Kinetics of V(V) Oxidation of Piperidinols

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Kinetics of oxidation of piperidinols by V(V) in different acetic acid-water mixtures are reported. The piperidinols being strong bases, most probably react in the corresponding protonated forms. The order of reactivity is N-methyl-piperidin-3-ol > piperidin-3-ol > N-methyl-piperidin-4-ol > piperidin-4-ol. This has been rationalized on the basis of conformational studies of piperidinols. Dependence on acidity is unity. Thermodynamic parameters have been evaluated. The mechanism involves C—H bond fission forming a free radical which in subsequent fast step leads to the corresponding ketones.

WHILE the conformational effects in the oxidation of substituted cyclohexanol have been extensively studied, little work seems to have been done in the field of piperidinols. Recently, the conformation of a few piperidinols has been investigated. This prompted us to study the kinetics of V(V) oxidation of piperidin-3-ol, piperidin-4-ol and their N-methyl derivatives.

Materials and Methods

All the piperidinols were of Fluka (AR) grade. Acetic acid (BDH, AR) was refluxed with CrO_3 and acetic anhydride (equivalent to the amount of water present in acetic acid) and distilled (b.p. 118°).

Ammonium metavanadate (AR grade) was weighed approximately and dissolved in a known amount of H_2SO_4 (AR) with slight warming. This solution after sufficient cooling, was made up with the appropriate solvent mixture, taking care to see that the solution was of the required acidity.

Both the V(V) solutions, from the oxidant flask before mixing and the aliquots from the reaction mixture, were analysed as follows: The V(V) solution (5 ml) was added to a known excess of acidified standard ferrous ammonium sulphate solution and the left over Fe(II) titrated against standard potassium dichromate solution using N-phenylanthranilic acid as an indicator.

Results and Discussion

The piperidinols being fairly strong bases most probably reacted in the corresponding protonated forms. These were oxidized to the respective ketones and gave good linear second order plots for over 60% of the reaction. The second order rate constants are given in Table 1.

The existing evidences and recent dipole moment measurements indicate that the N-hydrogen in these piperidinols has a small preference for the equatorial position whereas the N-methyl is found largely in the equatorial position. In piperidin-3-ol
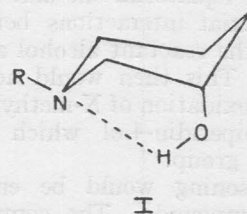
(R=H) and N-methyl-piperidin-3-ol intramolecular hydrogen bonding has been observed between the nitrogen and the hydrogen of the hydroxyl group, although the piperidinol assumes the less favourable conformation (I) with an axial-OH to make this possible[1].

Since no such stabilization would be possible in the chair conformation, both piperidin-4-ol and N-methyl-piperidin-4-ol exist in the usual conformations with —OH in the equatorial position.

TABLE 1 — SECOND ORDER RATE CONSTANTS FOR V(V) OXIDATION OF PIPERIDINOLS IN $1M$ H_2SO_4

Compound	$k_2 \times 10^3$ litre mole^{-1} min^{-1} HOAc (%, v/v)		
	50	60	70
TEMP.=60°C			
Piperidine-3-ol	8·52	1·429	20·68
N-Methyl-piperidin-3-ol	17·16	2·385	38·11
Piperidine-4-ol	5·14	8·12	12·43
N-Methyl-piperidin-4-ol	5·91	10·03	15·20
TEMP.=80°C			
Piperidin-3-ol	51·63	67·89	144·80
N-Methyl-piperidin-3-ol	100·5	136·2	207·3
Piperidin-4-ol	25·53	40·63	62·47
N-Methyl-piperidin-4-ol	35·39	48·42	83·79
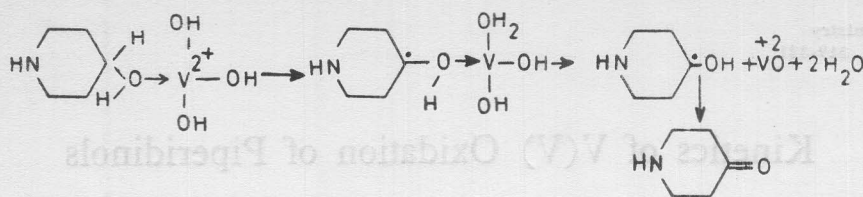
Scheme 1

However, the piperidine ring in 1,2,2,6,6-penta-methyl-4-phenyl-piperidin-4-ol has been shown to exist in a boat conformation. The *gem*-methyl groups on C-2 and C-6 the stabilization by the hydrogen bonding make the piperidine ring to exist in a boat conformation[2].

