,3-propanediol and ketones). Therefore, it was of interest to determine the formation constants of these six-membered chelates to see if they would show the corresponding gem-dialkyl effect. Thus, the object of this research was to synthesize the 2,2-dialkyl-1,3-diaminopropanes and the 1,1-di(aminomethyl)cycloalkane derivatives and to determine the acid dissociation constants of the diamines and the nickel (II) and copper (II) formation constants of the diamines.
III. RESULTS AND CONCLUSIONS

A. Organic Syntheses

The simplest and most direct synthesis of 2,2-dialkyl-1,3-diaminopropanes and the 1,1-di(aminomethyl)cycloalkane derivatives appeared to be the alkylation of malononitrile with the appropriate bromide or dibromide and base, followed by the reduction of the alkylated dinitrile.

Using sodium ethoxide in ethanol, a 13% yield of 1,1-dicyano-cyclopentane was obtained. The low yield was due to the formation of ethyl cyanoimidoacetate, \( \text{NCCH}_2\text{C(OC}_2\text{H}_5)\text{-NH} \) and a large undistillable residue. Attempts to alkylate malononitrile with ethylene dibromide in the presence of sodium ethoxide also resulted in low yields.\(^1\) The major products were the imido-esters. Because of the low yields, this method was abandoned.

Alkylation of malonamide using sodium amide in liquid ammonia and methyl bromide gave 46% of the desired 2,2-dimethylmalonamide, and 46% 2-methylmalonamide. The same reaction was performed using ethyl bromide, but only a 5% yield of the 2,2-diethylmalonamide was obtained. Realkylation of the mixture of monoethylmalonamide and malonamide gave a 64% yield of 2,2-diethylmalonamide.

The above alkylation method was also used to synthesize the 1,1-dicarboxamidocycloalkanes. The first attempt was 1,1-dicarboxamidocyclopentane. However, only 16% of the desired cyclopentyl compound was obtained, the major product being the tetraamide, 1,1,6,6-tetracarboxamidohexane (20%) and unalkylated malonamide (25%).

Because the above yield of diamide was low, this method was abandoned for the syntheses of the ring compounds. The cyclobutyl, cyclopentyl, and cyclohexyl diamides were synthesized by the following sequence: 1) alkylation of the diethyl malonate with the appropriate dibromide; 2) hydrolysis of the ester; 3) formation of the acid chloride; 4) ammonolysis. This sequence gave an overall yield of 31.3% of 1,1-dicarboxamidocyclobutane, 73% of 1,1-dicarboxamidocyclopentane, and 20.5% of 1,1-dicarboxamidocyclohexane based on diethyl malonate.

1,1-Dicarboxamidocyclopropane was synthesized in one step from the diethyl malonate by ammonolysis in 93% yield. Connors and Ross report the formation of 1,1-dicarboxamidocyclobutane from 1,1-dicarboxethoxycyclobutane using a concentrated aqueous solution of ammonia, and performing the reaction in a "pressure bottle". The same reaction was tried in a bomb, but no diamide was formed, and 95% of the diester was recovered.

The above diamides were subjected to reduction by the use of lithium aluminum hydride in Glyme (1,2-dimethoxyethane). Unfortu-

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nately, the reduction yields were very low: 1,3-diamino-2,2-dimethylpropane (16%); 1,3-diamino-2,2-diethylpropane (21%); 1,1-di(aminomethyl)cyclopropane (30%); 1,1-di(aminomethyl)cyclobutane (12%); 1,1-di(aminomethyl)cyclopentane (20%); and 1,1-di-(aminomethyl)cyclohexane (18%).

In hope that the dinitrile would be reduced in higher yield than the diamide, 1,1-dicarboxamidocyclopentane was treated with phosphorus pentoxide. However, only a 22% yield of 1,1-dicyanocyclopentane was obtained. Experimental difficulties made this route undesirable. Therefore, dehydration of the other diamides by this method was not performed.

Dehydration of 1,1-dicarboxamidocyclopentane using phosphorus pentachloride and phosphorus oxychloride was also unsuccessful as polymerization of the supposed dinitrile occurred on attempted distillation.

1,1-Di(aminomethyl)cyclopentane was also synthesized in 33.5% overall yield based on diethyl malonate by the following sequence. Reduction of 1,1-dicarboethoxycyclopentane with lithium aluminum hydride, conversation of the resulting diol to 1,1-di(mesitylmethyl)-cyclopentane, which in turn was converted to 1,1-di(phthalimido-methyl)cyclopentane which on hydrazinolysis gave the diamine.

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The synthetic route that gave the best results is the following.  
1) alkylation of diethyl malonate; 2) reduction of the diester to 
the diol with lithium aluminum hydride; 3) conversion of the diol to 
the dimesyl derivative; 4) formation of the diazide; 5) reduction 
of the diazide with lithium aluminum hydride to give the diamine. 
The over-all yields of diamine based on diethyl malonate were: 
1,1-di(aminomethyl)cyclopropane (32.7%); 1,1-di(aminomethyl)-
cyclobutane (32.1%); 1,1-di(aminomethyl)cyclopentane (50.7%); 
1,1-di(aminomethyl)cyclohexane (35.3%). And yields of diamine based 
on starting diol were: 1,3-diamino-2,2-dimethyl propane (43.2%) and 
1,3-diamino-2,2-diethyl propane (37.2%).

Good elemental analyses of the diamines were difficult to 
obtain. The diamines are very hygroscopic and absorb carbon 
dioxide rapidly on exposure to the atmosphere as indicated by the 
immediate formation of a white solid on the surface. (See experimental section). Hence, the diamines were converted in quantitative 
yields to the dihydrochloride derivatives which gave good analyses.

B. Complex Formation Constants

The acid dissociation constants for the diamines were deter-
mined as described in the experimental section. Three to five 
titration runs were made on each diamine and the resulting calcu-
lated pK_a1 and pK_a2 values were averaged. No individual calcula-
tion from any one run deviated by more than 0.05 of a pK_a unit 
from the average value. The results are given in Table 12. The
data for ethylene diamine, trimethylene diamine, and 1,3-diamino-2,2-dimethylpropane are in agreement with those of previous workers.

The formation constants for the nickel (II) and copper (II) complexes were determined by the Calvin-Bjerrum method. This technique consists of plotting \( \bar{n} \), the average number of ligands bound per metal ion, against \( pR \), the negative log of the concentration of the chelating species. The \( pR \) and the \( \bar{n} \) values were calculated for each point in the titration from 5.50 ml. to 14.00 ml. of NaOH added in the case of nickel, and from 5.20 to 11.00 ml. of NaOH for copper. A graph of \( \bar{n} \) versus \( pR \) was made for each amine.

With copper (II) ion a nearly constant value of \( \bar{n} = 2 \) was obtained toward the end of the titration indicating a maximum coordination number of four. The only exception is the trimethylene diamine plot, in which a maximum of \( \bar{n} = 1.5 \) was obtained, which shows that the stability of the disubstituted compound to be low.

Nickel (II) showed a maximum of \( \bar{n} \) equal to 2 for all 2,2-disubstituted 1,3-propanediamines. The ethylenediamine plot showed a maximum of \( \bar{n} \) equal to three. The values of \( pR \) at \( \bar{n} = 0.5, 1.0, \)

---


and 1.5 are equal to log \( K_1 \), log \( K_{AV} \), and log \( K_2 \), respectively.
(And \( n = 2.5 \) and 3.0 are equal to log \( K_{AV} \) and log \( K_3 \), pertaining to the ethylene diamine plot). 8

Tables 13 and 14 contain the stepwise formation constants for copper (II) and nickel (II) chelates. Figures 1 and 2 graphically represent the formation constants for copper and nickel chelates for 2,2-diethyl-1,3-diaminopropane, which are representative of all the 2,2-disubstituted diamines.

In general 5-membered chelate rings are the most stable in systems with saturated rings, as shown in other work. 6 A quantitative comparison is possible for the chelation of both nickel (II) and copper (II) ions with 1,3-propanediamine and 1,2-ethanedi amine. The chelates with the former diamine are approximately 10 times less stable than those with the latter, as shown in Tables 13 and 14.

