CHAPTER II

SCOPE OF THE WORK
A study of carbohydrates is one of the most exciting fields of organic chemistry. It extends from tremendously complicated problem of understanding the process of photosynthesis to the equally difficult problem of unraveling the tangled steps in the enzyme catalyzed reconversion of (+) glucose into carbon dioxide and water. The saying in the Hinselwood's words¹ that "Nature possesses the art of weaving simple threads into the pattern of wonderful complexity and beauty" is true here. Carbohydrates provide us with the most basic and bare necessities of life namely food, clothing and shelter in quite literal terms.

Carbohydrates are the class known since ancient times. Before 1887 four isomeric hexose sugars were known - glucose, fructose, galactose and sorbose. The fifth isomer mannose was added to the existing list by Emil Fischer in 1897 who is better known as the pioneer of carbohydrate chemistry.

Heinrich Kiliani and Bernard Christian Gottfried Tollens are credited with the structural studies of simple sugars in earlier times. Initial investigations in the chemistry of the carbohydrates led to the waning interest and among some of the earlier workers who forged their weapons of investigation to gain knowledge in this field, the names of Purdie, Irvine and Hamworth are worthy of being mentioned at this place².
Since author's chief concern is the oxidation reaction of glucose, a brief survey of literature will be quite appropriate here in this field only.

Oxidation reaction of glucose was studied as early as 1922 when Schonebaum studied the action of ozone on glucose, fructose and sucrose. Oxidation of glucose by yellow oxide of mercury resulting in the production of the gluconic acid was reported by D.H. Brauns and A. Blanchetier.

Alles and Winogarden, Vinilescu and Fatlis, Coebel and others used iodine as the oxidant in this reaction. Oxidation of glucose by air or atmospheric oxygen was studied by a number of workers, the more important ones being the names of Speech, Power and Upson, McCoull, Chakrabarti and Dhar, and Samuelson.

Oxidation of glucose by cupric salts has been studied by Jensen and Upson, Lundin, Forber, Dimitrov Khadiev, Singh and Swedberg in the alkaline media. Oxidation studies with the manganese oxide has been reported by C.D. Ingersoll.

Bernhauer and Schon studied the influence of chloramine on glucose while Louisa Ridgway used potassium permanganate as the oxidant in its reaction with glucose.
Sohnichiro Ochi\textsuperscript{22} oxidised glucose, fructose and sucrose with bleaching powder while barium hypobromite was used for the oxidation of glucose by Reichstein and Neracher.\textsuperscript{23} Busch, Clark, Genung, Schroeder and Evans\textsuperscript{24} oxidised the glucose with silver oxide.

Kakuno Suzuki studied the decomposition of glucose in solution containing excessive amount of calcium hydroxide while Nakhamovich\textsuperscript{25} studied the kinetics of the above reaction. Oxidation of glucose by cerium carbonate has been reported by Job\textsuperscript{26} whereas cerium sulphate was used for the oxidation of carbohydrates by Birstein and Shimental.\textsuperscript{27} Mechanism of Ce(IV) oxidation of glucose has been reported by Pottengar.\textsuperscript{28}

Kiyoshi Ashida\textsuperscript{29} and co-workers have studied the oxidation of glucose by Ketones. Oxides of nitrogen have been used as oxidant in the oxidation of glucose and related compounds by Degering and Berntsen.\textsuperscript{30}

Benjamin Warshovsky and W.M. Sandstrom\textsuperscript{31} have studied the action of oxygen on the glucose in the presence of potassium hydroxide.

Halogens and their acids have also been used in oxidation reaction of glucose. Course of oxidation of aldose
sugars by bromine water was studied by Isbell and Hudson.\textsuperscript{33} Isbell and Pigman\textsuperscript{34} oxidised $\alpha$- and $\beta$-aldoses with bromine and studied mutarotational phenomenon.

Hayman and Persky\textsuperscript{35} studied the influence of ionic strength and temperature on the bromine oxidation of glucose. Barker, Overend and Rees\textsuperscript{36} also studied this reaction.

Isbell\textsuperscript{37} has also determined the isotope effect by double labelling in the reaction of glucose with iodine as the oxidant. Sumio Nakamura\textsuperscript{38} reported the use of potassium hypiodite as oxidant whereas some others\textsuperscript{39} have reported the use of periodic acid. Hypochlorous acid and chlorine has been used as an oxidant for glucose by Bernardelli, Grigor and Tumanova,\textsuperscript{40} Fitis,\textsuperscript{41} Norman and Lichtin,\textsuperscript{42} Chlorine dioxide\textsuperscript{43} and sodium chlorite\textsuperscript{44} have also been used for oxidation reactions by some workers.

