Kinetics of Chlorination of Some Substituted Piperidin-4-ones by 1-Chlorobenzotriazole

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The title halogenation reaction is first order each in the substrate and the chlorinating agent in 30% aq. acetic acid at 303 K. While increase in [H+] decreases the rate, the rates are not much affected by the change in dielectric constant and by added salts. It is likely that the reaction occurs between two neutral species.

The earlier work from our laboratory reported the kinetics and mechanism of chlorination of organic substrates by 1-chlorobenzotriazole(CBT). The title investigation is in continuation of this earlier work.

1-Chlorobenzotriazole(CBT) and the ketones, viz. N-methyl-2,3,5,6-tetraphenyl-(I)-, N -methyl-2,6-diphenyl-(II)-, N,3-dimethyl-2,6-diphenyl-(III)-, N,3,3-trimethyl-2,6-diphenyl-(IV)- and N,3,5-trimethyl-2,6-diphenyl(V)-piperidin-4-ones were prepared by literature methods. The reactions were followed iodometrically under pseudo-first order conditions ([ketone]>>[CBT]). The stoichiometric runs indicated that one mol of ketone consumed one mol of CBT to give α-haloketone and benzotriazole.

The rate constants at varying [CBT] and [substrate], given in Table 1, show that the reaction is first order each in the reactants. The results on the effect of change of ionic strength, dielectric constant and [H+] on the reaction rate are given in Table 2. The various thermodynamic parameters calculated for the chlorination (followed at four temperatures) of the representative ketone(III) are: $E_a = 83.44$ kJ mol$^{-1}$; $\Delta H^\circ = 80.78$ kJ mol$^{-1}$; $\Delta S^\circ = -37.36$ JK$^{-1}$ mol$^{-1}$.

All these observations indicate that the chlorination does not proceed by an ion-dipole reaction in the rate-limiting step, but occurs between two neutral species. The rate expression should be of the form: Rate $= k_1$ [substrate][oxidant] and that the reaction is simple and straightforward involving CBT and piperidone.

The rate constants of chlorination of ketones (I-V) in 30% acetic acid are: $19.1 \times 10^{-4}$, $11.2 \times 10^{-4}$, $8.51 \times 10^{-4}$, $3.61 \times 10^{-4}$ and $3.35 \times 10^{-4}$ s$^{-1}$ respectively. All the ketones investigated in this study have been shown to exist in simple chair conformation with equatorial alkyl group(s) and further chlorination occurs by the displacement of hydrogens alpha to the carbonyl group because of stereo-electronic reasons.

Eventhough the electron density of both the H atoms at 3,5-positions is much less due to the inductive effect of the carbonyl function at position-4, the H atom at each of the equatorial position is easily approached by the molecule of CBT. Thus when 3 and 5 positions are being successively occupied by methyl groups there is striking retardation in the rate. Increasing substitution of the active H atoms by alkyl groups not only increases the steric hindrance to the attacking species but also enhances the shift of electron density towards the ring. The presence of electron releasing methyl group thus opposes the build-up of a partial positive charge on the hydrogen and counteracts the electron-withdrawing effect of the
carbonyl group. This effect may be more significant when there are two methyl groups at the same carbon of the ring.

Thus N-methyl-2,6-diphenylpiperidin-4-one(II), which has two equatorial H atoms that can be attacked, undergoes chlorination at a much faster rate as compared to other ketones. On the other hand, in N,3,5-trimethyl-2,6-diphenylpiperidin-4-one(V) both the bulky methyl groups at 3 and 5 positions are equatorially placed, the attacking CBT has to approach only the axial hydrogen atoms. Because of the steric hindrance the reaction is expected to be the slowest and this is found to be so.

The much faster rate of chlorination of N-methyl-2,3,5,6-tetraphenylpiperidin-4-one(I) indicates that in this compound the electronic effect outweighs the steric effect.

References