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Mechanism of Formation of Schiff Base Complexes. Part. I. Reaction of Ni(bis-Salicylaldehyde) with Primary Amines

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A kinetic study on the reaction between Ni(bis-salicylaldehyde) and primary amines is reported. Two stages were observed having the same kinetic law:

$$k_{obs} = a[RNH_2][CH_3O^-]/\{b + c[CH_3O^-]\}$$

which shows the occurrence of basic catalysis during the course of the reaction. Two alternative mechanisms, consistent with the kinetic law, are proposed and discussed for each stage. A comparison with analogous reactions of uncoordinated aldehydes is also included in the paper and the different kind of reactivity towards basic catalysis is also interpreted.

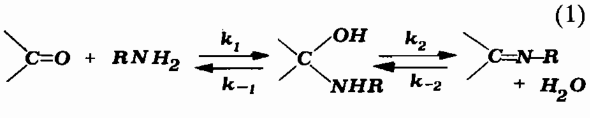
Either for free or for nickel coordinated aldehydes the second order rate values, k_0 (sec^{-1} M^{-1}), do not parallel the proton basicity of RNH_2. However a linear relationship between logk_0 and the free energies of dissociation of the corresponding addition compounds $RNH_2 \cdot B(CH_3)_3$ is observed, showing that similar structural effects are operating in the correlated processes.

Introduction

A large fraction of biochemical reactions involves the >C=O and the >C=N–groups. There is now evidence in the literature, for example, suggesting the involvement of azomethine intermediates in several enzimatic processes[1] and this has focused attention on the mechanism of Schiff base formation and hydrolysis in solution.

Many data, so far collected, support the following reaction path[2]:

(1)



and a transition from rate determining dehydration, at neutral pH, to rate determining amine attack, under acidic conditions, was also postulated for oxime and semicarbazone formation.[3,4]

Metal–Schiff base complexes have been very well known for long time. Preparation methods include reactions of Schiff bases with metal ions or reactions of salicylaldehyde complexes with primary amines[5].

Much of the chemistry regarding these compounds emphasized particulary the recognition of their structures principally by measurements of dipole and magnetic moments, X-ray diffraction and recently NMR investigations. The most significant stereochemical patterns so far examined were i) the variation of stereochemistry as a function of metal ions in a series of complexes with a constant ligand structure and ii) the variation of stereochemistry as a function of the ligand structure in a series of complexes with the same metal ion[6].

Factors affecting the change of the structure from planar to tetrahedral are now well recognized; however, the effect of the coordinated metal in promoting Schiff base formation was, in some way, neglected.

Therefore it seemed to us very interesting to begin a systematic investigation on the reactions between $M(SA)_2$ complexes (M = bivalent ion; SA^- = salicylaldehydato ion) and primary amines with the particular aim of elucidating the role of the metal in these reactions.

This paper reports our results about the reaction of $Ni(SA)_2$ with several amines (RNH_2) such as ethylamine, n-butylamine, sec-butylamine, t-butylamine and cyclohexylamine in methanol at 25° C:

$$Ni(SA)_2 + 2\,RNH_2 \rightarrow Ni(SN)_2 + 2\,H_2O \qquad (2)$$

(SN^- = salicylaldiminato ion)

A comparison, of course, will also be made with analogous reactions of uncoordinated aldehydes, also included in this work.

Studies concerning other $M(SA)_2$ complexes will be published in forthcoming papers.

Experimental

$Ni(SA)_2$ and $Ni(SN)_2$ complexes (SA^- = salicylaldehydato ion; SN^- = salicylaldiminato ion) were prepared as reported in the literature[7–9]. All amines were distilled before use and stored under argon in the dark.

Kinetics

Separate solutions of the complex and reagents were prepared in methanol. The concentration of CH_3O^- was determined by standard titrimetric methods. The ionic strength was maintained constant at the value of 0.15M. The reagent solutions were separately brought to reaction temperature, then mixed in the thermostated cell of an Optica CF4R double beam recording spectrophotometer and the kinetics followed by observing absorption changes in the U.V. region of the spectrum. Any single kinetic run was carried out with concentrations of amines large enough to provide pseudo-first-order conditions. Pseudo-first-order rate constants, k_{obs} (sec^{-1}), were calculated from slopes of linear plots of $\log(A_\infty - A_t)$ *vs.* time (A is the optical density).

Results

Kinetics of Reactions of Benzaldehyde with Amines

These reactions proceed through only one stage. Final spectra resemble those of authentic samples of benzaldimines, indipendently prepared. Table I lists kinetic rate constants, k'_{obs}(sec^{-1}), for reactions of benzaldehyde with amines, experimentally determined under various conditions.

Plots of k'_{obs}(sec^{-1}) values against the amine concentration are linear and no dependence of the rate on the added CH_3O^- was observed. Values of second order rate constants, k'_o (sec^{-1} M^{-1}), determined as slopes of linear plots, pertaining to these reactions, are included in Table I.

Kinetics of Reactions of Salicylaldehyde with Amines

The course of these reactions was followed spectrophotometrically in the U.V. region and two isosbestic points were always observed; furthermore only one stage was detected.

Experimental rate constants, k''_{obs}(sec^{-1}), for reactions of salicylaldehyde (SAH) with amines are reported in Table II and their plots against the concentration of amines are linear. The slopes of these plots, k_o'' ($sec^{-1}M^{-1}$), are included in Table II and the rate of these reactions is not affected by the presence in solution of CH_3O^-.