Fernelius and co-workers 6 determined the enthalpy changes in the above chelations, and found that the \(-\Delta H_1\) values for the chelation with 1,3-propanediamine are the larger, in agreement with the greater basicity of this diamine. Therefore, the large difference in stability of the chelates of these two diamines must arise from a less favorable entropy change in the formation of the 6-membered ring. This may be associated with an increase in strain in the ring and with a greater loss of freedom of the ligand when the 1,3-propanediamine molecule is fixed in a ring system.
<table>
<thead>
<tr>
<th>Amine</th>
<th>pK$_{a1}$</th>
<th>pK$_{a2}$</th>
</tr>
</thead>
<tbody>
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<td>10.18</td>
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</tr>
<tr>
<td>C$_2$H$_5$(\text{C}\text{H}_2\text{NH}_2)</td>
<td>7.59</td>
<td>10.23</td>
</tr>
<tr>
<td>C$_2$H$_5$(\text{C}\text{H}_2\text{NH}_2)</td>
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<td></td>
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<tr>
<td>CH$_2$(\text{N}\text{H}_2)</td>
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<td>10.32</td>
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<td>Diamine</td>
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<td>log $K_{AV}$</td>
</tr>
<tr>
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<td>-----------</td>
<td>--------------</td>
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<td>8.78</td>
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<td></td>
</tr>
<tr>
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<tr>
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<td>9.72</td>
</tr>
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<tr>
<td>$\text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2$</td>
<td>9.18</td>
<td>7.40</td>
</tr>
</tbody>
</table>
### TABLE II
Nickel (II) Formation Constants at 25°C.

<table>
<thead>
<tr>
<th>Diamine</th>
<th>log $K_1$</th>
<th>log $K_{AV}$</th>
<th>log $K_2$</th>
<th>log $K_{AV}$</th>
<th>log $K_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_3$NH$_2$</td>
<td>6.28</td>
<td>5.20</td>
<td>4.16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_3$CH$_2$NH$_2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$_2$H$_5$CH$_2$NH$_2$</td>
<td>6.54</td>
<td>4.30</td>
<td>4.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$_2$H$_5$CH$_2$NH$_2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_2$NH$_2$</td>
<td>6.42</td>
<td>5.00</td>
<td>4.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_2$NH$_2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$_2$H$_5$CH$_2$NH$_2$</td>
<td>6.36</td>
<td>4.80</td>
<td>4.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$_2$H$_5$CH$_2$NH$_2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_2$NH$_2$</td>
<td>6.60</td>
<td>5.40</td>
<td>4.30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_2$NH$_2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$_2$H$_5$CH$_2$NH$_2$</td>
<td>6.61</td>
<td>5.16</td>
<td>3.90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$_2$H$_5$CH$_2$NH$_2$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H$_2$NCH$_2$CH$_2$NH$_2$</td>
<td>7.30</td>
<td>6.60</td>
<td>5.95</td>
<td>5.09</td>
<td>4.08</td>
</tr>
<tr>
<td>H$_2$NCH$_2$CH$_2$NH$_2$</td>
<td>6.18</td>
<td></td>
<td></td>
<td></td>
<td>4.28</td>
</tr>
</tbody>
</table>
FIGURE 1

Formation Curve for Cu(II) Complex of 2,2-Diethyl-1,3-propanediamine

\[
\bar{n} = 0.5 \quad pR = 9.94 \\
\bar{n} = 1.0 \quad pR = 8.60 \\
\bar{n} = 1.5 \quad pR = 7.36
\]

\((C_2H_5)_2C(CH_2NH_2HCl)_2 : Cu\)  
16 : 1
FIGURE 2

Formation Curve for Ni(II) Complex of 2,2-Diethyl-1,3-propanediamine

\[
\bar{n} = 0.5 \quad p_R = 6.54
\]
\[
\bar{n} = 1.0 \quad p_R = 5.30
\]
\[
\bar{n} = 1.5 \quad p_R = 4.06
\]
FIGURE 3

Titration Curves for 2,2-Diethyl-1,3-propanediamine

\[
\text{Diamine} : Cu :: 16:1 \\
\text{Diamine} : Ni :: 16:1 \\
\text{Diamine} : Cu :: 8:1 \\
\text{Diamine} : Ni :: 8:1 \\
\text{Cu(ClO}_4\text{)}_2 \\
\text{Ni(ClO}_4\text{)}_2
\]
As shown in Tables 13 and 14, the nickel (II) and copper (II) formation constants of the 2,2-dialkyl-1,3-diaminopropanes and the 1,1-di(aminomethyl)cycloalkanes are slightly greater than those of 1,3-propanediamine and slightly less than those of 1,2-ethanediamine. Hence, introduction of gem-dialkyl groups into the 1,3-propanediamine increases the stability of the resulting chelates, and therefore, promotes ring stability in metal chelates.

Since Fernelius and co-workers have shown that the differences in the enthalpy values for the chelation of 1,3-propanediamine (\(\Delta H_1 = 10.2 \text{ kcal/mole for nickel, and 13.9 kcal/mole for copper} \)) and 1,2-ethanediamine (\(\Delta H_1 = 9.5 \text{ kcal/mole for nickel, and 12.8 kcal/mole for copper} \)), are small, the greater stability of the latter is attributed to the entropy effect. Likewise, the greater stability of the chelates of the 2,2-disubstituted 1,3-propanediamines over that of 1,3-propanediamine may be attributed to the entropy change.

Because of the substituents in the dialkylated 1,3-propanediamine, these compounds as free molecules will have less freedom of rotation and will exist in fewer conformations than 1,3-propanediamine. Therefore, on chelation 1,3-propanediamine experiences a greater entropy change. This is presumably associated with a greater loss of freedom of the ligand when the 1,3-propanediamine molecule is fixed in a ring system versus the chelation of the dialkylated 1,3-propanediamines.
It may be anticipated that the formation constants would vary with substituents on 1,3-propanediamine. A study of hydrogen bonding in 1,3-propanediols showed\textsuperscript{10} that $\Delta v$, ($\Delta v$ = spectral shift in the infrared spectrum of the free and intramolecularly hydrogen bonded diol) increases and therefore hydrogen bonding increases with methyl and ethyl disubstitution at the 2 position.

\begin{table}[h]
\centering
\begin{tabular}{ccc}
\hline
R & R & $v_{\text{free}}$ cm\textsuperscript{-1} & $v_{\text{bonded}}$ cm\textsuperscript{-1} & $\Delta v$ cm\textsuperscript{-1} \\
\hline
H & H & 3637.0 & 3559.8 & 77.7 \\
CH\textsubscript{3} & CH\textsubscript{3} & 3641.7 & 3553.7 & 88.0 \\
C\textsubscript{2}H\textsubscript{5} & C\textsubscript{2}H\textsubscript{5} & 3643.0 & 3553.0 & 90.0 \\
\hline
\end{tabular}
\caption{Hydrogen Bonding in 2,2-Dialkyl-1,3-propanediols}
\end{table}

Also studied were the 1,1-di(hydroxymethyl)cycloalkanes. The cyclobutyl compound showed a significantly decreased $\Delta v$, while the spectral shift for cyclopropane-1,1-dimethanol was the lowest for any compound studied. The other cyclic compounds had normal values. These results were attributed to the OH...O distance which is a function of the C-C-C bond angle containing the OH groups.

**TABLE 16**

Hydrogen Bonding in 1,1-Di(hydroxymethyl)cycloalkanes

<table>
<thead>
<tr>
<th>Cycloalkane</th>
<th>$v_{\text{free}}$ cm$^{-1}$</th>
<th>$v_{\text{bonded}}$ cm$^{-1}$</th>
<th>$\Delta v$ cm$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclopropyl</td>
<td>3635.7</td>
<td>3566.9</td>
<td>68.8</td>
</tr>
<tr>
<td>Cyclobutyl</td>
<td>3638.3</td>
<td>3653.0</td>
<td>85.3</td>
</tr>
<tr>
<td>Cyclopentyl</td>
<td>3638.3</td>
<td>3550.2</td>
<td>83.1</td>
</tr>
<tr>
<td>Cyclohexyl</td>
<td>3640.3</td>
<td>3550.8</td>
<td>89.5</td>
</tr>
</tbody>
</table>
Studies of the formation and hydrolysis of cyclic ketals showed that the ketals derived from ethylene glycol are more stable than those derived from 1,3-propanediol. The introduction of 2,2-dialkyl substituents into 1,3-propanediol increases the stability of the corresponding ketals so that the latter are almost as stable as those derived from ethylene glycol. The larger the substituent the more stable the cyclic ketal is.