Recently nitric acid oxidation of glucose has been studied by some workers.\textsuperscript{45} Last but not the least, mention should be made of chromic acid oxidations of aldoses including glucose which is the topic of the present work.

Before the chromic acid oxidations are reviewed, it will be appropriate to mention a word about some other modes of oxidation of glucose. Apart from the biochemical oxidation
in the metabolism of the living beings, considerable work has been done in the studies of electrolytical and photochemical oxidation of the compound. Contributions of some of the Indian chemists such as Ghosh, Mukherji, Banerjee and Bhattacharya and others are worth mentioning in the photochemical studies. Electrolytical oxidation of glucose has been studied by a number of workers - Isbell and Frusch, Helvig and Szwarc, Kapanna and Joshi and many others.

Chronic acid is an important and one of the most widely used oxidizing agent. Almost all forms of organic matter can be oxidized by this oxidant. Bobtelsky and Westheimer may be credited with the admirable contribution and pioneer work in this field.

Here it is intended to give a bird’s eye view over the oxidation reactions of chronic acid before passing over to intricacies of the oxidation and the system of glucose - chronic acid studied in this light.

Immense amount of work has been done in the oxidation reactions and in fact there is no dearth of papers appearing in the literature in this respect. The oxidation reactions of chronic acid involving organic compounds have been studied extensively. Perhaps none of the class of organic
compound is untouched by chromic acid oxidation.

To name a few of them are alcohols including aromatic, primary, secondary and tertiary, alicyclic and aliphatic; organic acids including carboxylic, hydroxy and aliphatic; hydrocarbons including branched chain and straight chain, unsaturated and saturated aromatic and alicyclic; allylic compounds, fatty acids, glycols and related compounds; paraffins and olefins; aldehydes and ketones including aromatic, alicyclic, aldehydic acids and amines. Some of the more complex classes of organic compounds which have been studies are: carbohydrates, including pentoses, hexoses, cellulose, lignin types, glucosides and other related compounds; viridin; steroidal copolymers; sterols and their related compounds; alkaloids; vitamins; organoboranes; organic nitrogen compounds; adamantane and its homologs; boron carbide and codriver oil etc.

The advantage of using chromic acid as oxidising agent is multifaceted in terms of both synthetic and mechanistic studies. The stability of its derivatives and the fact of its activity being a function of acidity constitutes chromic acid as a potent and very strong oxidising agent.

Five oxidation states are known for chromium ions,
from +2 to +6. All the lower oxidation states of chromium are excellent reducing agents converse to the higher oxidation states. The most stable state, however, is +3. Brown insoluble complexes of Cr$^{+3}$, and Cr$^{+6}$ with CH$_3$COO$^-$ are formed in anhydrous acetic acid or acetic anhydride resulting in the incomplete reduction of Cr$^{+6}$ even in the presence of large excess of reducing agent.

The highest oxidation state for chromium continues to be the one corresponding to the total number of 3d and 4s electrons i.e., Cr$^{+6}$ in addition to the peroxy compounds. In its higher oxidation state it forms oxo compounds which are potent and strong oxidizing agents. It is the aqueous chemistry of chromium which is the most important. In the basic solutions it exists as yellow tetrahedral chromate ion CrO$_4^{2-}$. With increasing acidity pH is lowered and yellow chromate turns orange giving birth to dichromate ion Cr$_2$O$_7^{2-}$ as a result of the protonation and dimerization. Following steps have been suggested in the whole process:

H$_2$O + CrO$_3$ $\rightarrow$ H$_2$CrO$_4$ Overall reaction.
CrO$_4^{2-}$ + H$^+$ $\rightarrow$ CrO$_3$(OH)$^-$ Protonation.
CrO$_3$(OH)$^-$(H$^+$)$^+$ $\rightarrow$ H$_2$CrO$_4$ Further protonation.
CrO$_3$(OH)$^-$(OH)$^-$(OH)$^+$ $\rightarrow$ Cr$_2$O$_7^{2-}$ + H$_2$O Dimerization.
Lee and Stewart\textsuperscript{97} have studied the nature of Cr(VI) in acid solution and applied its relation to oxidation studies. The details of these pH dependent equilibrium have been investigated by a number of workers such as Tong\textsuperscript{98}, Wiberg\textsuperscript{99}, Howard\textsuperscript{100} and others\textsuperscript{101}. It is worth adding that chromium(VI) does not give rise to the extensive and the complex series of polyacids and polyanions perhaps due to the greater extent of multiple bonding Cr = 0 for the smaller chromium ion, leaving aside the reported exceptions of trichromates $MgCr_3O_10$ and tetrachromates $MgCr_4O_{13}$\textsuperscript{102}.

