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# SYNTHESIS OF N-SUBSTITUTED HYDROXAMIC ACIDS

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## ABSTRACT

A series of N-substituted hydroxamic acids, R.N(OH).C(O).R', have been synthesized by reacting freshly prepared N-substituted hydroxylamines and acid chlorides in mixed diethyl ether and petroleum ether (boiling range 40 to $60^0$ C) media at 0 to $5^0$ C, and neutralizing the liberated hydrochloric acid with aqueous suspensions of sodium bicarbonate. These compounds have been prepared for analytical applications and physico-chemical studies. These are also to be examined for antibacterial, antifungieidal and antiviral activity. The melting points of these compounds are as under.

R=-$C_6H_4CH_3$-4, R'= -$C_6H_4F$-3, $99^0$ : -$C_6H_4Cl$-3, $99^0$; -$C_6H_3Cl_2$-2,4, $163^0$; -$CH_2$ Cl, $123^0$; -$(CH_2)_7$ $CH_3$, $82^0$; - $(CH_2)_8$ $CH_3$, $86^0$; - $(CH_2)_2C_6H_5$, $118^0$; - $(CH)_2C_6H_5$, $156^0$; - $(CH_3O)_2C_6H_3$-3,5, $130^0$; -$C_4H_3$, $131^0$

R=-$C_6H_4CH_3$-3, R'= -C $(CH_3)_3$, $105^0$ : R=-$C_6H_4Cl$-4, R'= -$(CH_2)_{14}CH_3$, $100^0$ :

R=- $CH_2C_6H_5$, R'= -C $(CH_3)_3$, $104^0$ : -$(CH_2)_{14}CH_3$, $94^0$ :

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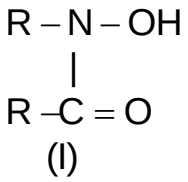
## INTRODUCTION:

Hydroxamic acids are becoming increasingly important class of compounds because of their applications in analytical chemistry (1 – 7) and biological science (8 – 12). Since introduction of certain groups and conjugated systems in the hydroxamic acid functional grouping alter the analytical properties, it was thought to synthesize some vividly substituted hydroxamic acids. In this communication, for the present purpose, preparation and infra-red spectroscopic data of hydroxamic acids, as represented by general formula I, are described



(I)

$R = p-CH_3C_6H_4-$, $m-CH_3C_6H_4-$, $p-ClC_6H_4-$ or $C_6H_5CH_2-$

R' = substituted phenyl, 2 – furyl or alkyl group, Twelve out of fourteen hydroxamic acids discussed here, are synthesized for the first time.

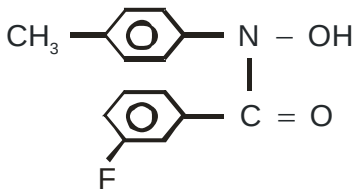
## EXPERIMENTAL:

### Apparatus and Materials:

A Perkin-Elmer Model 377 double beam recording spectrophotometer, equipped with potassium bromide discs and sodium chloride sealed cells of 0.1, 0.15 and 0.2 mm path length, was used for determining infra-red spectra of hydroxamic acids. The spectrophotometer was calibrated by standard methods using polystyrene film. The hydroxamic acids were dried over $P_2O_5$ for several hours. The spectra of all hydroxamic acids were determined from suspension in nujol. The spectra of some hydroxamic acids were determined in $CCl_4$ and $CH_3Cl$ also.

### Preparation of hydroxamic acids:

The method for preparing the typical compound N-p-tolyl-m-fluoro benzohydroxamic acid (II) is described below.



(II)

All other hydroxamic acids reported here were prepared similarly. 2.32 g (0.0188 mole) of freshly prepared and purified N-p-tolylhydroxylamine dissolved in 30 ml. diethyl ether and a suspension of about 4 g sodium-bicarbonate is 5.0 ml. water, were mixed together and stirred mechanically. External cooling was done to bring the temperature to $0^0$ C or lower. A solution of 3.0 g (0.0189) mole m-flurobenzoyl chloride in 30 ml of diethyl ether was added from a dropping funnel during the course of about 50-80 minutes. Some solid white product got precipitated. It was separated by filtrations. The filtrate was distilled under vacuum to remove the solvent diethyl ether, and by this some more light yellow product was obtained. Both products were mixed and triturated with 25 ml. saturated solutions of sodium bicarbonate for about fifteen minutes to remove the acidic impurities. The solution was filtered and the solid was washed with water and dried. The product was crystallized from a mixture of benzene and petroleum-ether. The yield of once crystallized product was 3.6 g (79%), m. p. $99^0$.

## RESULTS AND DISCUSSION:

**Preparation:** All of the hydroxamic acids are obtained as crystalline solids, the yield ranging from 55 – 90%. It is observed that the use of stoichiometric proportions of N-substituted hydroxylamine and acid chloride was most satisfactory for obtaining a pure product. With excess of acid chloride diderivative was formed and with excess of hydroxylamine the product was impure due to the decomposition products such as azobenzene, azoxybenzene, nitrosobenzene and aniline (13, 14). Low temperature and longer period of addition helped in improving the yield and N-acylation and minimizing the side reactions. The hydrolysis of acid chlorides, particularly of alkyl acid chlorides, is also minimized at low temperature.