**TABLE 17**

Relative Rates of Ketal Hydrolysis

<table>
<thead>
<tr>
<th>Glycols</th>
<th>Cyclohexanone</th>
<th>Cyclopentanone</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethylene glycol</td>
<td>1.0</td>
<td>13.0</td>
</tr>
<tr>
<td>1,3-propanediol</td>
<td>30.6</td>
<td>172.0</td>
</tr>
<tr>
<td>2,2-dimethyl-1,3-propanediol</td>
<td>2.01</td>
<td>16.5</td>
</tr>
<tr>
<td>2,2-diethyl-1,3-propanediol</td>
<td>0.888</td>
<td>7.65</td>
</tr>
<tr>
<td>2,2-diisopropyl-1,3-propanediol</td>
<td>0.335</td>
<td>2.67</td>
</tr>
</tbody>
</table>

*Solvent: 70-30 dioxane-water, 0.003 N HCl, at 30° C.*

The gem-dialkyl effect of small rings in acetal and ketal formation and hydrolysis has also been studied. The equilibrium constant is largest for the acetal of 1,1-di(hydroxymethyl)cyclohexane and 1-naphthaldehyde, and the smallest for the acetal of 1,1-di(hydroxymethyl)cyclopropane and 1-naphthaldehyde. If the relief of angle strain is an important factor in the stability of the acetals, and the hydrolysis thereof, the most stable ones would be the spirocyclohexyl acetals, and the least stable would be the cyclopropyl one. As seen from the following table (Table 18) the greatest change in equilibrium constants occurred between the cyclopropyl and cyclobutyl acetals with further but smaller changes between the other members of the series.

![Chemical Structure](image)

TABLE 18
Equilibrium Formation Constants and Rates of Hydrolysis of Acetals

<table>
<thead>
<tr>
<th>Diol</th>
<th>( k_{\text{hyd}} ) (mole/L-min)</th>
<th>( K_{eq} )</th>
<th>( k_f = k \times k_{\text{hyd}} ) (moles/L-min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,1-Di(hydroxymethyl)cyclopropane</td>
<td>4.2</td>
<td>0.92</td>
<td>4.0</td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)cyclobutane</td>
<td>0.28</td>
<td>11.0</td>
<td>3.1</td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)cyclopentane</td>
<td>0.14</td>
<td>26.2</td>
<td>3.6</td>
</tr>
<tr>
<td>1,1-Di(hydroxymethyl)cyclohexane</td>
<td>0.09</td>
<td>61.0</td>
<td>5.5</td>
</tr>
</tbody>
</table>

No comparative analogies of substituent effect can be made concerning the formation constants of the disubstituted diamine chelates studied. The formation constants of the disubstituted diamines did not vary greatly within the series, that is, increasing the size of the substituent from dimethyl to diethyl, and varying the ring size from cyclopropyl to cyclohexyl showed no measurable difference in the stability of the chelates. When it became apparent that the formation constants of the disubstituted diamines did not vary greatly, repeating and refining of the formation constant data were not performed.

A possible explanation for the small variations in the values of the formation constants for the disubstituted diamine chelates compared to the corresponding equilibrium constants for cyclic ketal formation from disubstituted 1,3-propanediols, and the internal hydrogen bonding of substituted 1,3-propanediols is the larger radius of nickel and copper. The metal - nitrogen bond distance is greater than the carbon - oxygen bond distance in the cyclic ketals. The nickel - nitrogen (ammonia) bond distance in octahedral Ni(NH$_3$)$_4$(NCS)$_2$ has been determined by x-ray crystallographic studies to be 2.15 Å, and the carbon - oxygen bond distance in comparable 1,4-dioxane has been determined by electron diffraction to be 1.42 Å.

---


This greater bond distance in the metal complexes may accommodate better any strain that may be introduced into the 6-membered ring system by the varying of the C-C-C bond angle due to substitution at the 2 position (e.g. cyclopropyl, cyclobutyl diamines).
IV. EXPERIMENTAL

A. Generalizations

1. All melting points were taken on a Thomas Hoover capillary melting point apparatus and are uncorrected.

2. The elemental analyses were determined by Galbraith Laboratories, Inc., Knoxville, Tennessee.

B. Organic Syntheses

1,1-Dicyanocyclopentane

To a cooled solution of 11.5 g. (0.5 g.-atom) of sodium in 200 ml. of absolute ethanol in a 1 l. three-necked round-bottom flask equipped with stirrer, condenser, and two dropping funnels was added dropwise with stirring a solution of 33 g. (0.5 mole) of malononitrile in 40 ml. of absolute ethanol, followed by the simultaneous addition of 119 g. (0.55 mole) of 1,4-dibromobutane and a solution of 11.5 g. (0.5 g.-atom) of sodium in 200 ml. of absolute ethanol. The mixture was refluxed for 2 hr., at which time the solution was neutral to phenolphthalein. Most of the ethanol was removed by distillation. When the residue was cool, 100 ml. of ether was added and decanted from the sodium bromide. The bromide was washed with additional ether. The ether solutions were combined and dried by passing through anhydrous magnesium sulfate. On stripping of the
ether under reduced pressure, a yellow solid precipitated and was filtered from the concentrated ether solution. After removal of the solvent, the dark red viscous residue was vacuum distilled. The distillation fractions gave the following results as shown by v.p.c. (2 ft. 10% silicone rubber, SE 30 on 60-80 WAW).

<table>
<thead>
<tr>
<th>Cut</th>
<th>Temp.</th>
<th>Pressure</th>
<th>Weight</th>
<th>% by v.p.c.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67-77°</td>
<td>2.8 mm.</td>
<td>17.76 g.</td>
<td>essentially A</td>
</tr>
<tr>
<td>2</td>
<td>78-85°</td>
<td>2.8 mm.</td>
<td>1.53 g.</td>
<td>53% B</td>
</tr>
<tr>
<td>3</td>
<td>85-92°</td>
<td>2.8 mm.</td>
<td>5.10 g.</td>
<td>75% B</td>
</tr>
<tr>
<td>4</td>
<td>93-97°</td>
<td>2.8 mm.</td>
<td>4.31 g.</td>
<td>83% B</td>
</tr>
</tbody>
</table>

A black undistillable oil remained (45.0 g.).

Compound A was shown to be malononitrile by its infrared spectrum and retention time on v.p.c. compared with an authentic sample of malononitrile.

Redistillation afforded 8.21 g. (13%) of 1,1-dicyanocyclopentane (B), b.p. 73-74° at 1 mm.

Analysis for C₇H₉N₂:

Calcd: C, 70.0; H, 6.7; N, 23.3

Found: C, 69.7; H, 6.5; N, 23.5

Recrystallization of the yellow solid in benzene yielded 5 g. (10%) of white crystals, m.p. 77-78°,¹ which was shown to be ethyl cyanoimidoacetate.

1,1-Dicarboxamidocyclopentane

Into a 2 l. three-necked round-bottom flask, equipped with a stirrer, dry-ice-acetone condenser, and packed in insulation was placed 1 l. of liquid ammonia, followed by 23.6 g. (0.6 mole) of sodium amide and 61.2 g. (0.6 mole) of malonamide. The mixture was stirred for one hr. and 134.6 g. (0.66 mole) of 1,4-dibromobutane was added by means of an addition funnel over a period of 1.5 hr. The mixture was stirred for another hour. Then 23.6 g. (0.6 mole) of sodium amide was added. The reaction mixture was stirred for 12 hr. and poured into an evaporating dish. After the removal of ammonia, the solids were washed with water to remove the sodium bromide. Recrystallization from 400 ml. of 1:1 water-ethanol gave 31 g. (20%) of the tetraamide, 1,1,6,6-tetracarboxamidohexane, m.p. 308°.

