BRIEF REVIEW OF HYDRAZONES
AS ANALYTICAL REAGENTS

CHAPTER 3
Hydrazones are azomethines characterized by the grouping \( \text{C} = \text{N-N} < \). They are distinguished from other members of this class (Imines, Oximes etc) by the presence of two interlinked nitrogen atoms. The hydrazone grouping occurs in organic compounds of the following types.

\[
\text{I} \quad \text{R} = \text{N} = \text{N} = \text{C} \\
\text{II} \quad \text{R} = \text{N} = \text{N} = \text{C} \\
\]

Where

- \( \text{R} \) and \( \text{R}^1 \) = H, Alk, Ar, RCO, Ht (Heterocyclic group)
- \( \text{Y} \) = H, Alk, Ar, RCO, Ht
- \( \text{X} \) and \( \text{X}^1 \) = H, Alk, Ar, Ht, Hal, OR\(^1\), SR, CN, SO\(_2\)R, NO\(_2\), NHR\(^{11}\), R\(^{11}\), N=NR\(^{11}\), COOR\(^{11}\), CONR\(^{11}\)R\(^{1}\)

The general name of hydrazone is used for all the compounds having structure (I). The compounds of structure (II) are called Azimes.

Hydrazones are usually named after the compounds from which they are derived.
Hydrazones in general are prepared by refluxing the stoichiometric amounts of the appropriate hydrazone and aldehyde or ketone dissolved in suitable solvent. The compound usually crystallizes out on cooling.

Many of the physiologically active hydrazones find application in the treatment of diseases such as tuberculosis, leprosy and mental disorder. Aroyl hydrazones (III) are reported to possess tuberculostatic activity. This is attributed to the formation of stable chelates with transition metals present in the cells.

\[ R-\text{CH}=\text{N}-\text{NH-CO-R} \]

(III)

Thus many vital enzymatic reactions catalysed by the transition metals can not take place in presence of hydrazones. Hydrazones also act as herbicides, insecticides, nematocides, rodenticides and plant growth regulators. They show spasmylytic activity, hypotensive action, and activity against leukaemia, sarcomas and other malignant neoplasms. Hydrazones are used as plasticizers and stabilizers for polymers and as polymerization initiators, antioxidants etc. Hydrazones of 2-methyl phthalazine are effective sterilants for house files. 3-N-methyl-N-(4-chloro-1-phthalazinyl) and 3-N-methyl-N-(4-oxo-1-phthalazinyl) hydrazones possess anthelmintic activity.
Besides, the metal chelates of some hydrazones are useful in industry as dyes for wool, nylon, rubber etc. and as photochromic materials. Jain and Singh reviewed critically the applications of hydrazones as analytical reagents. The formation of hydrazone is extensively used in the detection, determination and isolation of compounds containing the carbonyl group. Photometric methods for determining aldehydes and ketones are based on their reaction with 2,4-dinitrophenyl hydrazine to form the corresponding hydrazones.

Biscyclohexanone oxalyldihydrazone was one of the earliest used hydrazone for the spectrophotometric determination of copper. It gives a blue colour with traces of copper and is used for determination of copper in paper pulp products, human serum, steel, plants, nonferrous metals and alloys, and cadmium sulphide. Ethylidene oxalyldihydrazone has been used to determine copper in zinc and its alloys. A similar atype of reagent, bis(ethylacetoacetate) oxalyldihydrazone is very selective and sensitive for copper.

Lions and Martin introduced Pyndine-2 aldehyde pyridyl hydrazone (PAPH) and similar type of hydrazones and have made detailed physico-chemical investigations on their metal complexes. This has opened a wide field for their use in analytical chemistry, which began in 1963 when Cameron et al published a survey of the visible, spectra of aqueous solutions containing metal ions and PAPH. They also stated that PAPH is
useful as colorimetric reagents as well as an acid-base indicator. PAPH has been used for the determination of copper in food stuffs\textsuperscript{29}. The complexes of PAPH and Zn(II), Cd(II), Fe(II), Cu(II), Ni(II), Mn(II) and Pd(II) have been studied by Quddus and Bell\textsuperscript{30}.