Since the N-methyl-piperidin-3-ol molecule is known to exist predominantly with the —OH group in axial position and the N-methyl in equatorial position, this configurational relationship must be retained in the protonated form as well. It is a common fact that an axial —OH is more easily oxidized than the equatorial one and that this arises from the 1,3-diaxial interactions between the hydroxyl group of the reactant alcohol and the nearby axial hydrogen. This then would account for the increased rate of oxidation of N-methyl-piperidin-3-ol over N-methyl-piperidin-4-ol which has only an equatorial —OH group.

A similar reasoning would be enough for the unmethylated compounds. The comparison of the rate data of these piperidinols shows that the N-methyl compounds are oxidized faster than the parent piperidinols. The only rational explanation for the rate enhancement in the N-methyl derivatives is the inductive effect of the N-methyl group in an alicyclic unconjugated system like piperidine.

Thermodynamic parameters — The activation energies and other Arrhenius parameters in acetic acid-water mixture are given in Table 2. A linear plot is obtained by plotting $\log_{10} PZ$ against $1/\sqrt{E}$ in conformity with the thermo-dynamic considerations.

While the rates of oxidation of the piperidinols vary considerably, it is surprising that E values are all equal or nearly equal. Other factors seem to be more important than the parameter E.

Dependence on acidity — The data in Table 3 show that there is linear dependance on [H⁺] and

the order with respect to [H⁺] is unity. Plots of $\log_{10} k_2$ versus H_0 are linear but the order is half. This is due to the difference in the degree of hydration not only of the transition state of the reaction but also of the reversibly formed complex. The appropriate functions have been found to fit more closely than in reactions where the water molecule is taking part merely as a nucleophile.

Solvent effects — Increase in acetic acid content of the solvent medium enhances the rate pointing to the fact that the present reaction is a positive ion dipolar reaction.

Mechanism of oxidation of piperidinols — V(V) like Cr(VI), Mn(VII) and Pt(IV) has been found to act as a 1 or 2 electron oxidant[3] depending upon the nature of the reaction. Waters and Littler[4] during their studies on V(V) oxidation of alcohols, ketones and other substrates have favoured one electron transfer for V(V) oxidations. But it is not essential that all the organic compounds should oxidize by V(V) by one electron transfer. It may be mentioned that when oxidants of similar redox potential, viz. bromine and V(V) are compared it is often noticed that 2 electron transfer proceed

TABLE 2 — THERMODYNAMIC PARAMETERS

{[H₂SO₄] = 1 M; solvent: HOAc (50%, v/v)}

Compound	E k cal mole⁻¹	$\log_{10} PZ$	$\Delta S‡$ (e.u.)	$\Delta H‡$ k cal mole⁻¹
Piperidin-3-ol	19·68	9·06	−17·36	19·02
N-Methyl-piperidin-3-ol	19·48	9·23	−16·57	18·82
Piperidin-4-ol	18·55	8·10	−21·76	17·89
N-Methyl-piperidin-4-ol	19·70	8·92	−17·95	19·04

TABLE 3 — ACIDITY DEPENDENCE IN THE OXIDATION OF PIPERIDINOLS BY V(V) $k_2 = 10^3$ LITRE MOLE⁻¹ MIN⁻¹

{Solvent = HOAc (50%, v/v); [V(V)] = 0·003 M}

Substrate	[H₂SO₄]					
	1 M		1·75 M		2·5 M	
	60°	80°	60°	80°	60°	80°
Piperidin-3-ol	8·52	51·63	14·62	84·39	25·86	128·5
N-Methyl-piperidin-3-ol	17·16	100·50	30·04	168·30	49·11	298·5
Piperidin-4-ol	5·14	25·53	10·17	44·22	17·05	61·96
N-Methyl-piperidin-4-ol	5·90	35·93	11·88	54·39	20·23	95·00

faster than one electron transfer since (a) no high energy free radicals are formed during 2 electron process and (b) there is, overall, twice the free energy change. If a two electron path is available it is therefore likely to be the favoured reaction course.

On analogy of the oxidation of cyclohexanol[4], it can be safely argued that piperidinols also undergo a C—H bond fission. A mechanism (Scheme 1) involving cyclic transfer of this α-hydrogen atom to the metal ion-coordination sphere, can accommodate these facts.

The above scheme takes into account all the observed facts, viz. (a) dependence on [H+] being unity, (b) Drummond's and Waters tests being positive.

Hence it is concluded that the process is by a C—H fission involving formation of a free radical.

References

1. HITE, G., SMISSMAN, E. E. & WEST, R., *J. Am. chem. Soc.*, **82** (1963), 1207.
2. LYLE, R. E., *J. org. Chem.*, **22** (1957), 1280.
3. STEWART, R., *Mechanism of oxidation* (W. Benjamin), 1964.
4. LITTLER, J. S. & WATERS, W. A., *J. chem. Soc.*, (1959), 4046.