**Properties:**

The properties of hydroxamic acids are summarized in table I.Except cinnamic acid derivative which is yellow, almost are white compounds. These are stable towards heat, light and air and can be stored in-definitely in tightly stoppered bottles. Their alcoholic, chloroform, dioxane solutions, too, are stable and can be kept for several weeks, if stored in amber bottles. The aqueous solutions of some hydroxamic acids such as N-p-tolyl-3, 5-dimethorybenzohydroxamic acid and N-m-tolylpivalolhydroxamic acid turn yellowish red in keeping them for more than one day. The solutions in alkaline and acidic media are unstable due to catalysed hydrolysis. The alkaline solutions turn green or bluish-green within two three hours.

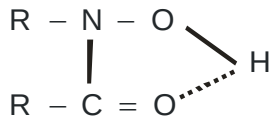
All the hydroxamic acids described here are sparingly soluble in water but are soluble in organic solvents such as benzene diethyl ether, chloroform, o-dichlorobenzene, ethanol, dioxane etc. and also in ammonia and caustic alkali solutions.

All hydroxamic acids give the characteristic purple colour test with ferric chloride. The chloroform solutions of all hydroxamic acids give violet extracts with $\lambda_{max}$ at 530± 30 nm, where there are shaken with ammonium –meta-vanadate solution in 4N HCl.

**Infra-Red spectra**:

The Changes in electron density around the characteristic group due to substitution in the molecule bring about displacements in the positions of absorption bands. The mesomeric (M) and inductive (I) effects, steric inhibition of resonance, intra and intermolecular interaction, physical state etc. alter the position, shape and intensity of absorption band in infra-red region.

**O-H Band:** The band due to O-H stretching vibrations is assigned in the region 3250 – 3110 $cm^{-1}$ (Table 1). The position and shape of the band depends upon the extent of hydrogen bonding. As the strength of hydrogen band increases the band becomes more broad and moves to lower frequencies. All the hydroxamic acids are involved in strong intramolecular hydrogen bonding (III) since the OH band




(III)

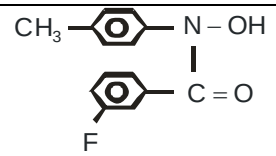
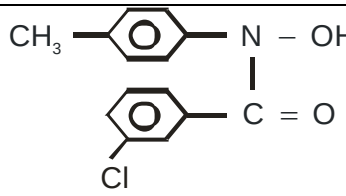
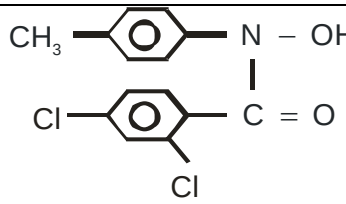
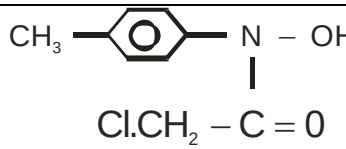
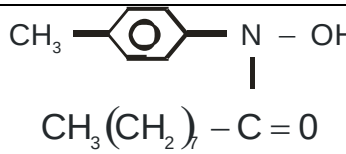
In shifted to lower frequencies is broad and is not displaced on dilution.

**C=O band:** This band appears in the region 1640 – 1580 $cm^{-1}$ (Table 1). The displacement of the band to lower frequencies/further confirms the formation of intramolecular hydrogen bond.

**N-O band:** In oximes, this band appears around 950 $cm^{-1}$. In N-arylhydroxylamines, this band appears around 928 $cm^{-1}$ (15). In the hydroxamic acids examined here, the absorption due to N – O stretching vibrations occurs in the range of 900 – 960 $cm^{-1}$ (Table 1).

**C – N Band:** The weak band observed near 1340 ± 20 $cm^{-1}$ in some of the spectra is probably due to C – N stretching vibrations. In aromatic tertiary amines, this band appears at 1360 – 1310 $cm^{-1}$ but its identification is difficult (7).