Oxidation states of Cr(V) and Cr(IV) formed as transient intermediates in the reduction of Cr(VI) solution, have no stable aqueous chemistry because of their rapid disproportionation to the rather stable Cr(III) and Cr(VI) states.\textsuperscript{104} Long has studied the effect of acidity on the intermediate reactions that may take place during the reduction of chronic acid. Westheimer et al\textsuperscript{103} have demonstrated the participation of these ions in the oxidation of organic substrates. Indeed these species have appeared to be more vigorous oxidising agents. In strongly acidic solutions higher polymers of Cr(VI) have also been detected.\textsuperscript{105}

Concentrating on the kinetic studies of the glucose-chronic acid system, one comes across the names of Kurtzel and
Monsheimer who studied the reduction of chromium(VI) with glucose in sulphuric acid - dichromate solution under the varying experimental conditions. Oxidation of glucose by means of chromic acid has been followed kinetically by Balseore and Tandon.

The author found it interesting to study certain aspects of the chromic acid oxidation of glucose in aqueous media under varying conditions. It is obvious from a perusal of literature that this system has not been much investigated.

It has been observed that the walls of the reaction vessels do manage to intervene in the system under study and to modify its character in one way or other, even if it does not itself react. Therefore it was ascertained in the system glucose-chromic acid whether it is homogeneous or heterogeneous in nature.

As mentioned earlier, the oxidizing character of chromic acid diminishes or enhances with the hydrogen ion concentration therefore presence of acids affects the reaction rate considerably. It has been evidenced by the work of a number of workers. The author has also studied the effect of acids on the course of the reaction. Four acids were selected for this purpose: hydrochloric, sulphuric, phosphoric and acetic acids. The first two are comparatively strong mineral acids whereas the third one, phosphoric acid is rather moderate.
The fourth and last one, acetic acid is a weak organic acid. Care was taken in choosing the concentration ranges of acids so that they did not interact with the system under study.

A glance over the literature will reveal that the reaction catalysed by acids or bases are affected by the mere presence of salts to a more or less extent. Effects of the salts on the reaction rates have been well observed by a number of workers namely, Mahajani, Dhar, Saraf, Sharma, Joshi and many others.

Arthur Harden and Kappanna have studied the effect and role of phosphate in the oxidation of glucose. Milton Levy and Edward A Doisy studied the effect of borate. Influence of addition of carbonates has been studied by Bernhauer and Distler. Honig and Ruzicka and Tulchinashii in the oxidation of glucose with different oxidants.

Singh, Krishna and Ghosh have found tartarate and citrate to affect the oxidation reaction of glucose by bivalent cupric ions. Colbran and Neveli report the effect of potassium iodide concentration on the oxidation of glucose in alkaline media by iodine. Recently Purhit and Shrivastava have observed the catalytic effect of silver ions on the velocity of the reaction of oxidation of glucose by potassium phosphate.
It, however, is clear that there exists significant scope to carry on further investigations in this field and hence the author has become interested in it.

The author has also studied the effect of salts on the reaction of glucose with chromic acid. The sulphate and chlorides of three alkali metals - potassium, sodium and lithium were selected and their effect on the rate constant was studied.

The correlation between rate constant and Hammett acidity constant $H_0$ has been well established in a number of oxidation reactions. The correlation has also been observed to hold good in the reaction involving chromic acid, chromate or dichromate ions as the oxidizing species for example in the case of oxidation of secondary alcohols by chromic acid. Going through the literature has again revealed that this field is relatively not studied and offered scope and opportunities for further exploration in this field also. Therefore the author has also attempted to step further in the study of the correlation of reaction rate with Hammett acidity constant $H_0$ in the oxidation reaction of glucose by chromic acid under varying conditions.

The author has also calculated energy of activation and entropy of activation for this system from the experimental data and results obtained from the kinetic measurement.
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