

## QUANTITATIVE TREATMENT OF HSAB PRINCIPLE IN MOLECULAR INTER-ACTIONS BETWEEN 4-NITROQUINOLINE-1-OXIDES AND SOME n-DONORS

Ranjana Shukla

Professor, Department of Chemistry, Babu Banarshi Das National Institute of Technology and Management,  
Lucknow, Uttar Pradesh, India

### ABSTRACT

4-Nitroquinoline-1-oxide (4-NQO) is a carcinogenic compound. In this paper 4-Nitroquinoline-1-oxide forms molecular complexes with n-donors. A theoretical attempt has been made to explore the side of interaction and the role of 4-nitroquinoline-1-oxide or its related derivatives in the charge transfer complexation processes involving n-donors based on Klopman's quantitative treatment of the HSAB principle.

**KEYWORDS:** 4-NQO, 4-HAQO, Ac-4-HAQO, (Ac)<sub>2</sub>-4-HAQO, 4-AQO, N-Donors (Pyridine, Aniline, DMA, Adenine, Guanine, Uracil, Thymine, Cytosine, Ph<sub>3</sub>N, Ph<sub>3</sub>P, Ph<sub>3</sub>As, Ph<sub>3</sub>Sb) Charge Transfer Complexation, Cancer, Quantitative Treatment Of HSAB Principle

---

### Article History

Received: 02 May 2019 / Revised: 21 May 2019 / Accepted: 28 May 2019

---

### INTRODUCTION

According to Klopman's<sup>1</sup> quantitative treatment of HSAB principle, softness values of 4-nitroquinoline-1-oxides, n-donors have been calculated and equilibrium constants of these charge transfer complexes have been established in terms of "matching constant" ( $\Delta E_{nm}^\ddagger$ ) as introduced by Singh *et al.*<sup>2</sup>. These values have been considered to explore the possibility and extent of charge transfer complexation on the basis of the fact that hard-hard interactions are recognized as charge transfer interactions.

### THEORETICAL

There have been enormous developments of HSAB principle introduced by Pearson.<sup>3</sup> Edward<sup>4</sup> proposed a four-parameter equation which was called an oxy-base scale to describe the stability of the compounds. According to the HSAB principle, hard acid reacts with a hard base, and soft acid reacts with a soft base. The hard-hard and soft-soft interactions did explain a wide range of chemical phenomena<sup>5-11</sup> qualitatively. Misono *et al.*<sup>12</sup> expressed the stability constants (log K) well for hard-hard and soft-soft complexes.

Klopman<sup>1</sup> has made a significant attempt to calculate softness values of various acids ( $E_n^\ddagger$ ) and bases ( $E_m^\ddagger$ ) taking the role of reactants as well as a solvent into consideration. The softness values of acid and base ions of both types of interactions and that of intermediate reactions were calculated with the help of the following equations:

$$\begin{aligned}
 & x_r (c_r^m)^2 \\
 E_m^\ddagger &= IP_m - a^2 (IP_m - EA_M) - \left\langle \frac{1}{\varepsilon} \right\rangle \\
 & R_r \\
 & [q_r + 2b^2 x_r (c_r^m)^2] \tag{1}
 \end{aligned}$$

$$\begin{aligned}
 & X_s (c_s^n)^2 \\
 E_m^\ddagger &= IP_n b^2 (IP_n - EA_n) - \left\langle \frac{1}{\varepsilon} \right\rangle \\
 & R_r \\
 & [q_s + 2b^2 x_s (c_s^n)^2] \tag{2}
 \end{aligned}$$

Where  $E_m^\ddagger$  = softness of a base,  $E_n^\ddagger$  = softness of acid,

IP = ionization potential of atom,

EA = electron affinity,  $\varepsilon$  = dielectric constant,

R = radius of the atom whose softness is to be calculated,

q = charge on the atom,  $x = q - (q-1)\sqrt{K}$  and  $K = 0.75$

A hard base ( nucleophile) is characterized by a low value of the energy of the occupied frontier orbital and a soft base by a higher value. A hard acid, on the contrary, is characterized by a higher value of the energy of the empty frontier orbital. The values of  $a^2$  and  $b^2$  depend on the nature of the reaction. When a complete charge transfer occurs (frontier controlled reaction)

$$a^2 = b^2 = 1/2$$

and when no charge transfer occurs (charge controlled reactions).

$$b^2 = 0, a^2 = 1.$$

For an intermediate situation,

$$A^2 = 3/4 \text{ and } b^2 = 1/4$$

Klopman<sup>1</sup> classified various acids and bases into hard, soft and borderline bases on  $E_m^\ddagger$  and  $E_n^\ddagger$  values and sequence of the softness of acids and bases suggested by Persons<sup>3</sup> on qualitative bases have been found in close agreement with these values.

Recently, Sahai and Kushwaha<sup>13,14</sup> have introduced a more convenient and accurate method in modification Singh et al.<sup>2</sup> method, considering the effect of shielding due to the partial charge of developed on coordinating atoms in the calculation of effective nuclear charge and its contribution towards the effective retail of coordinating atoms. The values of  $E_m^\ddagger$  and  $\Delta E_{nm}^\ddagger$  so calculated for a series of substituted phenoxyacetic acid have shown good correlation (with correlation coefficient r, greater

than 0.60) with Hammett substituent constant<sup>15</sup> ( $\sigma$ ).

### IONIZATION PITENTIAL (IP), ELECTRON AFFINITY (EA) SR AND PARTIAL CHARGE (Q)

Dewar and Martia<sup>16</sup> gave the following relation for calculation the ionization potential.

$$W = a + b.q + cq^2 \quad (3)$$

Where W = ionization potential,

Q = valence state electronic charge derived from the hybridization state of an atom in the molecule, a, b & c are the parameters derived from the electron affinity (EA), Its and 2nd ionization potential of the individual atom.

