Reactivity of Some Epimeric 4-Aminooxanes towards Oxidation by Cerium (IV)

NALLAPPAN CHANDRASEKARA & KRISHNASAMY RAMARAJAN*
Department of Chemistry, CBM College, Coimbatore 641 042

and

MATILAN SUJA & KUPPUSAMY SELVARAJ*
Department of Chemistry, PSG College of Arts and Science, Coimbatore 641 014

Received 17 February 1986; revised 29 April 1986; revised and accepted 11 November 1986

Kinetics of oxidation of four epimeric pairs of 4-aminooxanes by Ce(IV) in aqueous acetic acid in the presence of nitric acid, have been investigated. The oxidation is first order in [oxidant]. No definite order exists with respect to [substrate]. A mechanism involving the abstraction of a H-atom from the \( \sigma - C - H \) by Ce (IV) in the rate-limiting step is proposed. Equatorial amines react faster than axial amines. Added \( H^+ \) or \( NO_3^- \) increase the rate of oxidation. Rate is lowered by increase in the polarity of the medium. The conformational (steric) and electronic effects on the rate of oxidation are discussed.

Although considerable work has been reported\(^1\) -\(^{13}\) on the kinetics of oxidation of amines by a variety of oxidants, only meagre attention has been paid towards oxidation by Ce (IV)\(^{14,15}\). To the best of our knowledge no work has so far been reported on the kinetics of oxidation of heterocyclic amines by Ce (IV). The title investigation is an attempt to fill the gap.

Materials and Methods

4-Aminooxanes (1-8) used were prepared by literature procedures\(^{16,19}\). Acetic acid (AR, BDH) was refluxed over \( \text{CrO}_3 \) and used. Ceric ammonium nitrate (BDH) and nitric acid (BDH) were used as such. Other chemicals used were of AR grade.

Kinetic measurements

Pseudo-first order conditions were maintained ([S] \( \geq [\text{Ce(IV)}] \)). Before mixing, the two reactant solutions were equilibrated at 50 \( \pm 0.05 \) \( ^\circ \)C for 30 min. The rate was followed by withdrawing aliquots (2 ml each) from the mixture at regular time intervals, pouring into a known excess (10 ml) of Fe(II) solution and titrating the unused Fe(II) against standard \( K_2\text{Cr}_2\text{O}_7 \) using barium diphenylamine sulphonate as indicator. The rates were followed at least upto 60\% conversion of the oxidant and the results were found to be reproducible within \( \pm 5\% \).

Product analysis

In the oxidation of 4-aminooxanes (1-8) by Ce (IV), the corresponding 4-oxanones were identified as the products. A solution (25 ml) containing 4-aminooxane (0.25 mol), ceric ammonium nitrate (0.025 mol) and nitric acid (0.2 mol dm\(^{-3}\)) in aq acetic acid (70\% v/v) was kept at 50\(^\circ\)C for 24 hr. The solution was neutralized with aq ammonia (1:1), extracted with ether (3 x 50 ml) and the combined ether extract dried (Na\(_2\)SO\(_4\)) and evaporated. The residue was dissolved in minimum amount of cold benzene and chromatographed over a column of neutral alumina. Evaporation of petroleum ether (b.p. 60-80\(^\circ\)C)-benzene eluates gave a solid. This product was found to be identical with the corresponding 4-oxanone.

Results and Discussion

The pseudo-first order rate constants obtained with different 4-aminooxanes (1-8) are presented in Table 1. The effect of varying [substrate] on the pseudo-first order rate constant has been studied for \( t-2, t-6\)-diphenyl-c-3-methyl-\( r-4\)-aminooxane (2) as a typical case. Under the condition: \([\text{Ce(IV)}] = 2.5 \times 10^{-3}\), \([\text{HNO}_3]\) = 0.2 and \( \mu = 0.5 \) mol dm\(^{-3}\) in 70\% (v/v) aq acetic acid at 50\(^\circ\)C the values of \( 10^3 k_1(s^{-1}) \) are 7.97, 9.52, 10.92, 13.41 and 14.81 at 10\(^3\) [substrate] = 21.58, 28.57, 40.22, 59.92 and 80.11 mol dm\(^{-3}\) respectively. The absence of a simple relation between \( k_1 \) and...
Table 1—Pseudo-first Order Rate Constants for Oxidation of 4-Aminooxane (1-8) by Ce (IV)

<table>
<thead>
<tr>
<th>[Ce(IV)]</th>
<th>10^3 k_1 (s^-1)</th>
<th>[substrate]</th>
<th>10^3 k_1 (s^-1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5 x 10^-3 mol dm^-3; [substrate] = 21.25 x 10^-3 mol dm^-3, solv = 70% (v/v) aq HOAc</td>
<td>46.79</td>
<td>5</td>
<td>62.94</td>
</tr>
<tr>
<td>7.97</td>
<td>6</td>
<td>10.87</td>
<td></td>
</tr>
<tr>
<td>20.11</td>
<td>7</td>
<td>193.00</td>
<td></td>
</tr>
<tr>
<td>6.15</td>
<td>8</td>
<td>124.00</td>
<td></td>
</tr>
</tbody>
</table>

