A Kinetic Study of Aqua-DMSO Solvent on Alkali Catalyzed Hydrolysis of Methylpicolinate

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ABSTRACT
A kinetic study of alkali catalyzed hydrolysis of methylpicolinate in aqua-DMSO solvent was done at different temperature (20°C, 25°C, 30°C and 35°C) and composition of solvent varying from 10% to 50% (V/V). A depletion in rate of the reaction was found with increase in composition of solvent at all temperatures. To understand the effect of solvent on reaction rate and mechanism iso-composition activation energy, iso-dielectric activation energy and various thermodynamic parameters (ΔH*, ΔS* & ΔG*) were evaluated.

KEYWORD: Methylpicolinate, aqua-DMSO, iso-composition activation energy and iso-dielectric activation energy, transition state and di-electric constant.

INTRODUCTION
Numerous studies¹-¹⁰ have been carried out to show the effect of organic solvent on kinetic & mechanism of reaction highlighting the role of solvation dynamics and dielectric properties. But the study of influence of mixed solvent, aqua-DMSO on alkali catalyzed hydrolysis of heterocyclic acid ester methylpicolinate in terms of solvent-solute interaction, dielectric constant, various thermodynamic parameters, iso-composition activation energy and iso-dielectric activation energy pay special attraction to provide a comprehensive understanding of solvent effect. These parameters offer insights into the molecular interactions and transition state stabilization conferred by the solvent environment. So this study is different quite interesting and significant in pharmaceutical context.

EXPERIMENTAL
The quality of methylpicolinate used was Merck grade. Other chemicals used were high quality grade. NaOH of N/5 strength and aqueous DMSO solvent varying in composition (10% to 50%) were prepared using double distilled water. 8ml of aqua- DMSO was taken in hard glass tube and then mixed with 1ml of 0.2N NaOH solution. The conductivity cell was kept in this tube and the solution was thermostated. Then 1ml of methylpicolinate was added to it. Then conductance was recorded using conductivity meter at regular interval of time at different temperature 20°C, 25°C, 30°C and 35°C. Similar experiments were done for composition 10%, 20%, 30%, 40% & 50% of DMSO solvent. The specific rate constant calculated was given in Table-I. The reaction was found to obey second order kinetics. Using slope of Arrehrius plot of logk vs 1/T, Iso-composition activation energy (Ec) was calculated as given in Table-II and graph is shown in Fig-I. Iso-dielectric activation energy and various thermodynamic parameters were also calculated and given in Table- III and IV.
Table-I Specific rate constant (k) value of alkaline catalyzed hydrolysis of methylpicolinate in aqueous- DMSO medium

<table>
<thead>
<tr>
<th>Temp. (°C)</th>
<th>Composition of DMSO (% V/V)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10%</td>
</tr>
<tr>
<td>20</td>
<td>18.62</td>
</tr>
<tr>
<td>25</td>
<td>25.11</td>
</tr>
<tr>
<td>30</td>
<td>31.62</td>
</tr>
<tr>
<td>35</td>
<td>41.68</td>
</tr>
</tbody>
</table>

RESULT AND DISCUSSION

A depletion in specific rate constant values were observed with increasing proportion of solvent DMSO in accordance with the previous observation\(^{11-12}\). Dielectric constant value also decreases with increasing proportion of organic co-solvent in the medium leads to decrease in concentration of transition state. The transition state becomes desolvated and less stable. But the initial state experiences greater desolvation compared to the transition state means it is less stabilized, leading to an increased energy difference between initial and transition state, resulting in a slower rate of hydrolysis. This is also supported by decrease in iso-composition activation energy (Ec) as observed in Table-II.

![Fig-I Plots of logk value against 10^3/T in aqua–DMSO media.](image-url)
The iso-dielectric activation energy ($E_D$) were calculated in accordance with Wolford$^{13}$. The iso-dielectric activation energy increases with increasing dielectric constant. An increased value of iso-dielectric activation energy suggests that solvation effects are more influential than dielectric effect.

### Table-III Iso-dielectric activation energy values ($E_D$ in KJ mol$^{-1}$)

<table>
<thead>
<tr>
<th>Dielectric constant</th>
<th>68</th>
<th>70</th>
<th>73</th>
<th>76</th>
<th>78</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_D$</td>
<td>26.80</td>
<td>30.63</td>
<td>33.89</td>
<td>38.29</td>
<td>47.86</td>
</tr>
</tbody>
</table>

Various thermodynamic activation parameters like $\Delta H^*$, $\Delta S^*$ & $\Delta G^*$ were calculated using Wynne-Jons and Eyring$^{14}$ equation, shown in Table-IV.

### Table IV Thermodynamic activation parameters in aqua-DMSO medium at 25$^\circ$C ($\Delta H^*$, $\Delta G^*$ in KJ mol$^{-1}$ & $\Delta S^*$ in JK$^{-1}$mol$^{-1}$)

<table>
<thead>
<tr>
<th>% of DMSO (V/V)</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta H^*$</td>
<td>38.29</td>
<td>34.65</td>
<td>30.63</td>
<td>29.29</td>
<td>21.25</td>
</tr>
<tr>
<td>$-\Delta S^*$</td>
<td>89.69</td>
<td>102.43</td>
<td>112.64</td>
<td>119.46</td>
<td>128.95</td>
</tr>
<tr>
<td>$\Delta G^*$</td>
<td>65.00</td>
<td>65.17</td>
<td>65.34</td>
<td>65.45</td>
<td>65.60</td>
</tr>
</tbody>
</table>

It is obvious from the above data that $\Delta H^*$ value decreases with increase in proportion of organic co-solvent which should enhance the reaction rate, but the rate actually decreases. This unusual behavior can be attributed to an increase in entropy with the addition of more organic solvent. It causes higher degree of disorder. Slight increase in the value of $\Delta G^*$ was observed, which indicate that the stability of transition state is not significantly improved and further contributes to the reduction in reaction rate, as a higher Gibbs free energy corresponds to a less favorable reaction progression.

**CONCLUSION**

In alkaline hydrolysis of methylpicolinate, decrease in rate constant with composition of organic co-solvent is due to either decrease in dielectric constant or solvation of transition state. An increased value of iso-dielectric activation energy shows that solvation effect is more influential than dielectric effect. Decrease in value of iso-composition activation energy with increasing co-solvent inferred the solvation of transition state. Only increasing trend of entropy with addition of co-solvent favour the decrease in rate constant. Thus the reaction can be convinced as entropy controlled.

**REFERENCES**

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