Analysis for $C_{16}H_{18}N_4O_4$:

Calcd: $C$, 46.5; $H$, 7.0; $N$, 21.6

Found: $C$, 46.2; $H$, 6.9; $N$, 21.2

Concentrating the mother liquor gave 16.6 g. of crude solid, m.p. 260-1°. Further recrystallization in 150 ml. of 1:1 water-ethanol gave 15 g. (16%) of 1,1-dicarboxamidocyclopentane, m.p. 265°.

Analysis for $C_7H_{12}N_2O_2$:

Calcd: $C$, 53.8; $H$, 7.8; $N$, 17.9

Found: $C$, 54.0; $H$, 8.0; $N$, 17.7

Further concentration of the mother liquor gave 15.5 g. (25%) of malonamide, m.p. 170°.
2,2-Dimethylmalonamide

Into a 5 l. three-necked round-bottom flask, equipped with a stirrer, dry-ice-acetone condenser, and packed in insulation was placed 3.5 l. of liquid ammonia, followed by 39 g. (1.0 mole) of sodium amide and 102 g. (1.0 mole) of malonamide. The mixture was stirred for one hr. and 110 g. (1.1 mole) of methyl bromide (b.p. 40°) was added by means of controlled distillation from a filter flask connected through an atmospheric pressure equalizer by means of Tygon tubing and then to the neck of the flask. The addition was completed in 1.5 hr. The mixture was stirred for another hour. Then 39 g. (1.0 mole) of sodium amide was added, followed by the addition of 110 g. (1.1 mole) of methyl bromide by distillation. The reaction mixture was stirred for 12 hr. and poured into an evaporating dish. After the removal of ammonia, the solids were washed with water to remove the sodium bromide. Recrystallization in dimethylformamide gave 59.8 g. (46%) of 2,2-dimethylmalonamide, m.p. 268°.2

Analysis for C₅H₁₀N₂O₂:

Calcd:   C, 46.1;   H, 7.7;   N, 21.5

Found:  C, 46.2;   H, 7.7;   N, 21.3

Further concentration of the mother liquor gave 54.0 g. (46%) of 2-methylmalonamide, m.p. 206-7°.3


3Ibid., report m.p. 207-8°.
2,2-Diethylmalonamide

Into a 5 l. three-necked round-bottom flask, equipped with a stirrer, dry-ice-acetone condenser, and packed in insulation was placed 3.5 l. of liquid ammonia, followed by 49 g. (1.25 mole) of sodium amide and 127.5 g. (1.25 mole) of malonamide. The mixture was stirred for one hr. and 142 g. (1.35 mole) of ethyl bromide was added by means of an addition funnel over a period of 2 hr. The mixture was stirred for another hour. Then 49 g. (1.25 mole) of sodium amide was added. The reaction mixture was stirred for 12 hr. and poured into an evaporating dish. After the removal of ammonia, the solids were washed with water to remove the sodium bromide. Recrystallization in dimethylformamide gave 10 g. (5%) of 2,2-diethylmalonamide, m.p. 222-3°.\(^4\)

Analysis for C\(_7\)H\(_{14}\)N\(_2\)O\(_2\):

Calcd: C, 53.1; H, 8.9; N, 17.7

Found: C, 53.1; H, 8.7; N, 17.6

Concentrating the mother liquor gave 110.6 g. of a mixture, m.p. 190-190° assumed to be monoethylmalonamide and malonamide. This mixture was subjected to further alkylation using sodium amide (35.1 g. (0.9 mole)) and ethyl bromide (126.1 g. (1.15 mole)) as described above. Recrystallization afforded 87.4 g. (61%) of 2,2-diethylmalonamide, m.p. 221-22°.

2,2-Dialkylated diethyl malonate

Into a 5 l. three-necked round-bottom flask, equipped with a stirrer and water condenser, was placed 1000 ml. of absolute ethanol, and 50.6 g. (2.2 g.-atom) of sodium. After the complete formation of sodium ethoxide, 320 g. (2.0 mole) of diethyl malonate was added, and the flask was heated to keep the sodio malonate soluble in ethanol. Simultaneously, 2.2 mole of dibromide and a solution prepared by dissolving 41.4 g. (1.8 mole) of sodium in 1000 ml. of absolute ethanol were added. The reaction mixture was refluxed for 2 hr. at which time the solution was neutral to phenolphthalein. After the ethanol was removed by distillation, water was added to dissolve the sodium bromide and the water layer was extracted with ether. The ether extracts were combined and dried by passing through anhydrous magnesium sulfate. After removal of the ether, the residue yielded (A) of 2,2-dialkylated diethyl malonate, as shown in Table 19.

1,1-Dicarboxycycloalkane

To a solution of 100 g. (1.8 mole) of potassium hydroxide in 215 ml. of water in a 1 l. three-necked flask fitted with stirrer, condenser and addition funnel was added 0.8 mole of 1,1-dicarboxyethylxycycloalkane. The mixture was heated for 2 hr. until homogeneous and the alcohol from the ester was removed by distillation. After dissolving the salt in the minimum amount of hot water, the solution was poured onto concentrated hydrochloric acid, and the acid was extracted with ether. The ether solution was dried by passing it through anhydrous magnesium sulfate. After the removal of the solvent, recrystallization in ethyl acetate gave the acid. (See Table 20).
**TABLE 19**
Yields and Physical Constants of Diesters

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield (A)</th>
<th>b.p.</th>
<th>Dihalide</th>
</tr>
</thead>
<tbody>
<tr>
<td>![CO₂Et]</td>
<td>63%</td>
<td>121-23°/15 mm.</td>
<td>Br(CH₂)₂Br</td>
</tr>
<tr>
<td>![CO₂Et]</td>
<td>58%</td>
<td>80-82/1.7 mm.</td>
<td>Br(CH₂)₃Br</td>
</tr>
<tr>
<td>![CO₂Et]</td>
<td>94%</td>
<td>78-80/2 mm.</td>
<td>Br(CH₂)₄Br</td>
</tr>
<tr>
<td>![CO₂Et]</td>
<td>45%</td>
<td>92-95/1.5 mm.</td>
<td>Br(CH₂)₅Br</td>
</tr>
</tbody>
</table>

*aAlkylation performed by reverse addition, i.e., prepared sodio malonate added to dibromide, to reduce the possibility of elimination on the dibromide.*

---

8. Ibid., report b.p. 83° at 3 mm.
<table>
<thead>
<tr>
<th>Product</th>
<th>Yield</th>
<th>m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="CO2H" alt="Image" /> <img src="CO2H" alt="Image" /></td>
<td>72%</td>
<td>156-70°</td>
</tr>
<tr>
<td><img src="CO2H" alt="Image" /> <img src="CO2H" alt="Image" /></td>
<td>95%</td>
<td>190-1010</td>
</tr>
<tr>
<td><img src="CO2H" alt="Image" /> <img src="CO2H" alt="Image" /></td>
<td>65%</td>
<td>167-8011</td>
</tr>
</tbody>
</table>


1,1-Dicarbonylcycloalkane chloride and 1,1-dicarboxamidocycloalkane

In a 500 ml. Erlenmeyer flask fitted with a condenser with drying tube, thermometer, and stirred with a magnetic bar, was placed 0.67 mole of 1,1-dicarboxycycloalkane and 178 g. (1.5 mole) of thionyl chloride. The mixture was heated at 45-50° for 24 hr. until the reaction mixture became homogeneous. The excess thionyl chloride was distilled by the use of a water aspirator. Attempts to distill the acid chloride were unsuccessful. The darkening red-black liquid was then added dropwise to a cold concentrated aqueous solution of ammonia. The crude product was filtered and recrystallized in a 2:1 ethanol-water mixture giving the diamide. (See Table 21).