These values have been calculated as reported in the literature<sup>3,13,14</sup> and thereafter the values of EA and IP. The partial charge has been calculated using Sanderson's approach.<sup>17,18</sup> The values of stability ratios (SR) of the molecules have been calculated from the atomic stability ratios<sup>17,18</sup> and then using Sanderson's equation,

$$\text{Partial Charge} = \frac{\text{SR of molecule} - \text{SR of the atom}}{2.08\sqrt{\text{SR of the atom}}} \quad (4)$$

The values of partial charges have been calculated. Adding these values to the total electronic charges of orbital energy of the atoms, their EA and IP values and thereafter the values of orbital energy (OE) have been calculated. These values have been reported in Tables 1 and 2. The values of RS are used to be  $r + 0.82$  (Pauling' TABLE 1)

**Table 1: Calculated Values of SR, Q, EA, IP and OE for Various Bases**

Compound	Abbreviated Name	SR	-Q	EA (Ev)	IP (Ev)	OE (Ev)
C <sub>5</sub> H <sub>5</sub> N	Py	3.736	0.172	12.224	26.802	15.868
C <sub>6</sub> H <sub>7</sub> N	Aniline	3.713	0.177	20.163	26.727	21.804
C <sub>8</sub> H <sub>11</sub> N	DMA	3.687	0.182	12.086	26.634	15.724
C <sub>5</sub> H <sub>5</sub> N <sub>5</sub>	Ad	3.922	0.129	12.794	27.509	16.472
C <sub>5</sub> H <sub>4</sub> N <sub>5</sub> O (N-donor)	Gua	4.0237	0.107	13.088	27.849	16.779
C <sub>5</sub> H <sub>4</sub> N <sub>5</sub> O (O-donor)	Gua	4.0237	0.251	7.959	29.876	13.438
C <sub>4</sub> H <sub>4</sub> N <sub>2</sub> O <sub>2</sub> (N-donor)	Ura	4.022	0.104	13.128	20.495	16.970
C <sub>4</sub> H <sub>4</sub> N <sub>2</sub> O <sub>2</sub> (O-donor)	Ura	4.022	0.251	7.970	20.502	11.103
C <sub>5</sub> H <sub>6</sub> N <sub>2</sub> O <sub>2</sub> (N-donor)	Thym	3.938	0.125	12.841	27.548	16.518
C <sub>5</sub> H <sub>6</sub> N <sub>2</sub> O <sub>2</sub> (O-donor)	Thym	3.938	0.268	7.565	29.511	13.052
C <sub>4</sub> H <sub>5</sub> N <sub>3</sub> O (N-donor)	Cyto	3.938	0.120	12.913	27.634	16.593
C <sub>4</sub> H <sub>5</sub> N <sub>3</sub> O (O-donor)	Cyto	3.938	0.270	7.529	29.476	13.016
C <sub>18</sub> H <sub>15</sub> N (N-donor)	Ph <sub>3</sub> N	3.701	0.179	12.132	26.690	15.771
C <sub>18</sub> H <sub>15</sub> P (P-donor)	Ph <sub>3</sub> P	4.010	-0.176	-51.403	-42.366	-49.144
C <sub>18</sub> H <sub>15</sub> As (As-donor)	Ph <sub>3</sub> As	3.685	0.055	-27.961	-19.139	-25.756
C <sub>18</sub> H <sub>15</sub> Sb (Sb-donor)	Ph <sub>3</sub> Sb	3.669	-0.078	-25.027	-17.181	-23.065

**Table 2: Calculated Values of SR, Q, EA, IP and OE for 4-Nitroquinoline-1-Oxide and its Related Derivatives**

Compound	Abbreviated Name	SR	-Q	EA (Ev)	IP (Ev)	OE (Ev)
C <sub>9</sub> H <sub>6</sub> N <sub>2</sub> O <sub>3</sub> (1)	4-NQO	3.965	0.119	12.922	27.645	16.603
C <sub>9</sub> H <sub>6</sub> N <sub>2</sub> O <sub>3</sub> (2)	4-NQO	3.965	0.263	7.582	29.629	13.094
C <sub>9</sub> H <sub>8</sub> N <sub>2</sub> O <sub>2</sub> (1)	4-HAQO	3.872	0.140	12.642	27.308	16.309
C <sub>9</sub> H <sub>8</sub> N <sub>2</sub> O <sub>2</sub> (2)	4-HAQO	3.872	0.282	7.249	29.219	12.742
C <sub>11</sub> H <sub>10</sub> NO <sub>3</sub> (1)	Ac-4-HAQO	3.862	0.143	12.611	27.270	16.276
C <sub>11</sub> H <sub>10</sub> NO <sub>3</sub> (2)	Ac-4-HAQO	3.862	0.284	7.209	29.182	12.702
C <sub>13</sub> H <sub>12</sub> N <sub>2</sub> O <sub>4</sub> (1)	(AC) <sub>2</sub> -4-HAQO	3.892	0.136	12.702	27.379	16.371
C <sub>9</sub> H <sub>8</sub> N <sub>2</sub> O (1)	4-AQO	3.815	0.153	12.471	27.100	16.128
C <sub>9</sub> H <sub>8</sub> N <sub>2</sub> O (2)	4-AQO	3.815	0.294	5.978	28.964	11.724

- Calculated with respect to the nitrogen atom.
- Calculated with respect to an oxygen atom.

radil). The Pauling's radil of the coordination atoms have been used in the calculation of desolvation energy (DE).

#### Calculation of $E_M^\ddagger$ , $E_N^\ddagger$ and $\Delta E_{nm}^\ddagger$

Using Eqns. (1) and (2), the values of  $E_m^\ddagger$  and  $E_n^\ddagger$  for bases, and 4-NQO and its related derivatives in various solvents of varying dielectric constant ( $\epsilon$ ) have been calculated (Tables 3 to 4)

based on the values of EA, IP, SR and q, the matching of Lewis acids and bases on the basis of their softness has been made as it has been done by Singh *et al.*<sup>2</sup> A better match of hard-hard or soft-soft interaction can be expected to form a higher value of  $\Delta E_{nm}^\ddagger$  expressed by the following relation:

$$\text{Matching constant } (\Delta E_{nm}^\ddagger) = |E_n^\ddagger - E_m^\ddagger| \quad (5)$$

These values have been reported in Tables 5 to 7.