\[2,21^\text{B}-\text{Bipyridyl 2-Pyridyl hydrazone (BPPH)}\textsuperscript{31}\] reacts with cobalt(II) to form an orange coloured complex (\(\lambda_{\text{max}}=480\) mm) which shows a bathochromatic shift on addition of perchloric acid (\(\lambda_{\text{max}} = 500\) mm) giving a pink complex which is stable even in 50\% perchloric acid medium. This reaction has been utilized in the spectrophotometric determination of cyanocobalamine\textsuperscript{32} and of cobalt in sea-water and brine\textsuperscript{33}. BPPH also reacts with iron(II)\textsuperscript{34}, zinc(II)\textsuperscript{35} and cadmium(II)\textsuperscript{36}.

A new heterocyclic hydrazone, pyridine-2-aldehyde 2-Quinolylhydrazone (PAQH) was introduced by Heit and Raym\textsuperscript{37}. It was used selectively for the spectrophotometric determination of cobalt and Nickel\textsuperscript{38}. It was also used for the determination of cobalt in sea water\textsuperscript{39}. It can also complex with Fe(II), Cu(II) and Pd(II). Quinoline-2-aldehyde 2-quinolylhydrazone has been used for the determination of copper in sea water\textsuperscript{43-44} and tap water\textsuperscript{45}.

For vanadium(V), Co(II), Zn(II), Fe(II), Pd(II), Ni(II), Cu(II), Cd(II), Rh(III) another reagent called 2-2\textsuperscript{1} bipyridyl 2-pyrimidylhydrazone has been introduced by Singh and Co-workers as an analytical reagent\textsuperscript{46-50}. It has the advantages over the pyridyl and quinolyl hydrazones.
A series of 2-benzothiazolyl hydrazones have been described. Benzothiazole-2-aldehyde for Cu(II), thiophene-2-aldehyde for Cu(II), 2-furural for Cu(II), Ag(I), Co(II), Hg(II), Ni(II), Zn(II).

Libergott et al. used isatin-2-benzothiazolylhydrazone for the determination of lead in plastic milk cartons.

Many new hydrazones are prepared in situ and applied for the spectrophotometric determination of metal ions. For the determination of traces of iron, 2,2′-bipyridylglyoxal dihydrazone, biacetyl dihydrazone and phenyl-2-pyridyl ketone hydrazone have been employed.

Some other hydrazones have been prepared and proposed for the determination of different metal ions. These are presented in Table III.
**Table III.1**

Other important hydrazones used for the spectrophotometric determination of metal ions

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Name of Hydrazones</th>
<th>Metal ions</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>2,2',-bipyridyl phenylhydrazone</td>
<td>Pd II</td>
<td>55</td>
</tr>
<tr>
<td>2.</td>
<td>pyridoin phenylhydrazone</td>
<td>Cu(II), and Pd(II)</td>
<td>56,57</td>
</tr>
<tr>
<td>3.</td>
<td>Benzil bis (2-hydroxy benzoyl hydrazone)</td>
<td>Ti(V)</td>
<td>58</td>
</tr>
<tr>
<td>4.</td>
<td>Salicylaldehyde benzoyl hydrazone</td>
<td>Cu(II) and Pd(II)</td>
<td>59</td>
</tr>
<tr>
<td>5.</td>
<td>Di-2-pyridyl ketone 2-furan carbothiohydrazone</td>
<td>Ni(II),Cu(II),Co(II),</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fe(II) and Re(II)</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>2-Benzoyl(BPPH) hydrazone</td>
<td>Fe(II), Co(II), Ni(II)</td>
<td>61</td>
</tr>
<tr>
<td>7.</td>
<td>2,2'-pyridyl bishydrazone</td>
<td>Fe(II), Cu(II), Co(II), Ni(II)</td>
<td>62</td>
</tr>
<tr>
<td>8.</td>
<td>Phenanthridine-6-aldehyde pyridyl hydrazone</td>
<td>Zn(II)</td>
<td>63</td>
</tr>
<tr>
<td>9.</td>
<td>Benzil quinolylhydrazone</td>
<td>Cu(II)</td>
<td>64</td>
</tr>
<tr>
<td>10.</td>
<td>2 Benzoyl pyridine hydrazone</td>
<td>Fe(II)</td>
<td>65</td>
</tr>
<tr>
<td>11.</td>
<td>Naphtyl methylketone isonicotinic acid hydrazone</td>
<td>Ti(IV)</td>
<td>66</td>
</tr>
<tr>
<td>12.</td>
<td>O-hydroxyacetophnone hydrazone</td>
<td>Ni(II)</td>
<td>67</td>
</tr>
<tr>
<td>13.</td>
<td>Pyridine-2-carbaxaldehyde-2-hydroxy benzoyl hydrazone</td>
<td>Zn(II), Fe(II), V(IV), W(II)</td>
<td>68,70</td>
</tr>
<tr>
<td>14.</td>
<td>Pyridion phenyl hydrazone</td>
<td>Cu(I), Pd(II)</td>
<td>71,72</td>
</tr>
<tr>
<td>15.</td>
<td>Bis(4-hydroxyl benzoyl hydrazone)</td>
<td>Ca(II), Cd(II)</td>
<td>73</td>
</tr>
</tbody>
</table>
Isonicotinic acid hydrazide is an important anti-tubercular agent and has good potential for the formation of complexes with metal ions. A survey of literature reveals that only a few isonicotinoyl hydrazones of benzaldehyde and its derivatives are prepared and relatively less work is done with regard to their metal complexes. It is also observed that isonicotinic acid hydrazones and their metal complexes possess higher activity and lower resistivity to tuberculosis bacteria. Isonicotinoyl hydrazones are also potential analytical reagents for the determination of several metal ions by different physico-chemical techniques. Of these techniques the spectrophotometric determination occupy a special place.

