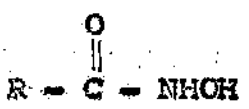
HYDROXAMIC ACIDS AND ORGANOTIN HYDROXAMATES

Since the present investigation is on hydroxamic acids it will be relevant to discuss some types of hydroxamic acids and their organotin derivatives in the greater detail.

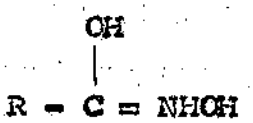
Although hydroxamic acids have been known for more than a century, the study of their chemistry and practical applications lagged for many years probably due to the uncertainity of their structures.

Sandler and Karo have published a review on the chemistry of hydroxamic acid in 1972 (153). The first stereochemical concepts of hydroxamic acids were proposed by Werner (154) who carefully differentiated between hydroxamic acids.



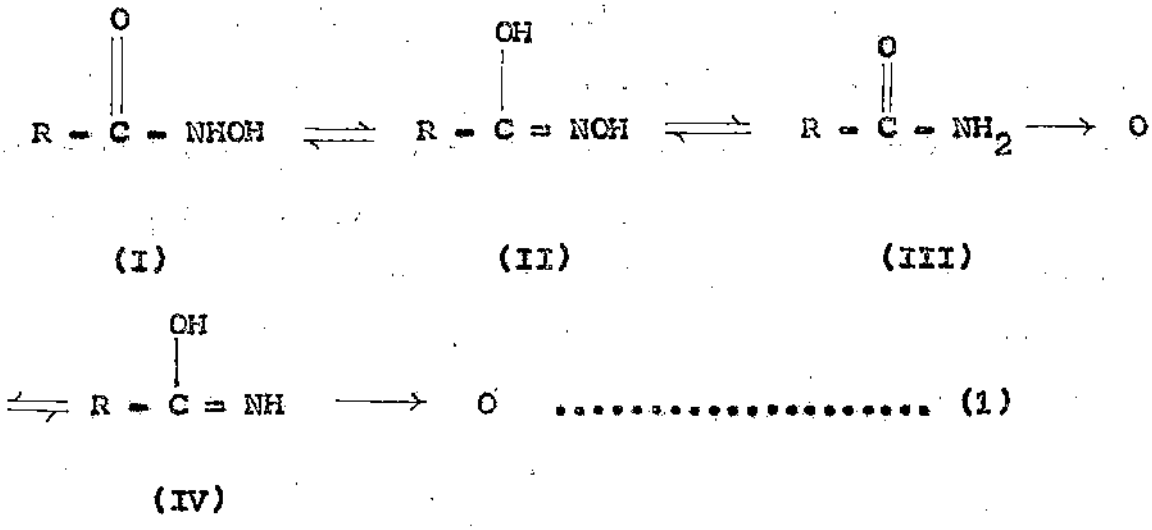
(I)

and their tautomers, the hydroximic acids



(II)

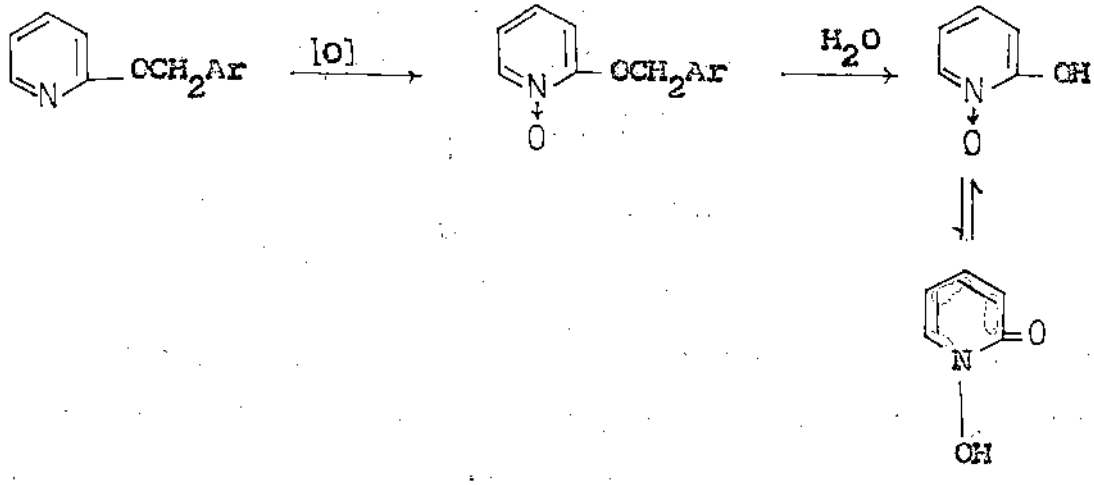
The above structures may be in equilibrium also with other tautomeric forms:



(I) (II) (III)

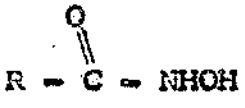
(IV)

Structure (II) termed as hydroximic acids constitute only a minor component of the tautomeric equilibrium mixture although derivatives of hydroximic acids are known. Structure (III) and (IV) have been added to the list of possible tautomeric forms relatively recently (155,156). Their importance becomes obvious from the standpoint of the preparation of cyclic hydroximic acid. For example N oxidation of an appropriately constituted molecule may produce a cyclic hydroxamic acid (157)

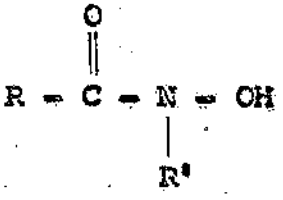


...(2)

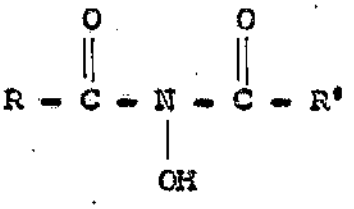
The variety of substituted hydroxamic acid is surprisingly large. If we consider only the structures which may be written upon alkylation and/or acylation of hydroxylamine but ignore the tautomeric derivatives, the following compounds result:



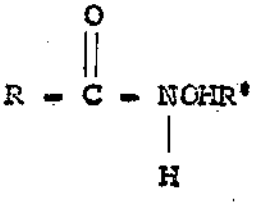
(I)



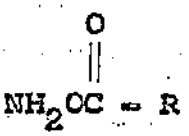
(V)



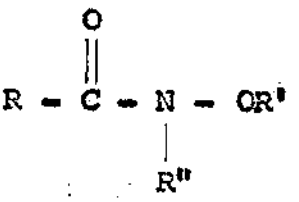
(VI)



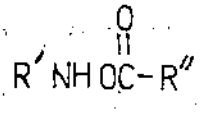
(VII)



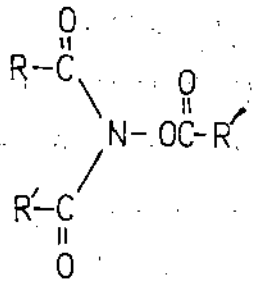
(VIII)



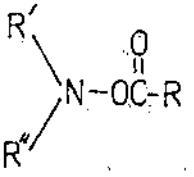
(IX)



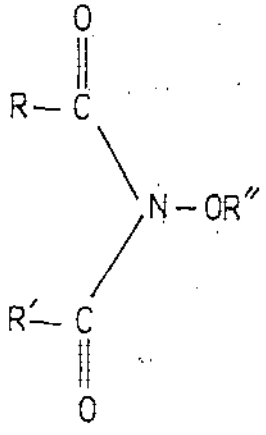
(X)



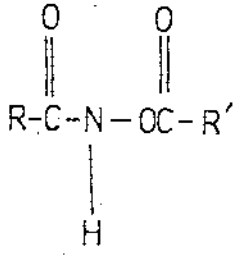
(XI)



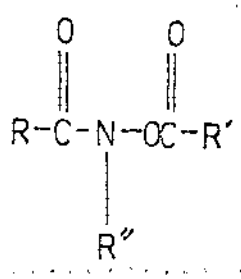
(XII)



(XIII)



(XIV)



(XV)

Compounds such as (VII), (IX) and (XIII) are esters of hydroxamic acids and in the case of structure (VII) are alkyl hydroxamates.