## RESULTS AND DISCUSSIONS

### The Partial Charge and SR Values

It is evident from Table 1 that partial negative charge (-q = electronic charger) on N atom is high for any alkyl

**Table 3: Calculated Values<sup>a</sup> of dE and - E<sup>‡</sup><sub>M</sub> Values for Bases of Different Solvents**

Abbreviated Name of Compound	Dioxane	Benzene	Toluene	Carbon Tetra Chloride	Chloroform	Dimethyl Ether	Pyridine	Acetone	Ethyl Alcohol	Methyl Alcohol	Acetonitrile
	ε=2.209	ε=2.284	ε=2.379	ε=4.520	ε=4.806	ε=5.02	ε=12.3	ε=20.7	ε=24.3	ε=32.6	ε=37.5
Py	0.177 (15.691)	0.182 (15.686)	0.187 (15.681)	0.195 (15.673)	0.256 (15.612)	0.259 (15.609)	0.297 (15.571)	0.307 (15.561)	0.310 (15.558)	0.313 (15.555)	0.314 (15.554)
Aniline	0.161 (21.643)	0.165 (21.639)	0.170 (21.634)	0.177 (21.627)	0.232 (21.572)	0.235 (21.569)	0.270 (21.534)	0.279 (21.525)	0.281 (21.523)	0.284 (21.520)	0.286 (21.518)
DMA	0.157 (15.567)	0.162 (15.562)	0.167 (15.557)	0.173 (15.551)	0.228 (15.496)	0.230 (15.494)	0.264 (15.460)	0.274 (15.450)	0.276 (15.448)	0.279 (15.445)	0.280 (15.444)
Ad	0.249 (16.223)	0.217 (16.255)	0.224 (15.248)	0.233 (16.239)	0.306 (16.166)	0.310 (16.162)	0.355 (16.117)	0.368 (16.104)	0.371 (16.101)	0.375 (16.097)	0.376 (16.096)
Gua(N-donor)	0.229 (16.550)	0.235 (16.544)	0.242 (16.537)	0.252 (16.527)	0.331 (16.448)	0.335 (16.444)	0.384 (16.395)	0.398 (16.381)	0.401 (16.378)	0.405 (16.374)	0.407 (16.372)
Gua(O-donor)	0.137 (13.301)	0.140 (13.298)	0.145 (13.293)	0.151 (13.287)	0.198 (13.240)	0.200 (13.238)	0.229 (13.209)	0.238 (13.200)	0.239 (13.199)	0.242 (13.196)	0.243 (13.195)
Ura (N-donor)	0.214 (16.756)	0.220 (16.750)	0.227 (16.743)	0.236 (16.734)	0.310 (16.660)	0.314 (16.656)	0.360 (16.610)	0.373 (16.597)	0.376 (16.594)	0.380 (16.590)	0.381 (16.589)
Ura (O-donor)	0.137 (10.966)	0.140 (10.963)	0.145 (10.958)	0.151 (10.952)	0.198 (10.905)	0.200 (10.903)	0.229 (10.874)	0.238 (10.865)	0.239 (10.864)	0.242 (10.861)	0.243 (10.860)
Thym(N-donor)	0.199 (16.319)	0.204 (16.314)	0.210 (16.308)	0.219 (16.299)	0.288 (16.230)	0.291 (16.227)	0.338 (16.184)	0.346 (16.172)	0.348 (16.170)	0.352 (16.166)	0.354 (16.164)
Thym(O-donor)	0.121 (12.930)	0.125 (12.926)	0.129 (12.922)	0.134 (12.917)	0.176 (12.875)	0.178 (12.873)	0.204 (12.847)	0.211 (12.840)	0.213 (12.838)	0.215 (12.836)	0.216 (12.835)
Cyto(N-donor)	0.218 (16.375)	0.224 (16.369)	0.231 (16.362)	0.241 (16.352)	0.316 (16.277)	0.319 (16.274)	0.366 (16.227)	0.379 (16.214)	0.382 (16.211)	0.387 (16.206)	0.388 (16.205)
Cyto(O-donor)	0.120 (12.896)	0.123 (12.893)	0.127 (12.889)	0.132 (12.884)	0.173 (12.843)	0.175 (12.841)	0.201 (12.815)	0.208 (12.808)	0.210 (12.806)	0.211 (12.804)	0.213 (12.803)
	ε=2.209	ε=2.284	ε=2.379	ε=4.520	ε=4.806	ε=5.02	ε=12.3	ε=20.7	ε=24.3	ε=32.6	ε=37.5
Ph <sub>3</sub> N	0.159 (15.612)	0.164 (15.607)	0.169 (15.602)	0.176 (15.593)	0.231 (15.540)	0.233 (15.538)	0.267 (15.504)	0.277 (15.494)	0.279 (15.492)	0.282 (15.489)	0.283 (15.488)
Ph <sub>3</sub> P	0.025 (-49.169)	0.025 (-49.169)	0.026 (-49.170)	0.027 (-49.171)	0.036 (-49.180)	0.036 (-49.180)	0.042 (-49.186)	0.043 (-49.187)	0.043 (-49.187)	0.044 (-49.188)	0.044 (-49.188)
Ph <sub>3</sub> As	0.145 (-25.901)	0.149 (-25.905)	0.154 (-25.910)	0.160 (-25.916)	0.210 (-25.966)	0.213 (-25.969)	0.244 (-25.000)	0.253 (-25.009)	0.255 (-25.010)	0.257 (-25.013)	0.259 (-25.015)
Ph <sub>3</sub> Sb	0.079 (-23.144)	0.081 (-23.146)	0.084 (-23.149)	0.087 (-23.152)	0.114 (-23.179)	0.115 (-23.180)	0.132 (-23.197)	0.137 (-23.202)	0.138 (-23.203)	0.139 (-23.205)	0.140 (-23.205)

The value in the parentheses are due to - E<sup>‡</sup><sub>m</sub>

**Table 4: Calculated Values<sup>a</sup> of De and - E<sup>‡</sup><sub>N</sub> for 4-Nitroquinoline Oxide and its Related Derivatives in Different Solvents**