Salicylaldehyde isonicotinoyl hydrazone is used for the spectrophotometric determination of gallium and indium at pH6.0-6.5 ($\lambda_{\text{max}}$ 390 and 380 nm). These complexes are extractable into pentanol. Since the aluminium complex is not extractable it does not interfere.

Belal and Chaaban determined Fe(II) and Fe(III) colorimetrically in presence of each other and other metal ions and applied to various pharmaceuticals by using 2-hydroxy-1-napthaldehyde isonicotinoyl hydrazone. Mo(VI) in steels was also determined.

The complexes formed by vanadium(V) in acidic 50% aqueous ethanolic medium with acetone isonicotinoyl hydrazone and with 4-hydroxybenzaldehyde isonicotinoylhydrazone have been examined and used for the spectrophotometric determination of vanadium.
Uno and Taniguchi\textsuperscript{78} have studied the fluorescent activity of the isonicotinic acid hydrazones of a number of carbonyl compounds, viz 2-hydroxy-1-napthaldehyde, salicylaldehyde-3-chloro-2-hydroxy benzaldehyde, 5-chloro-2-hydroxybenzaldehyde and 2-hydroxy acetophenone. In presence of aluminium these hydrazones give an yellowish-green fluorscence in an acetate buffer. While under similar conditions the parent carbonyls exhibit only feeble fluorescent activity. The fluorescent intensity of the hydrazones of 2-hydroxy-1-napthaldehyde (in the presence of aluminium) is particularly strong. Hence the aldehyde is found to be a good reagent for the fluorimetric determination of 0.1-1 ppm of isonicotinic acid hydrazide.

Isonicotinoyl hydrazone of salicylaldehyde and its 5 methyl, 5-chloro, 5,6-benzo derivatives and 2-OH acetophenone and its 5-methyl, 5-chloro derivatives react with manganese(II)\textsuperscript{79} to form four and six coordinated complexes. The aldehyde derivatives react in the keto form, while the keto derivatives react in the enol form.

Isoniazid(INH) and its acetone derivaties are employed for the spectrophotometric determination of V(V)\textsuperscript{80}, the complexes formed are 1:1 and the molar absorptivities at 420 nm and 435 nm are $9.4 \times 10^3 \text{ l.mol}^{-1}.\text{cm}^{-1}$ and $8.0 \times 10^3 \text{ l.mol}^{-1}.\text{cm}^{-1}$ respectively. V(V) was determined in vanadium iron alloy and iron ores in which iron was masked using fluoride.
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