When the distribution of electrons of hydroxamic acid and hydroximic acids are considered it will be noted that several sites exist with which these compounds may act as neucleophilic agents. Furthermore the hydroxamic acid may act as chelating groups. The classical color test for hydroxamic acid with ferric chloride involves chelation. Also a common method of isolating these compounds by precipitation with cupric ions frequently referred to as a formation of copper hydroxamate salts is a case of the formation of copper chelates. Because of its unusual electron distribution, the chemistryof hydroxamic

acid is complex and still present a fruitful area of research and development both from the theoretical and technological standpoint.

The acid strength of hydroxamic acids has been reported to be of the same order of magnitude as that of the carboxylic acids. At least some of these acids are said to be soluble in sodium bicarbonate solution. Moreover the acid strength of hydroxamic acids vary over a wide range and some of pK_a values of above 9 (e.g. O-methoxy benzo hydroxamic acid) may be precipitated from an alkaline solution with carbon dioxide, provided of course, that the free acid is insoluble in water (158).

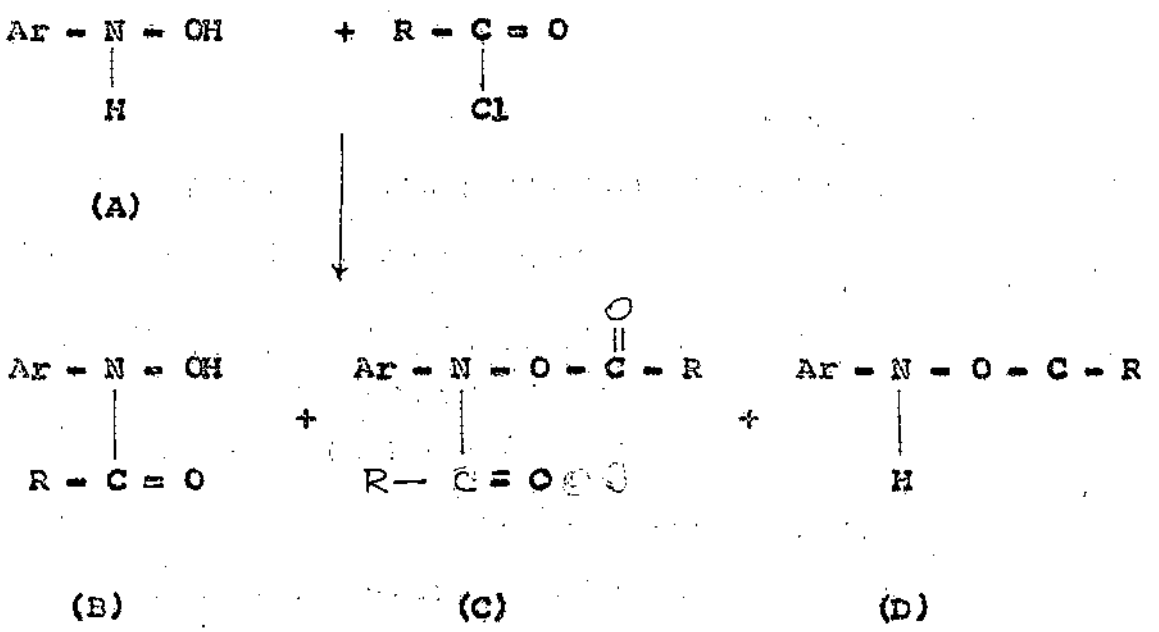
Hydroxamic acids in general are synthesised by reacting an alkyl or acyl ester (RCO_2Et) with hydroxylamine in the presence of alkali and the free acid is obtained by the addition of acid in the appropriate quantity in cold solution (159).

$$RCO_2Et + NH_2OH + KOH \longrightarrow RCONHOK + EtOH + H_2O$$

$$RCONHOK + HX \longrightarrow RCONHOH + KX.$$

The general method employed in the synthesis of N-aryl hydroxamic acids are outlined by Yale (160) in a well documented review article.

One of the widely used procedure for the preparation of hydroxamic acids is based on Schotten Baumann reaction (161). This involves the partial acylation of the N-aryl hydroxylamine (A) with acid chloride in aqueous (162) or benzene (163,164) or diethyl ether medium (165,166).