Abbreviated Name of Compound	Dioxane	Benzene	Toluene	Carbon Tetra Chloride	Chloroform	Dimethyl Ether	Pyridine	Acetone	Ethyl Alcohol	Methyl Alcohol	Acetonitrile
	ε=2.209	ε=2.284	ε=2.379	ε=4.520	ε=4.806	ε=5.02	ε=12.3	ε=20.7	ε=24.3	ε=32.6	ε=37.5
4-NQO (1)	0.219 (16.384)	0.225 (16.378)	0.232 (16.371)	0.241 (16.362)	0.317 (16.286)	0.320 (16.283)	0.368 (16.235)	0.381 (16.222)	0.384 (16.219)	0.388 (16.215)	0.389 (16.214)
4-NQO (2)	0.105 (12.989)	0.108 (12.986)	0.112 (12.982)	0.116 (12.978)	0.153 (12.941)	0.154 (12.939)	0.177 (12.917)	0.183 (12.911)	0.185 (12.909)	0.187 (12.907)	0.188 (12.906)
4-HAQO (1)	0.202 (16.107)	0.207 (16.102)	0.213 (16.096)	0.222 (16.087)	0.292 (16.017)	0.295 (16.014)	0.338 (15.970)	0.350 (15.959)	0.353 (15.956)	0.357 (15.952)	0.358 (15.951)
4-HAQO (2)	0.091 (12.651)	0.093 (12.649)	0.096 (12.646)	0.099 (12.642)	0.131 (12.611)	0.132 (12.609)	0.152 (12.590)	0.158 (12.584)	0.159 (12.583)	0.161 (12.581)	0.161 (12.580)
Ac-4-HAQO (1)	0.199 (16.076)	0.205 (16.071)	0.220 (16.056)	0.289 (15.987)	0.293 (15.983)	0.336 (15.940)	0.335 (15.940)	0.347 (15.928)	0.350 (15.926)	0.354 (15.922)	0.356 (15.920)
Ac-4-HAQO (2)	0.089 (12.613)	0.092 (12.610)	0.094 (12.608)	0.098 (12.604)	0.129 (12.573)	0.131 (12.571)	0.149 (12.552)	0.155 (12.547)	0.156 (12.546)	0.158 (12.544)	0.159 (12.543)
(Ac) <sub>2</sub> -4-HAQO(1)	0.206 (16.165)	0.211 (16.160)	0.218 (16.153)	0.226 (16.145)	0.297 (16.074)	0.301 (16.070)	0.345 (16.026)	0.357 (16.013)	0.360 (16.010)	0.364 (16.007)	0.365 (16.006)
	ε=2.209	ε=2.284	ε=2.379	ε=4.520	ε=4.806	ε=5.02	ε=12.3	ε=20.7	ε=24.3	ε=32.6	ε=37.5
4-AQO (1)	0.192 (15.936)	0.197 (15.931)	0.203 (15.925)	0.212 (15.916)	0.278 (15.850)	0.281 (15.847)	0.322 (15.806)	0.334 (15.794)	0.336 (15.792)	0.340 (15.788)	0.342 (15.786)
4-AQO (2)	0.082 (11.640)	0.084 (11.637)	0.087 (11.637)	0.090 (11.634)	0.118 (11.606)	0.119 (11.604)	0.137 (11.587)	0.142 (11.582)	0.143 (11.581)	0.145 (11.580)	0.145 (11.579)

- The values in the parentheses are due to - E<sup>‡</sup><sub>n</sub>

- Calculated with respect to a nitrogen atom.
- Calculated with respect to oxygen atom.

**Table 5: Calculated Values of  $\Delta E_{Nm}^{\ddagger}$  for 4-Nitroquinoline-1-Oxide and its Related Derivatives with Pyridine Complexes in Different Solvents**

Abbreviated Name of Compound	Dioxane	Benzene	Toluene	Carbon Tetra Chloride	Chloroform	Dimethyl Ether	Pyridine	Acetone	Ethyl Alcohol	Methyl Alcohol	Acetonitrile
	$\epsilon=2.209$	$\epsilon=2.284$	$\epsilon=2.379$	$\epsilon=4.520$	$\epsilon=4.806$	$\epsilon=5.02$	$\epsilon=12.3$	$\epsilon=20.7$	$\epsilon=24.3$	$\epsilon=32.6$	$\epsilon=37.5$
4-NQO (1)	0.693	0.692	0.690	0.688	0.674	0.673	0.664	0.662	0.661	0.660	0.660
4-NQO (2)	2.702	2.700	2.698	2.695	2.671	2.670	2.654	2.650	2.649	2.648	2.647
4-HAQO (1)	0.416	0.416	0.415	0.414	0.405	0.405	0.399	0.398	0.398	0.397	0.397
4-HAQO (2)	3.040	3.038	3.035	3.031	3.001	3.000	2.981	2.976	2.975	2.273	2.273
Ac-4-HAQO (1)	0.385	0.384	0.383	0.382	0.374	0.374	0.369	0.368	0.367	0.367	0.367
Ac-4-HAQO (2)	3.079	3.076	3.073	3.070	3.039	3.038	3.019	3.014	3.013	3.011	3.010
(Ac) <sub>2</sub> -4-HAQO(1)	0.474	0.473	0.473	0.471	0.461	0.461	0.455	0.453	0.453	0.452	0.452
4-AQO (1)	0.245	0.244	0.244	0.243	0.238	0.238	0.234	0.233	0.233	0.233	0.233
4-AQO (2)	4.049	4.046	4.043	4.039	4.007	4.005	3.985	3.979	3.978	3.976	3.975

**Table 6: Calculated Values of  $\Delta E_{Nm}^{\ddagger}$  for 4-Nitroquinoline-1-Oxide and its Related Derivatives with Various Bases in Carbon Tetrachloride**

Abbreviated Name of Compound	4-NQO (1)	4-NQO (2)	4-HAQO (1)	4-HAQO (2)	Ac-4-HAQO (1)	Ac-4-HAQO (2)	(Ac) <sub>2</sub> -4-HAQO(1)	4-AQO (1)	4-AQO(2)
Py	0.688	2.695	0.414	3.031	0.382	3.070	0.471	0.243	4.039
Aniline	5.265	8.649	5.540	8.984	5.571	9.023	5.482	5.711	9.993
DMA	0.811	2.573	0.536	2.908	0.505	2.947	0.594	0.366	3.917
Ad	0.123	3.260	0.152	3.597	0.183	3.635	0.094	0.322	4.605
Gua (N-donor)	0.165	3.549	0.440	3.880	0.471	3.923	0.382	0.610	4.893
Gua (O-donor)	3.074	0.310	2.799	0.645	2.768	0.684	2.857	2.629	1.654
Ura (N-donor)	0.372	3.756	0.647	4.091	0.678	4.130	0.589	0.817	5.110
Ura (O-donor)	5.409	2.025	5.134	1.690	5.103	1.651	5.192	4.964	0.681
Thym (N-donor)	0.063	3.321	0.212	3.657	0.243	3.695	0.154	0.383	4.665
Thym (O-donor)	3.444	0.061	3.170	0.275	3.138	0.313	3.227	2.999	1.283
Cyto (N-donor)	1.292	3.745	0.266	3.710	0.297	3.749	0.208	0.436	4.719
Cyto (O-donor)	3.478	0.094	3.205	0.242	3.172	0.280	3.261	3.032	1.250
Ph <sub>3</sub> N	0.766	2.618	0.492	2.953	0.460	2.992	0.549	0.321	3.962
Ph <sub>3</sub> p	65.533	62.149	65.258	61.813	65.227	61.775	65.316	65.087	60.805
Ph <sub>3</sub> As	42.278	38.894	42.003	38.558	41.972	38.520	42.061	41.833	37.550
Ph <sub>3</sub> Sb	39.514	36.130	39.239	35.794	39.208	35.756	39.296	39.068	34.786
Py	0.688	2.695	0.414	3.031	0.382	3.070	0.471	0.243	4.039
Aniline	5.265	8.649	5.540	8.984	5.571	9.023	5.482	5.711	9.993
DMA	0.811	2.573	0.536	2.908	0.505	2.947	0.594	0.366	3.917
Ad	0.123	3.260	0.152	3.597	0.183	3.635	0.094	0.322	4.605
Gua (N-donor)	0.165	3.549	0.440	3.880	0.471	3.923	0.382	0.610	4.893
Gua (O-donor)	3.074	0.310	2.799	0.645	2.768	0.684	2.857	2.629	1.654
Ura (N-donor)	0.372	3.756	0.647	4.091	0.678	4.130	0.589	0.817	5.110
Ura (O-donor)	5.409	2.025	5.134	1.690	5.103	1.651	5.192	4.964	0.681
Thym (N-donor)	0.063	3.321	0.212	3.657	0.243	3.695	0.154	0.383	4.665
Thym (O-donor)	3.444	0.061	3.170	0.275	3.138	0.313	3.227	2.999	1.283
Cyto (N-donor)	1.292	3.745	0.266	3.710	0.297	3.749	0.208	0.436	4.719
Cyto (O-donor)	3.478	0.094	3.205	0.242	3.172	0.280	3.261	3.032	1.250
Ph <sub>3</sub> N	0.766	2.618	0.492	2.953	0.460	2.992	0.549	0.321	3.962
Ph <sub>3</sub> p	65.533	62.149	65.258	61.813	65.227	61.775	65.316	65.087	60.805
Ph <sub>3</sub> As	42.278	38.894	42.003	38.558	41.972	38.520	42.061	41.833	37.550
Ph <sub>3</sub> Sb	39.514	36.130	39.239	35.794	39.208	35.756	39.296	39.068	34.786