1,1-Dicarboxamidocyclopropane

In a 150 ml. Erlenmeyer flask was placed 13 g. (0.07 mole) of 1,1-dicarboethoxycyclopropane and 60 ml. of a concentrated aqueous solution of ammonia and stirred with a magnetic bar for 24 hr. The yellow crystals were filtered and recrystallization in a 1:1 ethanol-water mixture gave 8.2 g. (93%) of 1,1-dicarboxamidocyclopropane, m.p. 198-90°.12

### TABLE 21
Yields and Physical Constants of Diamides

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield</th>
<th>m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="CONH2" alt="Structure" /></td>
<td>75%</td>
<td>279-80(^\circ)(^{13})</td>
</tr>
<tr>
<td><img src="CONH2" alt="Structure" /></td>
<td>82%</td>
<td>265-60(^\circ)(^{11})</td>
</tr>
<tr>
<td><img src="CONH2" alt="Structure" /></td>
<td>70%</td>
<td>254-50(^\circ)(^{15})</td>
</tr>
</tbody>
</table>

\(^{13}\)Ibid., report m.p. 280-30\(^\circ\).


2,2-Dialkyl-1,3-diaminopropane by the Reduction of 2,2-Dialkyl-
malonamide with Lithium Aluminum Hydride.

In a 3 l. three-necked round-bottom flask equipped with a
stirrer and soxhlet extractor with condenser was placed 1440 ml.
of dry Glyme and 30.4 g. (0.8 mole) of lithium aluminum hydride.
In the soxhlet thimble was placed 0.3 mole of 2,2-dialkylmalon-
amide. After complete extraction of the diamide which took 15
days, the mixture was heated for an additional 12 hr. and cooled.
After the slow addition of 60 ml. of water, the lithium and
aluminum salts were filtered. The Glyme was dried by passing it
through anhydrous magnesium sulfate. After the removal of solvent,
the residue absorbed carbon dioxide rapidly on exposure to the
atmosphere as indicated by the immediate formation of solid on
the surface.

Continuous extraction of the lithium and aluminum salts with
ether did not yield any additional amine.

Distillation of the residue gave the diamine. Yields are
given in Table 22.

1,1-Di(hydroxymethyl)cycloalkanes

Into a 1 l. three-necked round-bottom flask, equipped with
stirrer, addition funnel, and condenser with drying tube were
placed 400 ml. of dry ether and 14.5 g. (0.38 mole) of lithium
aluminum hydride. The hydride slurry was heated for one hr. A
solution of 0.3 mole of ethyl 2,2-dialkyl malonate in 150 ml. of
dry ether was added over a period of 3 hr. The mixture was heated
<table>
<thead>
<tr>
<th>Product</th>
<th>Yield</th>
<th>b.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{CH}_3\text{CCH}_2\text{NH}_2 )</td>
<td>16%</td>
<td>84-87° at 10 mm.</td>
</tr>
<tr>
<td>( \text{CH}_3\text{CCH}_2\text{NH}_2 )</td>
<td>16%</td>
<td>84-87° at 10 mm.</td>
</tr>
<tr>
<td>( \text{C}_2\text{H}_5\text{CHCH}_2\text{NH}_2 )</td>
<td>21%</td>
<td>81-83° at 9 mm.</td>
</tr>
<tr>
<td>( \text{C}_2\text{H}_5\text{CHCH}_2\text{NH}_2 )</td>
<td>21%</td>
<td>81-83° at 9 mm.</td>
</tr>
<tr>
<td>( \text{CH}_2\text{NH}_2 )</td>
<td>30%</td>
<td>71-74° at 12 mm.</td>
</tr>
<tr>
<td>( \text{CH}_2\text{NH}_2 )</td>
<td>30%</td>
<td>71-74° at 12 mm.</td>
</tr>
<tr>
<td>( \text{CH}_2\text{NH}_2 )</td>
<td>12%</td>
<td>82-85° at 6 mm.</td>
</tr>
<tr>
<td>( \text{CH}_2\text{NH}_2 )</td>
<td>12%</td>
<td>82-85° at 6 mm.</td>
</tr>
<tr>
<td>( \text{CH}_2\text{NH}_2 )</td>
<td>20%</td>
<td>70-71° at 1 mm.</td>
</tr>
<tr>
<td>( \text{CH}_2\text{NH}_2 )</td>
<td>20%</td>
<td>70-71° at 1 mm.</td>
</tr>
<tr>
<td>( \text{CH}_2\text{NH}_2 )</td>
<td>18%</td>
<td>92-94° at 5 mm.</td>
</tr>
<tr>
<td>( \text{CH}_2\text{NH}_2 )</td>
<td>18%</td>
<td>92-94° at 5 mm.</td>
</tr>
</tbody>
</table>


18 Analyzed as dihydrochlorides, see p.

for 12 hr., cooled and 40 g. of water was added to decompose the lithium and aluminum salts. The salts were dissolved in 6 N. hydrochloric acid, and sodium chloride was added to saturation. The ether layer was separated and the aqueous layer subjected to continuous ether extraction for 36 hr. The combined ether extracts were washed with 5% sodium bicarbonate solution, a saturated solution of sodium chloride, and passed through anhydrous magnesium sulfate. After the removal of the ether, the crude liquid was distilled or the crude solid was recrystallized in benzene to give the purified diol. The results are given in Table 23.

2,2-Dialkyl-1,3-dimesatylpropane

Into a 1 l. three-necked round-bottom flask equipped with a stirrer, pressure-equalizing addition funnel, and thermometer was placed 39 g. (0.3 mole) of 2,2-dialkyl-1,3-propanediol in 75 ml. of dry pyridine. The solution was cooled to 5° by an ice bath. To this solution was added 75 g. (0.66 mole) of methanesulfonyl chloride over a period of 30 min., never allowing the temperature to rise above 5°. The mixture was stirred for 3 hr. at 5° and then poured onto ice water. Concentrated hydrochloric acid was added until the solution was acidic. The cold solution was filtered and the white crystals were washed with water. Recrystallization from ethanol gave the results given in Table 24.
TABLE 23
Yields and Physical Constants of Diols

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield</th>
<th>b.p. or m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₂OH</td>
<td>70%</td>
<td>126-30° at 13 mm.²⁰</td>
</tr>
<tr>
<td>CH₂OH</td>
<td>71%</td>
<td>90-93° at 0.8 mm.²¹</td>
</tr>
<tr>
<td>CH₂OH</td>
<td>95%</td>
<td>m.p. 92-92.5°²²</td>
</tr>
<tr>
<td>CH₂OH</td>
<td>80%</td>
<td>m.p. 96-97°²³</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Product</th>
<th>Yield</th>
<th>M.p.</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CH₂OSO₂Me</td>
<td>95%</td>
<td>70-71°</td>
<td>C₇H₁₆S₂O₆</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calcd: C, 32.3 H, 6.2 S, 24.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Found: C, 32.1 H, 6.3 S, 24.4</td>
</tr>
<tr>
<td>C₂H₅CH₂OSO₂Me</td>
<td>91%</td>
<td>94-95°</td>
<td>C₉H₂₀S₂O₆</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calcd: C, 37.5 H, 7.0 S, 22.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Found: C, 37.7 H, 7.1 S, 22.0</td>
</tr>
<tr>
<td>CH₂OSO₂Me</td>
<td>90%</td>
<td>58-60°</td>
<td>C₇H₁₄S₂O₆</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calcd: C, 32.6 H, 5.4 S, 24.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Found: C, 32.7 H, 5.4 S, 24.6</td>
</tr>
<tr>
<td>CH₂OSO₂Me</td>
<td>86%</td>
<td>72-73°</td>
<td>C₈H₁₆S₂O₆</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calcd: C, 35.3 H, 5.9 S, 23.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Found: C, 35.2 H, 5.8 S, 23.5</td>
</tr>
<tr>
<td>CH₂OSO₂Me</td>
<td>99%</td>
<td>91-92°</td>
<td>C₉H₁₈S₂O₆</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calcd: C, 37.8 H, 6.3 S, 22.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Found: C, 37.8 H, 6.4 S, 22.3</td>
</tr>
<tr>
<td>CH₂OSO₂Me</td>
<td>93%</td>
<td>67-70°</td>
<td>C₁₀H₂₀S₂O₆</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calcd: C, 40.0 H, 6.7 S, 20.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Found: C, 40.1 H, 6.8 S, 20.0</td>
</tr>
</tbody>
</table>

**TABLE 24**

Yields and Physical Constants of Dimethylsulfonates
2,2-Dialkyl-1,3-diazidopropene

In a 1 l. three-necked round-bottom flask equipped with a stirrer, condenser, and thermometer were placed 0.1 mole of 2,2-dialkyl-1,3-dimesatylpropane, 19.5 g. (0.3 mole) of sodium azide, and 400 ml. of dimethylsulfoxide. The reaction mixture was heated for 16 hr. at 65°, cooled, poured onto 400 ml. of water, and extracted 3 times with 50 ml. portions of petroleum ether (b.p. 30-60°). The petroleum ether solution was washed with water and dried. After the removal of the solvent, the residue was distilled. The results are given in Table 25.