The course of acylation is very sensitive to the proper choice of experimental conditions, otherwise the concomitant formation of disubstituted hydroxamic acid (and possibly the O-acetylated aryl hydroxylamine, D) takes place.

Most of the workers isolated the desired mono derivative (B) from the crude product by tedious and repeated extraction

with concentrated ammonium hydroxide, in which the di derivative (and D, if present) is insoluble. Subsequent acidification with hydrochloric acid (167) of the ammoniacal solution liberates the hydroxamic acid.

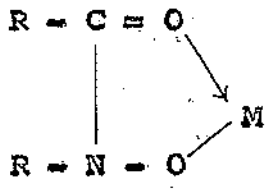
On the basis of Schotten Baumann reaction, Tandon and coworkers (168,169) have prepared several N-aryl hydroxamic acids by reacting phenyl hydroxylamine (PhNHOH) with acyl chloride or its derivatives ($R'COCl$) in the presence of dilute alkali

$$RNHOH + R'COCl + NaOH \longrightarrow R-N(-OH)-C(=O)-R' + NaCl + H_2O$$

Ghosh and Sarkar have synthesised succinyl bis N-phenyl hydroxamic acid (170) and adipyl bis N-phenyl hydroxamic acid (171) with phenyl hydroxylamine and corresponding acid chlorides in ice cold diethyl ether using a base (pyridine).

The acidic properties of hydroxamic acids have been reported to be associated with the hydrogen of the "hydroxylamino" hydroxyl group and the hydrogen associated with the nitrogen atom itself. But in case of N substituted hydroxamic acid the acidic nature of hydroxamic acid is due only to

"hydroxylamino" hydroxyl group, which may react with suitable metal moieties and also with the coordination from the carbonyl group to produce a chelate compound.



(Fig. 5)

A large number of metal hydroxamate chelate have been isolated with various metal cations (172) but organometallic chelate hydroxamates have so far not investigated extensively.

The hydroxylamine derivatives of organotin has been synthesised by Harrison (173,174) by the azeotropic removal of water from the mixture of appropriate hydroxylamine and the organotin oxides or hydroxides.

$$\begin{matrix}(R_3Sn)_2O \\ \text{or} \\ R_3SnOH\end{matrix} + HONR'R'' \longrightarrow R_3SnONR'R'' + H_2O$$

(where R = Me, R' = R'' = Et; R' = Ph, R'' = COPh; R = N-Pr, R' = Ph, R'' = COPh; R = Ph, R' = Ph, R'' = COPh; R = Me, R' = H, R'' = COPh; R = n-Pr, R' = H, R'' = COPh).

However attempts to prepare $Ph_3SnONHCOPh$ by the same method only resulted in the formation of tetra phenyl tin in high yield, presumably by a disproportion reaction although no pure diphenyl tin derivatives could be isolated.

$$Ph_3SnOH + HONOHCOPh \xrightarrow{-H_2O} [Ph_3SnONHCOPh]$$

$$\longrightarrow Ph_4Sn + [Ph_2Sn(ONHCOPh)_2]$$

The organotin derivatives of N-benzoyl hydroxylamines are extremely stable in moisture. The $Ph_3SnONHCOPh$ is monomeric in both crystal and solution phases, whereas the trimethyl tin derivatives are associated in the solid (173, 174).

Diorganotin derivatives of N-substituted benzo hydroxamic acids have been prepared (175,176,177,178) according to the following reaction schemes:

$$R_2SnO + 2\ HONR'R'' \longrightarrow R_2Sn(ONR'R'')_2 + H_2O$$

$$R_2SnCl_2 + 2\ HONR'R'' \longrightarrow R_2Sn(ONR'R'')_2 + HCl.$$

The liberated hydrochloric acid was neutralised by 25% aqueous ammonia and removed as precipitated ammonium chloride.

Phenyl tin halide bis (N-phenyl benzo hydroxamates) have been prepared by the reaction of tri phenyl tin N-phenyl benzohydroxamate with mercuric chloride, mercuric bromide and mercuric iodide (178).