- Calculated with respect to a nitrogen atom.
- Calculated with respect to an oxygen atom

**Table 7: Calculated Values of  $\Delta E_{Nm}^{\ddagger}$  for 4-Nitroquinoline-1-Oxide and its Related Derivatives with Various Bases in Chloroform**

Abbreviated Name of Compound	4-NQO (1)	4-NQO (2)	4-HAQO (1)	4-HAQO (2)	Ac-4-HAQO (1)	Ac-4-HAQO (2)	(Ac) <sub>2</sub> -4-HAQO(1)	4-AQO (1)	4= AQO(2)
Py	0.674	2.671	0.405	3.001	0.371	3.039	0.462	0.238	4.006
Aniline	5.286	8.631	5.555	8.961	5.589	8.999	5.498	5.722	9.966
DMA	0.790	2.555	0.521	2.885	0.487	2.923	0.578	0.354	3.890
Ad	0.120	3.225	0.149	3.555	0.183	3.593	0.092	0.316	4.560
Gua (N-donor)	0.162	3.507	0.431	3.837	0.465	3.875	0.374	0.598	4.842
Gua (O-donor)	3.046	0.299	2.777	0.629	2.743	0.667	2.834	2.610	1.634
Ura (N-donor)	0.374	3.719	0.643	4.049	0.677	4.087	0.586	0.810	5.054
Ura (O-donor)	5.381	2.036	5.112	1.706	5.078	1.668	5.169	4.945	0.701
Thym (N-donor)	0.056	3.289	0.213	3.619	0.247	3.657	0.156	0.380	4.624
Thym (O-donor)	3.411	0.066	3.142	0.264	3.108	0.302	3.199	2.975	1.269
Cyto (N-donor)	0.009	3.336	0.260	3.666	0.294	3.704	0.203	0.427	4.671
Cyto (O-donor)	3.443	0.098	3.174	0.232	3.140	0.270	3.231	3.007	1.237
Ph <sub>3</sub> N	0.746	2.599	0.477	2.929	0.443	0.033	0.534	0.310	3.934
Ph <sub>3</sub> P	65.466	62.121	65.197	61.791	65.163	61.753	65.254	65.030	60.786
Ph <sub>3</sub> As	42.252	38.907	41.983	38.577	41.949	38.539	42.040	41.816	37.572
Ph <sub>3</sub> Sb	39.465	36.120	39.196	35.790	39.162	35.752	39.253	39.029	34.785

- Calculated with respect to nitrogen atom.
- Calculated with respect to oxygen atom.

substituted base. The partial charge in bases decreases in the following order: N,N- dimethylaniline > aniline > pyridine.

The partial charge of N in adenine is more than that of N in guanine. This may be due to the fact that guanine contains an oxygen atom attached to the ring carbon atom that reduces the partial charge of N atom. Among pyrimidine bases, N of thymine has a more partial charge which is due to the presence of one methyl group attached directly to the ring. Further, the partial charge of cytosine is more than that of uracil because cytosine has one oxygen atom attached to the ring is less than uracil. Obviously, O-atom will decrease the partial charge of nitrogen to a considerable extent. The presence of oxygen atom in cytosine, thymine, and uracil decrease the partial charge on nitrogen atom which is indicated by its high partial charge compared to that of nitrogen. This decreases the donor capability of N-atom of cytosine, thymine, and uracil which may decrease the stability of charge transfer complexes of these molecules. Among triphenyl compounds, the partial charges on phosphorous and antimony are positive whereas on nitrogen and arsenic atoms are negative.

The partial negative charge and SR values of acceptors are listed in Table 2. From this table, it is evident that partial charge of N-atom in 4-NQO and its related derivatives are in the order of

$$4\text{-NQO} < \text{diacetyl ester of } 4\text{-HAQO} < 4\text{-HAQO}$$

< monoacetyl ester of 4-HAQO <4-AQO

Lower the partial charge on N-atom of 4-NQO and its related derivatives, lesser would be the acceptor nature of its  $\pi^*$ -orbital of nitrogen in the 4-nitro group of 4-NQO. Thus, the  $\pi^*$ -electron acceptor property increases along with the series mentioned above. In brief, higher the partial charge on N-atom, higher would be the possibility of the formation of the charge transfer complexes through  $\pi^*$ -orbital of nitrogen. Similar conclusions can be drawn considering O as acceptor atom in these molecules.