Elemental analysis was performed only on 1,1-di(azidomethyl)cyclopentane.

Analysis for C7H12N6:

Calcd:  C, 46.6;  H, 6.7;  N, 46.6

Found:  C, 47.5;  H, 6.8;  N, 45.6

Slowly heating a sample of 1,1-di(azidomethyl)cyclopentane in a test tube from 25° in a water bath showed that decomposition begins at 50° indicated by the slow evolution of nitrogen, which was collected by the displacement of water. All the azides decompose slowly with starting range of 45 to 55°.

2,2-Dialkyl-1,3-diaminopropane by the Reduction of 2,2-Dialkyl-1,3-diazidopropene with Lithium Aluminum Hydride.

In a 1 l. three-necked round bottom flask, fitted with a stirrer, addition funnel, and condenser with drying tube were placed 500 ml. of dry ether and 11.4 g. (0.3 mole) of lithium aluminum
### TABLE 25
Yields and Physical Constants of Diazenes

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield</th>
<th>b.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_3$-C-CH$_2$N$_3$</td>
<td>70%</td>
<td>76-3° at 5 mm.</td>
</tr>
<tr>
<td>CH$_3$-CH$_2$N$_3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$_2$H$_5$-CH$_2$N$_3$</td>
<td>87%</td>
<td>68-72° at 1 mm.</td>
</tr>
<tr>
<td>C$_2$H$_5$-CH$_2$N$_3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_2$N$_3$</td>
<td>81%</td>
<td>73-4° at 4.8 mm.</td>
</tr>
<tr>
<td>CH$_2$N$_3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_2$N$_3$</td>
<td>94%</td>
<td>64-7° at 1.4 mm.</td>
</tr>
<tr>
<td>CH$_2$N$_3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_2$N$_3$</td>
<td>94%</td>
<td>72-3° at 0.9 mm.</td>
</tr>
<tr>
<td>CH$_2$N$_3$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_2$N$_3$</td>
<td>93%</td>
<td>85-7° at 0.8 mm.</td>
</tr>
<tr>
<td>CH$_2$N$_3$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
hydride. The hydride slurry was heated for 1 hr. A solution of 0.064 mole of 2,2-dialkyl-1,3-diazidopropane in 100 ml. of dry ether was added over a period of 3 hr. An immediate evolution of gas occurred as shown by its displacement of water. The reaction appeared to be finished in 15 min. after the complete addition of the diazide. The mixture was heated for an additional hour and no noticeable amount of gas was evolved. After the mixture was cooled, 50 ml. of moist ether was added, followed by the addition of 40 g. of water to decompose the lithium and aluminum salts. The salts were filtered and the solution dried by passing it through anhydrous magnesium sulfate. After the removal of the ether, the residue was distilled, the vacuum being broken with dry nitrogen. The results are given in Table 26.

A good elemental analysis of 1,1-di(aminomethyl)cyclopentane was difficult to obtain. Determination of per cent nitrogen by a primary amino Van Slyke determination was also unsuccessful. The diamines are very hygroscopic and absorb carbon dioxide rapidly on exposure to the atmosphere as indicated by the immediate formation of a white solid on the surface. To prevent the addition of carbon dioxide to the diamines, the compounds were distilled into ampoules, which were either sealed under vacuum or under dry nitrogen. Such samples failed to give good elemental analyses, also. (Other
TABLE 26
Yields and Physical Constants of Diamines

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield</th>
<th>b.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CH₂NH₂</td>
<td>65%</td>
<td>75-77° at 8 mm.</td>
</tr>
<tr>
<td>C₂H₅CH₂NH₂</td>
<td>47%</td>
<td>78-80° at 8 mm.</td>
</tr>
<tr>
<td>C₂H₅CH₂NH₂</td>
<td>64%</td>
<td>77-79° at 15 mm.</td>
</tr>
<tr>
<td>CH₂NH₂</td>
<td>56%</td>
<td>87-90° at 8 mm.</td>
</tr>
<tr>
<td>CH₂NH₂</td>
<td>62%</td>
<td>77-80° at 2 mm.</td>
</tr>
<tr>
<td>CH₂NH₂</td>
<td>51%</td>
<td>90-93° at 4.8 mm.</td>
</tr>
</tbody>
</table>
diamines, e.g., cis-1,3-diaminocyclohexane, which absorbs carbon
dioxide rapidly, have not been analyzed directly. Only the
analysis of their dihydrochloride salts have been reported).

Good analyses of the dihydrochloride salts were obtained.

2,2-Dialkyl-1,3-diaminopropane Dihydrochloride

To a 25 ml. round-bottom flask was added 10 ml. of dry benzene.
The flask was fitted with a cork containing a Newman drying tube and
pipette through which dry hydrogen chloride gas was bubbled through
the benzene solution until saturation. To this solution 1 g. of
diamine was added slowly by means of a pipette, and the mixture went
stirred for 10 min. The solid was filtered, washed with dry benzene,
and dried. The results of the analyses are given in Table 27.

# TABLE 27
## Analyses of Diamine Dihydrochlorides

<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CH₂NH₂HCl</td>
<td>C₅H₁₆N₂Cl₂</td>
<td>Calcd: C,34.3; H,9.2; N,16.0; Cl,40.5</td>
</tr>
<tr>
<td>CH₃CH₂NH₂HCl</td>
<td>C₅H₁₆N₂Cl₂</td>
<td>Found: C,34.5; H,9.2; N,16.1; Cl,40.5</td>
</tr>
<tr>
<td>C₂H₅CH₂NH₂HCl</td>
<td>C₇H₂₀N₂Cl₂</td>
<td>Calcd: C,41.4; H,9.9; N,13.8; Cl,34.9</td>
</tr>
<tr>
<td>C₂H₅CH₂NH₂HCl</td>
<td>C₇H₂₀N₂Cl₂</td>
<td>Found: C,41.3; H,10.0; N,13.8; Cl,34.8</td>
</tr>
<tr>
<td>CH₂NH₂HCl</td>
<td>C₅H₁₄N₂Cl₂</td>
<td>Calcd: C,34.7; H,8.1; N,16.2; Cl,40.9</td>
</tr>
<tr>
<td>CH₂NH₂HCl</td>
<td>C₅H₁₄N₂Cl₂</td>
<td>Found: C,34.6; H,8.0; N,16.2; Cl,40.6</td>
</tr>
<tr>
<td>CH₂NH₂HCl</td>
<td>C₆H₁₆N₂Cl₂</td>
<td>Calcd: C,38.5; H,8.6; N,14.9; Cl,37.9</td>
</tr>
<tr>
<td>CH₂NH₂HCl</td>
<td>C₆H₁₆N₂Cl₂</td>
<td>Found: C,38.4; H,8.4; N,15.0; Cl,38.0</td>
</tr>
<tr>
<td>CH₂NH₂HCl</td>
<td>C₇H₁₈N₂Cl₂</td>
<td>Calcd: C,41.8; H,9.0; N,13.9; Cl,35.3</td>
</tr>
<tr>
<td>CH₂NH₂HCl</td>
<td>C₇H₁₈N₂Cl₂</td>
<td>Found: C,41.9; H,9.0; N,13.7; Cl,35.4</td>
</tr>
<tr>
<td>CH₂NH₂HCl</td>
<td>C₈H₂₀N₂Cl₂</td>
<td>Calcd: C,44.6; H,9.4; N,13.0; Cl,32.9</td>
</tr>
<tr>
<td>CH₂NH₂HCl</td>
<td>C₈H₂₀N₂Cl₂</td>
<td>Found: C,44.8; H,9.6; N,13.1; Cl,32.9</td>
</tr>
</tbody>
</table>
C. Potentiometric Titrations

1. General Considerations

The potentiometric titration technique employed throughout this study was that developed by Bjerrum, and later extended by Calvin and Wilson, and Sen.