Phenyl tin thiocyanate bis (N-phenyl benzohydroxamate) has been prepared (178) from the corresponding chloride by the displacement of chloride by thiocyanate.

$$PhSnCl(PBHA)_2 + KCNS \longrightarrow PhSn(CNS)(PBHA)_2 + KCl$$

(HPBHA = N-phenyl-N-benzohydroxamic acid).

Compounds of the type R_2SnX (PBHA) have also been prepared by Pradhan and Ghosh (178, 179) where R = Ph, X = Cl, I, SCN; R = Bu, X = SCN) through disproportion reaction.

$$R_2SnX_2 + R_2Sn(PBHA)_2 \longrightarrow 2R_2SnX(PBHA)$$

But $Ph_2Sn(SCN)(PBHA)$ has been prepared by the reaction of corresponding chloride complex with KCNS (180).

$$Ph_2SnCl\ (PBHA) + KCNS \longrightarrow Ph_2Sn(SCN)(PBHA) + KCl.$$

Pradhan and Ghosh (178) have shown that penta coordinated diorganotin halide N-phenyl-N-benzo hydroxamates disproportionate to the more stable hexa coordinated tin compounds when refluxed with non polar solvent like benzene for long time.

$$Ph_2SnX(PBHA) \longrightarrow PhSnX(PBHA)_2 + Ph_3SnX.$$

(where X = Cl, SCN)

However in polar solvents like methanol, Ph_2SnX (PBHA) was found not to give any triphenyl tin halide and $PhSnX(PBHA)_2$ instead another hexa coordinated compound phenyl tin halide methoxy N-phenyl-benzo hydroxamate was found along with the liberation of one equivalent of benzene (178).

The methoxy compound was also obtained when phenyl tin halide bis-N-phenyl-benzohydroxamate was refluxed in methanol with the liberation of one mole of ligand (178).

$$Ph_2SnX(PBHA) \xrightarrow{\text{in } CH_3OH} PhSnX(OCH_3)(PBHA) + C_6H_6$$

$$PhSnX(PBHA)_2 \xrightarrow{\text{in } CH_3OH} PhSnX(OCH_3)(PBHA) + HPBHA.$$

Some mono organotin derivatives of hydroxamic acids was prepared by Nanula and Gupta (180). They have synthesised five, six and seven coordinated mono organotin derivatives of hydroxamic acid. They have isolated the compounds of the general formulae $R_2Sn_2O_2L_2$, $(RSnL_2)_2O$ (LH = hydroxamic acid derivatives).

Harrison et al (176) have prepared a number of new organotin hydroxamates following the usual procedures (173,174). These compounds are of the types R_2SnL_2 (where R = Me, ^nBu, ^{n}Octyl, Ph and LH = N-benzoyl N phenyl hydroxylamine), R_2SnXL (where R = Me; X = Cl, Br, I) and $RSnL_3$ (where R = ^nBu).

Chaudhuri, Roy and Ghosh (181) also synthesised organotin hydroxamate of the type R_2SnL_2, R_2SnXL and $RSnXL_2$ (where R = methyl, butyl; X = Cl^-, Br^-, I^-, SCN; and LH = N phenyl p-chloro benzo hydroxamic acid) and nine new organotin N-phenyl-p-nitro benzo hydroxamates (182) of the types R_2SnL_2 and R_2SnXL (where R = methyl, butyl; X = Cl, Br, I, SCN and LH = N-phenyl p-nitro benzohydroxamic acid). These compounds have been characterised on the basis of their elemental analyses, molar conductance, IR and PMR spectral data.

They have also synthesised (183) two new ligands viz. Oxalyl bis N-phenyl hydroxamic acid (L) and Oxalyl bis N-p-tolyl hydroxamic acid (L'). These have been used to prepare some new types of organotin coordination compounds $(R_3Sn)_2L$

(R = phenyl), $(R_3Sn)_2L'$ (R = phenyl, cyclohexyl), $(R_2SnL')_n$ (R = phenyl, butyl benzyl), $[(R_2SnCl)_2L]_2$ and $[(R_2SnCl)_2L']_2$ (R = p-tolyl). Some of these derivatives are polymeric in nature.