**Table : 1 Properties of N-Substituted Hydroxamic Acids.**

| S.No. | Hydoxamic Acid | Mol. Formula & Mol. Weight | M.P. $^0C$ | Yield % | Infra-red Spectra, nujol, $cm^{-1}$ | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | V (O- H) | V (C=O) | V (C–N) | V (N-O) |
| 1. | N-p-tolyl-m-fluorobenzo | | | | | | | |
| |  | $C_{14}H_{12}O_2NF$ 245 | 99 | 78 | - 3260 [C] | 1630 1620[C] | - 1358[C] | 940 928[C] |
| 2 | N-p-tolyl-m-chlorobenzo | | | | | | | |
| |  | $C_{14}H_{12}O_2NCl$ 261.5 | 99 | 67 | 311 3264[C] 3255[d] | 1640 1620[c] 1638[d] | - 1355[c] - | 938 928[c] - |
| 3. | N-p-tolyl-2, 4-dichlorobenzo | | | | | | | |
| |  | $C_{14}H_{11}O_2NCl_2$ 296 | 163 | 67 | 3120 3270 [c] | 1605 1620[c] | - 1359[c] | - 924[c] |
| 4. | N-p-tolylchoroaceto | | | | | | | |
| |  | $C_9H_{10}O_2NCl$ 199.5 | 123 | 58 | 3195 | 1638 | - | 940 |
| 5. | N-p-tolyl-pelargono | | | | | | | |
| |  | $C_{16}H_{25}O_2N$ 263 | 82 | 73 | 3180 | 1626 | 1328 | - |
| 6. | N-p-tolyldecane- | | | | | | | |

| | | | | | | | | |
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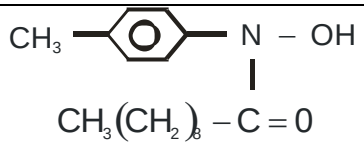
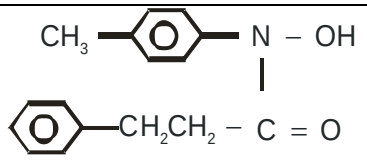
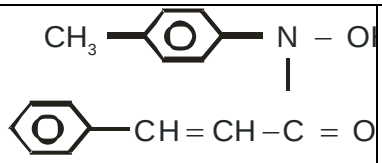
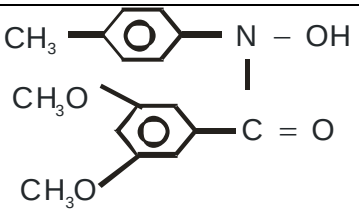
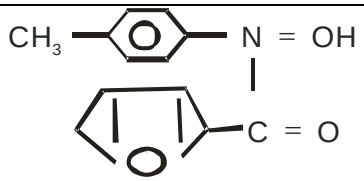
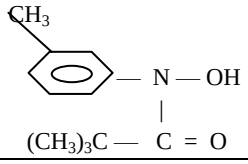
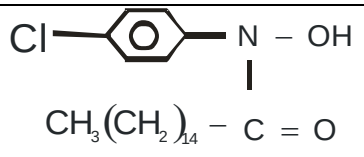
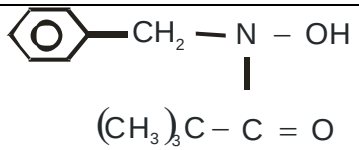
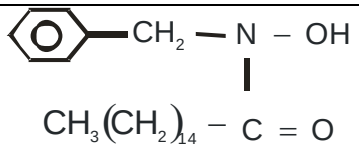
| |  | $C_{17}H_{27}O_2N$ 277 | 86 | 61 | 3164 | 1626 | 1338 | 940 |
| 7. | N-p-tolylhydrocinnamo | | | | | | | |
| |  | $C_{16}H_{17}O_2N$ 255 | 118 | 61 | 3182 | 1625 | 1345 | 942 |
| 8. | N-p-tolylcinnamo | | | | | | | |
| |  | $C_{16}H_{15}O_2N$ 253 | 156[a] | 78 | 3132s | 1634 | - | 950 |
| 9. | N-p-tolyl-3, 5-dimethoxy | | | | | | | |
| |  | $C_{16}H_{17}O_4N$ 287 | 130 | 88 | 3240 | 1580 | 1330 | 950 |
| 10. | N-p-tolyl-2-funo- | | | | | | | |
| |  | $C_{12}H_{11}O_3N$ 217 | 131[b] | 82 | 3130 | 1608 | - | 942 |
| 11. | N-m-tolyl-pivalo | | | | | | | |
| |  | $C_{12}H_{17}O_2N$ 105 | 105 | 68 | 3190 | 1596 | - | 938 |
| 12. | N-p-chloropenyl-palmito | | | | | | | |
| |  | $C_{20}H_{36}O_2NCl$ 357.5 | 100 | 90 | 3179 | 1622 | 1350 | - |
| 13. | N-benzyl-pivalo | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| |  | $C_{12}H_{17}O_2N$ 207 | 104 | 56 | 3155 | 1583 | 1350 | 938 |
| 14. | N-benzyl-palmito | | | | | | | |
| |  | $C_{23}H_{39}O_2N$ 361.5 | 94 | 55 | 3172 3200[d] | 1602 1640[d] | 1366 1370[d] | 930 |

Abbreviations :
a. Reported 159$^0$C , Tandon, S. G. ; Bhattacharya, S.C.; J. Chem. Engg. Data, 7,553 (1962)
b. Reported 142$^0$ C, ibid.
c. Spectra in Chloroform.
d. Spectra in Carbon Tetra chloride.

**Acknowledgement :**

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