### Effect of Solvent on $E_m^\ddagger$ Values

The behavior of bases in various solvents (dioxane, benzene, toluene,  $\text{CCl}_4$ ,  $\text{CHCl}_3$ , diethyl ether, pyridine, acetone,  $\text{C}_2\text{H}_5\text{OH}$ ,  $\text{CH}_3\text{OH}$ , acetonitrile) has been shown in terms of quantitative softness values,  $E_m^\ddagger$  (Table 3). It is evident from this table that the softness increases in parallel with increases in the dielectric constant of the medium. Similar observations have also been confirmed from the softness values of bases (Table 3) where the change in solvent results in an appreciable change in their  $E_m^\ddagger$  values. The change in the values on this account is so pronounced that a soft base can act as a hard base and vice-versa. For example, the softness values of pyridine in dioxane, benzene, toluene, carbon tetrachloride,

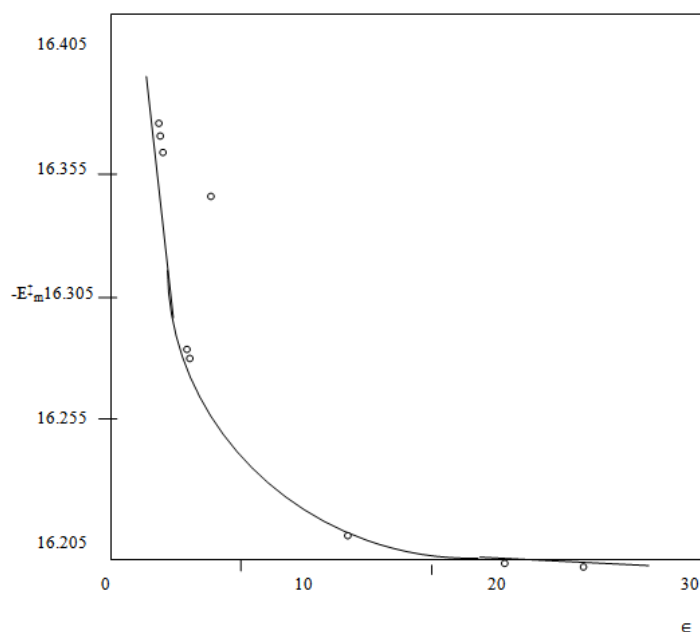
15.686, -15.681, -15.673, -15.612,

15.609, -15.571, -15.561, -15.558, -15.555 and -15.554,

Respectively. These values are in the order of decreasing hardness. In general, the behavior of the bases in solvents having high dielectric constant is softer. The order of dielectric constants of various solvents is: dioxane < benzene < toluene < carbon tetrachloride < chloroform < dimethyl ether < pyridine < acetone < ethyl alcohol < methyl alcohol < acetonitrile.

The softness for n-donor increases with increase in the dielectric constant of the medium (Table 3) following the same trend as stated above. Since the charge transfer interactions are characterized as hard-hard acid-base interactions, therefore, it seems from the above discussion that the charge transfer may best be favorable in the medium of low dielectric constant. The correlation between  $E_m^\ddagger$  and  $\epsilon$  has been predicted in Figure 1. The Figure 1 shows that softness increases on increasing the dielectric constant of the medium. Consequently, hardness decreases and hence better would be the possibility of the formation of charge transfer complexes in the medium of low dielectric constant.





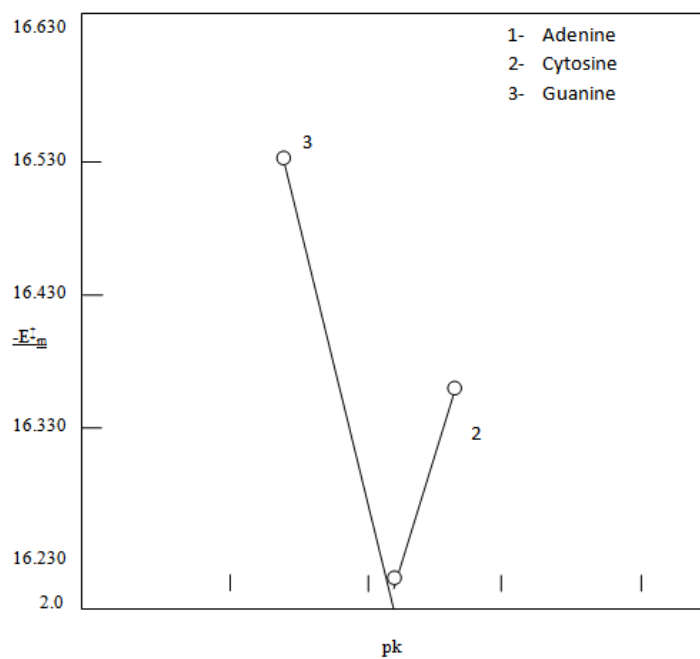
**Figure 1: Plot of  $E_M^{\ddagger}$  Vs  $\epsilon$  For for Cytosine**

The variation of the softness of donors their dissociation constant (pk) has been graphically represented in Figure 2.

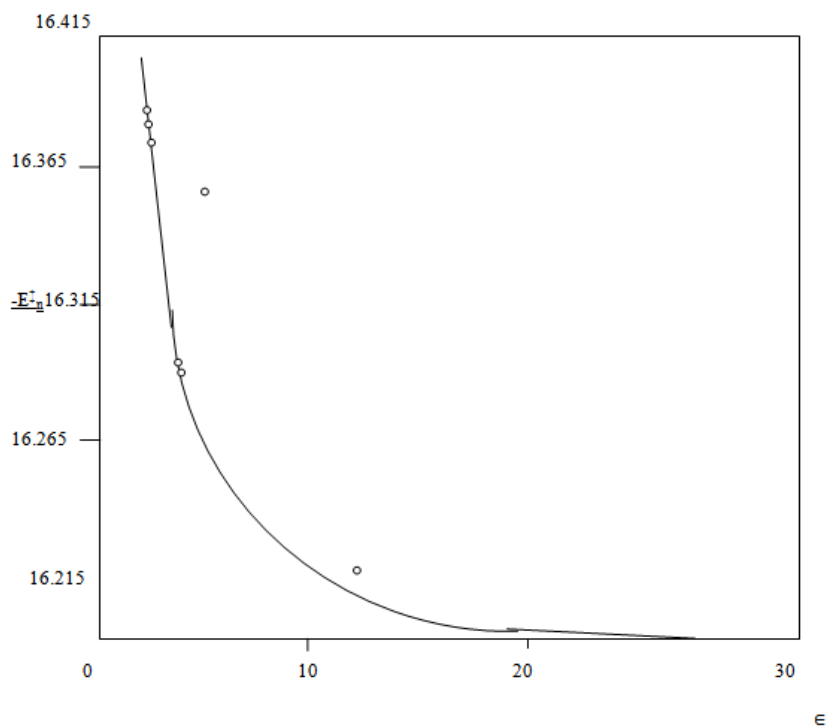
### Effect of Solvent on $E_n^{\ddagger}$ Value

The values of  $E_n^{\ddagger}$  in various solvents (Table 4) show that that the change of solvent affects the softness values 4-NQO and its related derivatives appreciably. For example, the softness value of 4-NQO in dioxane, benzene, toluene, carbon tetrachloride, chloroform, dimethyl ether, pyridine, acetone, ethyl alcohol, methyl alcohol, acetonitrile are: -16.384, -16.378, -16.371, -16.362, -16.286, -16.283, -16.235, -16.222, -16.219, -16.215, -16.214, respectively. These values are in the order of decreasing softness. The variation of  $E_n^{\ddagger}$  against  $\epsilon$  is shown in Figure 3. in general, the behavior of the Lewis acids in solvents having high dielectric constant is harder. From the above theoretical results, it may be anticipated that the charge acceptance prefer the medium of high dielectric constant and hence this general approximation may suggest scientists select the suitable medium for any reaction in the laboratory.