The chelation reaction involving the diamine and a divalent metal ion may be represented by the following equation.

\[ M^{+2} + 2 RH_{2}^{+2} \leftrightarrow M(R)_{2}^{+} + 4H^{+} \]

This equation involves the stepwise formation constants of the chelate

\[ M^{+2} + RH_{2}^{+2} \xrightleftharpoons{K_{1}} M(R)^{+2} + 2H^{+} \]
\[ M(R)^{+2} + RH_{2}^{+2} \xrightleftharpoons{K_{2}} M(R)_{2}^{+2} + 2H^{+} \]

and the acid dissociation constant of the conjugate acid of the complexing species.

\[ RH_{2}^{+2} \xrightleftharpoons{K_{a1}} H^{+} + RH^{+} \]
\[ RH^{+} \xrightleftharpoons{K_{a2}} H^{+} + R \]

---

25. J. Bjerrum, Metal Ammine Formation in Aqueous Solution, P. Haase and Son, Copenhagen, 1941.


The operative principle consists of the measurement of the amount of hydrogen ion released by the conjugate acid of the chelating agent during complex formation. Hence the solution of an explicit equation, derived as a function of the stepwise chelate formation constants, in terms of the hydrogen ion concentration at any point in the reaction, the total amount of chelating agent and the total amount of metal ion present in the solution and the acid dissociation constants of the chelating agent will yield the formation constants, \( K_1 \) and \( K_2 \).

The determination of the formation constants of the chelates was performed experimentally by titrating a known initial concentration of chelating agent and metal ion with standard alkali, and following the change in pH potentiometrically. The determination of the acid dissociation constants of the diamines were performed similarly.

A known excess of perchloric acid was added initially to determine if all the diamine was present as a dihydrochloride salt, and also to repress the extent of initial chelate formation. Perchloric acid was selected because of the minimum tendency of the perchlorate ion to coordinate with metal ions.

2. Apparatus

A pyrex vessel with an outer jacket was used for the potentiometric titrations. The temperature of the solvent system was kept constant to within ±0.1°C by circulating water from a constant
temperature bath through the outer jacket of the titration vessel. A Wilkens Anderson "Lo Temp Bath" was used.

The time required for solution equilibrium was lowered by the use of a magnetic stirrer. A piece of asbestos was placed between the stirrer motor and the titration vessel to reduce the transfer of heat from the motor to the solution. The titration vessel was covered with a plastic top in which holes had been drilled to accommodate the two electrodes, two ten-milliliter microburets, two nitrogen inlet tubes, a thermometer, and a glass rod, which was used to remove drops from the buret tips.

The standard sodium hydroxide was contained in a polyethylene bottle. The delivery system was equipped with appropriate towers of indicating drierite which prevented carbon dioxide and water vapor from coming in contact with the standard alkali. The atmosphere in the titration vessel was rendered free from carbon dioxide by passing moist nitrogen above and through the solution. The nitrogen had previously been saturated with the solvent, water, by bubbling through a tower containing water at the same temperature at which the titration was being performed.

The pH readings were obtained with a Beckman Model "G" pH meter equipped with a Beckman E-2 glass and saturated calomel electrode pair. The pH meter was standardized with Beckman buffers at pH 4.01, 7.00, and 9.18 at 25.0°C.
3. Titration Procedure

A weighed amount of sample was placed in the titration vessel. The initial volume for each titration was 110 ml. In the determination of the acid dissociation constants of the diaminedihydrochlorides, the 110 ml. was made up by 60 ml. of water and 50 ml. of standard perchloric acid. In the determination of the formation constants, the 110 ml. was made up by 55 ml. of water, 50 ml. of standard perchloric acid, and 5 ml. of standard metal ion. The mole ratio of diamine to metal ion was 16 to 1.

Each solution was degassed with nitrogen before the start of the titration. The addition of standard sodium hydroxide was done initially by 0.1 - 0.2 ml. increments and decreased in regions of rapidly rising pH values.

4. Standard Solutions

The standard sodium hydroxide (0.0992N) was obtained from The Ohio State University Reagents Laboratory and stored in a polyethylene bottle. The sodium hydroxide was standardized against potassium acid phthalate.

The perchloric acid was prepared to approximately 0.01 M by dilution of 70% Baker and Adamson reagent grade acid. This solution was standardized against the standard sodium hydroxide solution.

Approximately 0.01 M stock solution of metal ions were prepared by dissolving the metal perchlorate, obtained from G. F. Smith Co., in water. The copper (II) solution was standardized by titration with a standard solution of disodium ethylenediamine tetraacetic
acid (EDTA) using 1-(2-pyridylazo)-2-naphthol (PAN) as indicator. The nickel (II) solution was standardized by back titration of its EDTA complex with standard copper solution and PAN as indicator.

5. Titration Equations

The potentiometric titration technique involves the determination of the number of hydrogen ions displaced from the ligand during the formation of the chelate according to the following scheme.

\[
\begin{align*}
M^{n+} + HA &\rightleftharpoons MA^{n-1} + H^+ \\
MA^{n-1} + HA &\rightleftharpoons MA_2^{n-2} + H^+ \\
M^{n+} + H_mA &\rightleftharpoons MA^{n-m} + mH^+
\end{align*}
\]

From this it follows that ligands containing a large number of acidic groups will cause a significant drop in the initial pH due to the release of hydrogen ions during complex formation. The magnitude of this pH depression, is used as a quantitative measure of the stability of the metal chelate compound. The titration data is most commonly interpreted by the application of Bjerrum's technique. This technique consists of plotting \( \bar{n} \), the average number of ligands bound per metal ion, against \( pR \), the negative log of the concentration of the chelating species. The values of


\[29\] H. A. Flaschka, ibid., p. 83.
pR at  \( \bar{n} = 0.5, 1.0, \) and 1.5 are equal to \( \log K_1, \log K_{AV}, \) and \( \log K_2 \) respectively.

The equations needed to evaluate \( \bar{n} \) and pR from the titration data were obtained by a consideration of the following expressions.

Acid Dissociation Constants of the Reagent:

\[
K_{a1} = \frac{H^+ \cdot RH^+}{RH_2^{+2}}; \quad K_{a2} = \frac{H^+ \cdot R}{RH^+}
\]

where \( RH_2^{+2} \) is \( R'_{2-C-(CH_2NH_3)^2}^{+2} \)

\( RH^+ \) is \( R'_{2-C-CH_2NH_3^+} \)

\( R \) is \( R'_{2-C-(CH_2NH_2)} \)

Material Balance for the Metal Ion:

\[
T_M = M^{+2} + M(R)^{+2} + M(R)_2^{+2}
\]

Material Balance for the Reagent:

\[
T_R = RH_2^{+2} + RH^+ + R + M(R)^{+2} + 2M(R)_2^{+2}
\]

Charge Balance:

\[
2M^{+2} + 2M(R)^{+2} + 2M(R)_2^{+2} + 2RH_2^{+2} + RH^+ + H^+ + Na^+ = ClO_4^- + OH^- + Cl^{-}
\]

where \( T \) refers to the total concentration of a species.
The definition of \( \bar{n} \) employed was:

\[
\bar{n} = \frac{M(R)^{+2} + 2M(R)^{+2}}{T_M}
\]

These expressions were combined as shown in the Appendix to give:

\[
\bar{n} = \frac{1}{T_M} \left( T_R - \frac{S \left( (H^+)^2 + H^+K_{a1} + K_{a1}K_{a2} \right)}{H^+ \left( 2H^+ + K_{a1} \right)} \right)
\]

and

\[
R = \frac{S K_{a1}K_{a2}}{H^+ \left( 2H^+ + K_{a1} \right)}
\]

where \( S \) was defined as

\[
S = 2T_R + T_A + OH^- - H^+ - Na^+
\]
V. APPENDIX

Derivation of Equations for Acid Dissociation Constant Calculation of Diaminedihydrochlorides.