Table 2—Dependence of Rate on [H^+] at Fixed Ionic Strength and [NO_3^-] for Oxidation of c-2, c-6-Diphenyl-r-3-methyl-r-4-aminooxane (6) by Ce (IV)

<table>
<thead>
<tr>
<th>[HNO_3] (mol dm^-3)</th>
<th>10NaNO_3 (mol dm^-3)</th>
<th>10^3 k_1 (s^-1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>3</td>
<td>13.94</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>22.83</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>27.52</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>34.77</td>
</tr>
</tbody>
</table>

[substrate] indicates the operation of a complex mechanism.

It is evident, from the data presented in Table 2, that increase in [H^+] at fixed ionic strength and [NO_3^-] increases the rate of reaction, suggesting that the reaction is susceptible to acid catalysis.

Increase in polarity of the medium decreases the rate suggesting a charge dispersal in the transition state; for example, 10^3 k_1 (s^-1) = 2.91, 3.43, 4.50, 6.01 and 7.97 in 50, 55, 60, 65 and 70% (v/v) aq acetic acid, respectively under the conditions: [Ce (IV)] = 2.5 x 10^-3 mol dm^-3; [HNO_3] = 0.2 mol dm^-3, and temp. = 50°C.

Addition of sodium nitrate at fixed [HNO_3] increases the rate of the reaction; for example, in the presence of 1.0, 2.0 and 3.0 mol dm^-3 NaNO_3 and [Ce (IV)] = 2.5 x 10^-3 mol dm^-3, [substrate] = 21.07 x 10^-3 mol dm^-3, [HNO_3] = 0.2 mol dm^-3 in 60% (v/v) aq acetic acid at 50°C, 10^5 k_1 (s^-1) are 4.96, 6.00 and 7.49 respectively. This increase in k_1 in the presence of NO_3^- may partly be due to catalytic effect of NO_3^- and partly due to increase in ionic strength of the medium. A plot of log k_1 versus ionic strength is linear with a positive slope. A small positive salt effect is characteristic of reactions involving a positive ion and a neutral species in the rate-limiting step.

The involvement of a free radical mechanism is evidenced by the polymerization of acrylamide or acrylonitrile when added to the reaction mixture.

In all the cases investigated, a deep yellow solution was formed immediately after mixing the reactants, suggesting the formation of a complex between 4-aminooxane and Ce (IV) in a rapid equilibrium step.

Although in the acid solution (0.2 to 0.5 mol dm^-3) the amine will almost entirely exist in the conjugate acid form prior to the addition of Ce (IV), the addition of Ce (IV) may shift the equilibrium.

\[
\text{R} - \text{NH}_3 \rightarrow \text{R} - \text{NH}_2 + \text{H}^+ 
\]

to the amine side, as only the latter could form a complex with Ce (IV). Also, protonated amine has been reported\(^{14}\) to be less reactive than the free amine itself towards oxidation by Ce (IV). The equilibrium complex formation between Ce (IV) and the free amine has been further confirmed by a Michaelis-Menten type plot of 1/k_1 versus 1/[substrate], which is linear with a non-zero intercept.

**Mechanism and rate law**

In the range of acid and Ce (IV) concentrations used in the present investigation, Ce (IV) should exist\(^{21}\) predominantly as Ce^{4+} and Ce (OH)_3^{3+}. The observed small positive salt effect indicates that the reactants (in the rate-limiting step) are either a positive Ce (IV) species and a neutral free amine or a protonated amine and a neutral Ce (IV) species. However, the greater reactivity of a free amine (in contrast to a protonated amine) towards Ce (IV) and the preponderant existence of Ce (IV) as Ce^{4+} and Ce (OH)_3^{3+} in the reaction medium, clearly point towards a reaction between neutral free amine molecule and a positive Ce (IV) species.

If we assume the existence of the following equilibria: Ce (OH)^{3+} + H^+ \rightleftharpoons Ce^{4+} + H_2O; and Ce (OH)^{3+} + NO_3^- \rightleftharpoons Ce (OH) (NO_3)^{2+}, and Ce^{4+} and Ce (OH) (NO_3)^{2+} as the reactive species, the observed catalytic effects of the added H^+ and NO_3^- ions can be easily understood.