The electronic are also invariably in the formation of molecular complexes. Therefore, It seems to be



**Figure 2: Plot of PK  $E_M^+$  for Adenine, Guanine, and Cytosine in Carbon Tetra Chloride**



**Figure 3: Plot of  $E_n^+$  Vs  $\epsilon$  for 4-NQO**

fruitful to consider the effect of substituents on  $E_m^+$  and  $E_n^+$  values and hence on their stability. The effect of the substituent on the softness Value of an atom in the molecule is never so pronounced which may convert a soft base into a hard

base or vice-versa. But there is no doubt that the charge transfer interaction must be influenced by them.

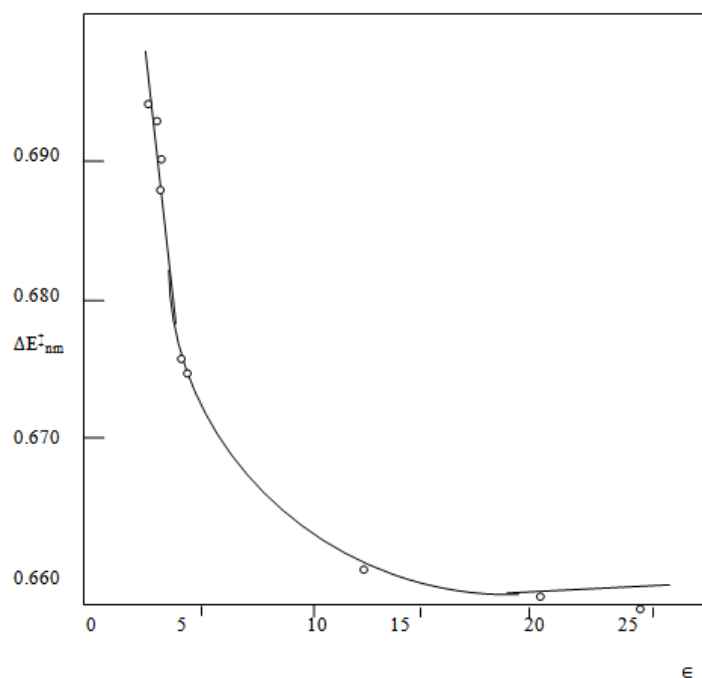
Within the framework of the molecules considered in the present investigation, it is, however, worth predicting that an electron releasing substituents increase the softness which thereby decreases the hardness of donor or acceptor. This makes the charge transfer complex interaction less favorable. On the other hand, if electron attracting groups are present they would favor the charge transfer reaction.

### Matching and Stability

It is evident from Tables 3 and 4 that the acceptors having lower values of  $E_n^\ddagger$  and donors having higher values of  $E_m^\ddagger$  are more soft with respect to the solvent considered. Hence, a better match of hard-hard or soft-soft interaction can be expected from a higher difference between  $E_n^\ddagger$  and  $E_m^\ddagger$  values. Thus in the form of an equation, it may be expressed as follows:

$$\text{Matching constant } (\Delta E_{nm}^\ddagger) = |E_n^\ddagger - E_m^\ddagger|.$$

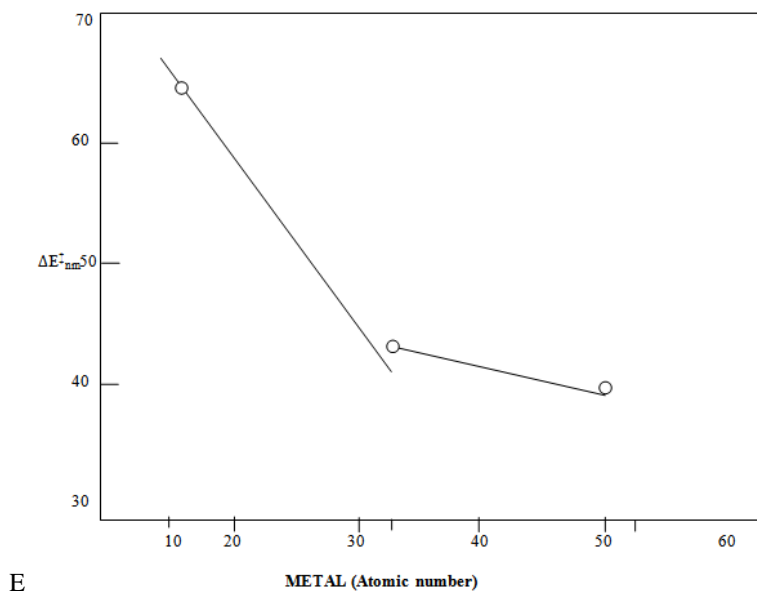
Hence, from this relation, the matching of a donor with acceptor can be established. This fact may be stated by taking an example of the interaction of pyridine with 4-NQO (N-acceptor) and 4-HAQQO (N-acceptor) in carbon tetrachloride (Table 5) where  $\Delta E_{nm}^\ddagger$  are found to be 0.688 and 0.414, respectively. Since the value in the former interaction is higher than the value in the latter interaction, better matching may be expected for the interaction of pyridine with 4-NQO (N-acceptor). Hence, with 4-NQO (N-acceptor) it may be anticipated that the value  $\Delta E_{nm}^\ddagger$  indicate better match in the former interaction, but this alone cannot explain the stability of these molecular complexes, because it depends upon a number of factors. The matching between other acceptor and donor in terms of  $\Delta E_{nm}^\ddagger$  has been expressed in Tables 5 to 7. The effect of solvent on  $\Delta E_{nm}^\ddagger$  for the interaction of 4-NQO and its related derivatives with pyridine has been shown in terms of  $\Delta E_{nm}^\ddagger$  in Table 5. A representative plot of  $\Delta E_{nm}^\ddagger$  versus  $\epsilon$  of the solvents for 4-NQO-pyridine interacting has been shown in Figure 4. It is clear from this figure that  $\Delta E_{nm}^\ddagger$  is also affected by the change in the dielectric constant of the medium. The general order of  $\Delta E_{nm}^\ddagger$  for the interaction of  $\text{Ph}_3\text{M}$  with 4-NQO and its related derivatives considered has been found to be:  $\text{P} > \text{As} > \text{Sb} > \text{N}$  (as central atoms in triphenyl compounds). It can be concluded that the values of  $\Delta E_{nm}^\ddagger$  also depends on the nature of the solvent in addition to the atomic of the central atom.