The equilibria being considered are:

\[ \begin{align*}
&\text{RH}_2^{+2} \rightleftharpoons K_{a1} \text{ RH}^+ + H^+ \\
&\text{RH}^+ \rightleftharpoons K_{a2} \text{ R} + H^+
\end{align*} \]

Material Balance for Reagent:

\[ T_R = \text{RH}_2^{+2} + \text{RH}^+ + \text{R} \quad (1) \]

Charge Balance:

\[ 2\text{RH}_2^{+2} + \text{RH}^+ + H^+ + \text{Na}^+ = \text{ClO}_4^- + \text{Cl}^- + \text{OH}^- \quad (2) \]

And for the system:

\[ \text{Cl}^- = 2T_R \quad \text{and} \quad \text{ClO}_4^- = T_A \quad (3) \]

The acid dissociation constants of the reagent are:

\[ K_{a1} = \frac{H^+ \cdot \text{RH}^+}{\text{RH}_2^{+2}} \quad (4) \]

\[ K_{a2} = \frac{H^+ \cdot \text{R}}{\text{RH}^+} \quad (5) \]
For $K_{a1}$, $R$ is small so equation (1) becomes

$$T_R = RH_2^{+2} + RH^+ \quad (6)$$

Substitute equations (3) and (6), equation (2) becomes

$$RH_2^{+2} + H^+ + Na^+ = T_A + T_R + OH^- \quad (7)$$

On rearranging equation (7) and defining $S$ as

$$S = T_A + OH^- - H^+ - Na^+$$

and substituting $S$, equation (7) becomes

$$RH_2^{+2} = T_R - S \quad (8)$$

Substitute equation (8), equation (6) becomes

$$RH^+ = S \quad (9)$$

Substitute equations (8) and (9) into equation (4), the first acid dissociation constant becomes:

$$K_{a1} = \frac{S \cdot H^+}{T_R - S}$$

For $K_{a2}$, $RH_2^{+2}$ is small so equation (1) becomes

$$T_R = RH^+ + R \quad (10)$$
and equation (2) becomes

\[
RH^+ + H^+ + Na^+ = ClO_4^- + Cl^- + OH^- \quad (11)
\]

Substitute equation (3) and on rearrangement equation (11) becomes

\[
RH^+ = T_A + 2TR + OH^- - H^+ - Na^+ \quad (12)
\]

Substituting the definition of S into equation (12)

\[
RH^+ = 2TR + S \quad (13)
\]

Substituting equation (13), equation (10) becomes

\[
R = -(TR + S) \quad (14)
\]

Substitute equations (13) and (14) into equation (5), the second acid dissociation constant becomes:

\[
K_{a2} = \frac{H^+ (-TR - S)}{2TR + S}
\]
Derivation of Equations for Stability Constant Calculation of Diamine Chelates with Divalent Metal Ions.

The equilibria being considered are:

\[ \begin{align*}
M^{+2} + RH^2+2 & \rightleftharpoons M(R)^{+2} + 2H^+ \\
M(R)^{+2} + RH^2+2 & \rightleftharpoons M(R)_{2}^{+2} + 2H^+ \\
M(R)_{2}^{+2} + RH^2+2 & \rightleftharpoons M(R)_{3}^{+2} + 2H^+ \\
\end{align*} \]

Material Balance for Metal:

\[ T_M = M^{+2} + M(R)^{+2} + M(R)_{2}^{+2} \]  \hspace{1cm} (1)

Material Balance for Reagent:

\[ T_R = RH^2+2 + RH^+ + R + M(R)^{+2} + 2M(R)_{2}^{+2} \]  \hspace{1cm} (2)

Charge Balance:

\[ 2M^{+2} + 2M(R)^{+2} + 2M(R)_{2}^{+2} + 2RH^2+2 + RH^+ + H^+ + Na^+ = ClO_4^- + OH^- + Cl^- \]  \hspace{1cm} (3)

And for the system:

\[ Cl^- = 2T_R \]  \hspace{1cm} (4)

\[ ClO_4^- = T_A + 2T_M \]  \hspace{1cm} (5)
The acid dissociation constants of the reagent are:

\[ K_{a1} = \frac{H^+ \cdot RH^+}{RH_2^{+2}} \]  

(6)

\[ K_{a2} = \frac{H^+ \cdot R}{RH^+} \]  

(7)

and \( \bar{n} \), the average number of reagent molecules per metal ion, is defined by:

\[ \bar{n} = \frac{M(R)^{+2} + 2M(R)_2^{+2}}{T_M} \]  

(8)

**Derivation of \( \bar{n} \)**

To obtain the equivalent numerator of equation (8), rearrange (2)

\[ M(R)^{+2} + 2M(R)_2^{+2} = T_R - RH_2^{+2} - RH^+ - R \]  

(9)

Solve equation (6) and (7) for \( RH^+ \), and substitute them into (9)

\[ M(R)^{+2} + 2M(R)_2^{+2} = T_R - \frac{H^+ \cdot RH^+}{K_{a1}} - RH^+ - \frac{RH^+ \cdot K_{a2}}{H^+} \]

\[ = T_R - RH^+ \left[ \frac{H^+}{K_{a1}} + 1 + \frac{K_{a2}}{H^+} \right] \]

\[ = T_R - RH^+ \left( \frac{[H^+]^2 + H^+ \cdot K_{a1} + K_{a1}K_{a2}}{H^+ \cdot K_{a1}} \right) \]  

(10)
To obtain RH+, (a) substitute equations (1), (4), and (5) into (3).

\[
2T^*_M + 2RH_2^{+2} + RH^+ + H^+ + Na^+ = OH^- + 2TR + TA + 2TR
\]

and substituting into equation (6), equation (11) becomes

\[
2 \frac{H^+ \cdot RH^+}{Kal} + RH^+ = OH^- + 2TR + TA - H^+ - Na^+
\]

which on rearrangement to collect terms for RH+ gives

\[
RH^+ = \left(2TR + OH^- + TA - H^+ - Na^+\right)\left(\frac{Kal}{2H^+ + Kal}\right)
\]

Let \( S = 2TR + TA + OH^- - H^+ - Na^+ \)

and substitute into equation (12)

\[
RH^+ = \frac{S \cdot Kal}{2H^+ + Kal}
\]

Substitute equation (13) into equation (10)

\[
M(R)^{+2} + 2M(R)_2^{+2} = TR - \frac{S \cdot Kal}{2H^+ + Kal} \left(\frac{(H^+)^2 + H^+Kal + KalKa2}{H^+Kal}\right)
\]

\[
= TR - \frac{S \left((H^+)^2 + H^+Kal + KalKa2\right)}{H^+ (2H^+ + Kal)}
\]
Substitute equation (14) into equation (8):

\[ n = \frac{1}{T_M} \left( T_R - \frac{S \left( (H^+)^2 + H^+K_{a1} + K_{a1}K_{a2} \right)}{H^+ \left( 2H^+ + K_{a1} \right)} \right) \]  \hspace{1cm} (15)

**Derivation of R**

Solve equation (2) for \( R \)

\[ R = T_R - RH_2^{+2} - RH^+ - M(R)^{+2} - 2M(R)_2^{+2} \]  \hspace{1cm} (16)

Substitute the value of \( M(R)^{+2} + 2M(R)_2^{+2} \) from equation (14) into equation (16)

\[ R = T_R - RH_2^{+2} - RH^+ - \frac{S \left( (H^+)^2 + H^+K_{a1} + K_{a1}K_{a2} \right)}{H^+ \left( 2H^+ + K_{a1} \right)} \]  \hspace{1cm} (17)

Solve equation (6) for \( RH_2^{+2} \) and substitute into equation (17)

\[ R = -\left( \frac{(RH^+)(H^+)}{K_{a1}} + RH^+ \right) + S \left( \frac{(H^+)^2 + H^+K_{a1} + K_{a1}K_{a2}}{H^+ \left( 2H^+ + K_{a1} \right)} \right) \]  \hspace{1cm} (18)

\[ R = \frac{S \ K_{a1}K_{a2}}{H^+ \left( 2H^+ + K_{a1} \right)} \]  \hspace{1cm} (19)