All the evidences presented thus far are in conformity with a mechanism outlined in Scheme 1. The rate law for this mechanism is given by Eq. (1) where [Ce (IV)]_T represents the total [Ce (IV)].

\[
\text{C} + \text{NH}_2 + \text{Ce (IV)} \rightleftharpoons \text{complex} \quad \text{K} \\
\text{Complex} \underset{k_s \text{slow}}{\rightarrow} \text{C} + \text{NH}_2 + \text{Ce (III)} \quad \text{fast} \\
\text{C} + \text{NH} + \text{H}_2 \text{O} \quad \text{fast} \rightarrow \text{C} + \text{H}_2 \text{O} + \text{Ce (III)} \\
\]

**SCHEME 1**
The pseudo-first order rate constant \( k_1 \) is given by Eq. (2)

\[
k_1 = \frac{k_s K[S]}{K[S] + 1}
\]

The fact that equatorial amines react faster than axial amines (Table 1) is consistent with the proposed mechanism (Scheme 1), which involves the formation of a complex in a rapid equilibrium step followed by the cleavage of an \( \alpha-C-H \) bond in a rate-limiting step. As evidenced by \( ^{15}N \) NMR spectral data, the lone pair of an axial amino nitrogen as in 9 is subjected to a greater steric compression (due to 1, 3-steric interaction) than that of an equatorial amino nitrogen, as in 10.

Hence, an amino group in the equatorial position is more accessible (sterically) towards complex formation than one in the axial position. Hence, the equilibrium constant for complex formation may be expected to be greater for equatorial amines than for axial amines. The cleavage of the \( \alpha-C-H \) bond in the rate-limiting step results in a reduction in size of the group at the cleavage location. A reduction in size will be more welcome at the axial location (equatorial amines) than at the equatorial location (axial amines).

Further evidence for the proposed mechanism comes from the following two observations:

(i) Under comparable conditions, c-2, c-6-diphenyl-1-t-3-methyl-r-4-aminooxan (6) and c-2, c-6-diphenyl-1-t-3-methyl-r-4-dimethylaminooxan (11) reacted at nearly equal rates \( (k_1 \text{ values for } 6 \text{ and } 11 \text{ respectively are } 3.477 \times 10^{-4} \text{s}^{-1} \text{ and } 3.715 \times 10^{-4} \text{s}^{-1}) \). Had there been a N-H abstraction in the rate-limiting step, 6 would have reacted faster than 11 and the latter, lacking a N-H group, would have undergone oxidation via different complex pathway.

(ii) Running the reaction in HOAc - D\(_2\)O medium (instead of HOAc - H\(_2\)O medium) did not result in any appreciable change in the rate of oxidation (compare \( k_1 \) values of \( 3.477 \times 10^{-4} \text{s}^{-1} \) and \( 3.702 \times 10^{-4} \text{s}^{-1} \) in HOAc - H\(_2\)O medium and HOAc - D\(_2\)O medium for 6). Under the conditions of the reaction, the amino group may be expected to undergo rapid deuterium exchange with the medium. Hence, if the mechanism involved a N-H cleavage rather than a C-H cleavage in the rate-limiting step, then the reaction in HOAc - D\(_2\)O medium would have been slower than that in HOAc - H\(_2\)O medium. Not only does this not happen but also there is a slight enhancement of rate in HOAc - D\(_2\)O medium.

**Structure and reactivity**

All the 4-aminooxanes (1-8) used in the present investigation were shown by their \(^1H\) and \(^{13}C\) NMR spectral data, to exist in the chair conformation. The observed influence on the rates due to the introduction of alkyl groups in the \( \beta \)-position can be rationalized on the basis of the combined but mutually opposing electronic and steric factors. An alkyl group in the \( \beta \)-position experiences a gauche interaction with the amino group, whether the latter is axial or equatorial, and this should retard the rate. However, the presence of an electron releasing group in the neighbourhood is expected to facilitate the formation of the complex and thus increase the rate. Since alkyl groups are electron releasing, a \( \beta \)-alkyl group should enhance the rate.

In both the axial and equatorial series, introduction of a methyl group in \( \beta \)-position lowers the rate and this is probably due to the dominance of steric factor. However, an ethyl group in the same position has no effect on the rate, indicating ascendancy of the electronic factor. In fact in the equatorial series, the ethyl substituted compound 7 reacts even faster than the unsubstituted 5. While the steric factor is dominant in the oxidation of 4, it is the electronic factor that predominates in the case of oxidation of 8. From the results, it appears that the equatorial amino compounds are more sensitive to electronic factors and the axial amino compounds are more sensitive to steric factors.

While a substituent in the para- positions of the phenyl groups at 2- and 6- positions cannot engage in any steric interaction with the amino group, it can still affect the reaction through its electronic influence. With the epimeric pair of 2, 6-di(p-anisyl)-3-methyl-4-aminooxan (12) and (13) the oxidation is so fast as to preclude any kinetic investigation by the conventional method. This is attributed to the electron releasing effect of the \( p-OCH_3 \) group. As anticipated chloro
substituent in the para-positions of the phenyl groups at 2- and 6- positions lower the reaction rates as revealed by $k_1$ values of $4 \times 10^{-5} \text{s}^{-1}$ and that $(k_1 = 5.285 \times 10^{-5} \text{s}^{-1})$ of t-2, t-6-di-p-chlorophenyl-c-3, c-5-dimethyl-r-4-aminoxooxane (14).

Acknowledgement
We thank Prof. DKP Varadarajan and Dr D Sethu Rao for constant encouragement and Mr G Varadaraj, for financial support.

References