**Figure 4: Plot of  $\Delta E_{nm}^*$  Vs  $\epsilon$  for 4-NQO- Pyridine Complex**

A representative plot of  $\Delta E_{nm}^*$  versus the atomic number in  $\text{CCl}_4$  is shown in Figure 5. For 4-NQO and its related derivatives, a better matching has been observed (Table 5) in a solvent of low dielectric constant in determining the extent of donor capability of various bases considered. The pyridine base with electron attracting group has been found to be more effective while electron releasing group less. As is evident from the results reported in Table 5, the dielectric constant of the solvent influences the stability of charge transfer complexes between 4-NQO (N-acceptor) and its related derivatives with pyridine under investigation, it is seen that the increase in dielectric constant, decreases the magnitude of  $\Delta E_{nm}^*$  indicating that a solvent of low dielectric constant is better to carry out charge transfer interaction between donor and acceptor. Further the extent of donor capability for the formation of charge transfer complexes with any of the acceptor's increases in the order: Pyridine < N,N-dimethylaniline < aniline, because the same sequence is theoretically found for matching constant of these bases with 4-NQO (N-acceptor) and its related derivatives.

A few exceptional results are obtained for some systems like adenine -4-NQO (N-acceptor), and guanine - 4-NQO (N-acceptor). In these systems, the matching constant values are estimated to be 0.123 and 0.165, respectively (Table 6 and 7). This may be due to the presence of oxygen atom in guanine attached directly to



**Figure 5: Plot of  $\Delta E_{nm}^*$  for  $\text{Ph}_3\text{M-4-NQO I Ccl}_4$  Vs the Atomic Number of M (M=P, As, Sb)**

The ring. Matching constant for charge transfer complexes of uracil, thymine, cytosine, and 4-NQO (N-acceptor) follow the trend:

thymine < uracil < cytosine.

The high matching constant of cytosine partly is due to only one oxygen atom directly attached to the ring unlike that in uracil and thymine. The exceptionally less matching constant for thymine is expected due to the presence of an electron releasing methyl group. Almost a parallel conclusion can be drawn by considering 4-NQO as an O-acceptor.

In triphenyl compounds the value of  $\Delta E_{nm}^*$  follow the trend,

$\text{Ph}_3\text{N} < \text{Ph}_3\text{Sb} < \text{Ph}_3\text{As} < \text{Ph}_3\text{P}$ .

It is interesting to note that except triphenylamine, the matching constant is inversely proportional to the atomic numbers of the central atoms. This indicates that smaller the size of the central atom, better would be the possibility of hard-hard interaction. Thus better would be the possibility of charge transfer interaction.

## CONCLUSIONS

The high value of matching constant indicated that charge transfer complexation may be the mode of carcinogenic activity of 4-nitroquinoline-1-oxide and its related derivatives.

The biomolecules considered in the present investigation show potential affinity towards these carcinogens to produce charge transfer complexes of sufficient stability. This may influence the mobility and hence may create imbalance in the several biochemical and biophysical processes occurring in the organism. Certain processes may be accelerated whereas others get retarded or damaged. The accelerated process may stimulate the replication of cells in an uncontrolled manner which may cause malignant tumors.<sup>19,20</sup> Thus, theoretical derivation of matching constant may be considered to be a fruitful scale which

may predict the quantitative relationship between the (molecular/electronic) structure and biological activity of carcinogens. This work presented in this paper supports the charge transfer complexation mechanism as the possible mode of action of 4-nitroquinoline-1-oxide in the chemical initiation of cancer.

## REFERENCES

1. Klopman, G. *J. Am. Chem. Soc.* 1968, 90, 223.
2. Singh, P.P.; Srivastava, S.K.; Srivastava, A.K. *J. Inorg. Nucl. Chem.* 1980, 42, 521, 533.
3. Pearson, R.G., Ed., "Hard and Soft Acids and Bases." Dowden, Hutchinson and Ross. Inc., 1973, and references cited therein.
4. Edwards, D.O. *J. Am. Chem. Soc.* 1954, 76, 1540.
5. Ahrland, S. "Structure and Bonding" 1966, 1, 249.
6. Jorgenson, C.K. *Inorg. Chem.* 1964, 3, 1201.
7. Basolo, F.; Burmeister, J. *Inorg. Chem.* 1964, 3, 1587.
8. Wayland, B.B.; Gold, R.H. *Inorg. Chem.* 1966, 5, 154
9. Mitchell, P.C.H. *Quart. Rev. (London)* 1966, 20, 103.
10. Schmidts, H.H. *J. Am. Chem. Soc.* 1965, 87, 2522.
11. Jorgenson, C.K. *Structure and Bonding* 1966, 1, 234.
12. Misono, M.; Ochiai, P.; Saito, Y.; Yoneda, Y. *J. Inorg. Nucl. Chem.* 1967, 29, 2685.
13. Kushwaha, S.S.S. "Studies on Structure Activity Correlation of Phenoxyacetic acid Herbicides and their Complexation with Some Metal Ions of Biological Interest," Ph.D. Thesis, Kanpur University, Kanpur 1981
14. Sahai, R.; Kushwaha, S.S.S. *Indian J. Chem.* 1983, 22, 512.
15. Jaffe, H.H. *Chem. Rev.* 1953, 53, 191.
16. Dewar, M.J.S.; Martia, T. *J. Am. Chem. Soc.* 1968, 91, 796.
17. Sanderson, R.T. "Chemical Bond and Bond Energy," Academic press, London and New York, 1971. pp, 19-20 and 57.
18. Sanderson, R.T. "Chemical Periodicity," Reinhold Publishing Co., New York, 1960.
19. Harris, R.J.C. "Cancer," Allen and Unwin, London, 1970.
20. Ambrose, E.J.; Roe, F.J.C. "The Biology of Cancer." Von Nostrand, London, 1966.