TABLE I. Values of Kinetic Constants for the Reaction of Benzaldehyde with Primary Amines at 25° C.

Amine	10^2[RNH_2]	10^2[CH_3O^-]	[ClO_4^-]	$10^4k'_{obs}$ (sec^{-1})	$10^2k'_o$ ($sec^{-1}M^{-1}$)
n-Butylamine	1.29		0.15	12.9	
	2.58		0.15	25.9	
	6.46		0.15	63.7	9.6
	12.9		0.15	124	
	1.29	7.5	0.075	12.3	
Ethylamine	2		0.15	18.2	
	5.2		0.15	46	
	10.4		0.15	94	8.8
	52		0.15	460	
	2	5	0.10	17.9	
Cycloexylamine	1.32		0.15	3.7	
	3.3		0.15	11	
	6.6		0.15	22	3.4
	13.2		0.15	45.2	
	1.32	5	0.10	3.5	
s-Butylamine	2.26		0.15	7.14	
	4.52		0.15	11.9	
	9.04		0.15	24.6	2.6
	18		0.15	50.6	
	45.2		0.15	117	
	2.26	5	0.10	6.9	
t-Butylamine	4.75		0.15	2	
	11.9		0.15	4.1	
	23.7		0.15	8.18	0.34
	47.5		0.15	16.1	
	4.75	5	0.10	1.9	

TABLE II. Values of Kinetic Constants for the Reaction of Salicylaldehyde with Primary Amines at 25° C.

Amine	$10^2[RNH_2]$	$10^2[CH_3O^-]$	$[ClO_4^-]$	$10^5k''_{obs}$ (sec^{-1})	$10^2k''_o$ ($sec^{-1}M^{-1}$)
n-Butylamine	0.454		0.15	150	26
	0.908		0.15	290	
	2.27		0.15	650	
	4.54		0.15	1200	
	0.454	5	0.10	148	
Ethylamine	1.0		0.15	217	19.6
	2.0		0.15	420	
	5.2		0.15	1030	
	10.4		0.15	2040	
	1.0	5	0.10	216	
Cycloexylamine	1.3		0.15	120	7.0
	3.3		0.15	240	
	6.6		0.15	490	
	13.2		0.15	940	
	1.3	5	0.10	122	
s-Butylamine	2.26		0.15	17.7	6.1
	4.52		0.15	31.5	
	9.04		0.15	60	
	18.0		0.15	117	
	2.26	5	0.10	17.8	
t-Butylamine	2.37		0.15	21.7	0.65
	4.74		0.15	36	
	11.8		0.15	77	
	23.7		0.15	155	
	2.37	5	0.10	21.7	

TABLE III. Values of Kinetic Constants for the First Stage of Reactions of $Ni(SA)_2$ with Primary Amines at 25° C; $[Ni(SA)_2] = 10^{-4}$.

Amine	$10^3[RNH_2]$	$10^3[CH_3O^-]$	$[ClO_4^-]$	$10^5k'''_{obs(1)}$ (sec^{-1})	$10^2k'''_{o(1)}$ ($sec^{-1}M^{-1}$)
n-Butylamine	1.9		0.15	108	52
	2.2		0.15	134	
	2.75		0.15	148	
	3.7		0.15	196	
	4.5		0.15	240	
	5.45		0.15	290	
	2.2	0.375	0.1496	199	
	2.2	0.55	0.1495	230	
	2.2	1.25	0.1487	267	
	2.2	1.87	0.1481	282	
	1.1	1.00	0.1490	120	
	2.2	1.00	0.1490	250	
	3.3	1.00	0.1490	365	
Ethylamine	0.9		0.15	34	40.5
	4.3		0.15	205	
	5.1		0.15	238	
	8.7		0.15	375	
	10		0.15	420	
	20		0.15	830	
	21.7		0.15	905	

TABLE III. (Cont.)

Amine	$10^3[RNH_2]$	$10^3[CH_3O^-]$	$[ClO_4^-]$	$10^5k'''_{obs(1)}$ (sec^{-1})	$10^2k'''_{o(1)}$ ($sec^{-1}M^{-1}$)
Ethylamine	5.1	0.62	0.1494	382	
	5.1	1.24	0.1487	489	
	5.1	1.87	0.1481	555	
	1.3	1.00	0.1490	107	
	2.55	1.00	0.1490	215	
	5.1	1.00	0.1490	440	
Cycloexylamine	13.0		0.15	81.5	
	19.4		0.15	128	
	26		0.15	149	
	52		0.15	326	
	130		0.15	810	
	19.4	3.75	0.1462	141	6.4
	19.4	11.2	0.1388	166	
	19.4	30	0.12	195	
	4.85	3.75	0.1462	38	
	9.7	3.75	0.1462	70	
	19.4	3.75	0.1462	141	
s-Butylamine	5.05		0.15	26	
	10.1		0.15	66	
	20.2		0.15	125	
	38		0.15	239	
	50.5		0.15	316	
	38	3.75	0.1462	278	6.3
	38	5.25	0.1447	303	
	38	15	0.135	336	
	9.5	3.75	0.1462	71	
	19	3.75	0.1462	140	
	38	3.75	0.1462	278	
t-Butylamine	20.1		0.15	13.8	
	40.3		0.15	22.2	
	201		0.15	116	
	225		0.15	128	
	403		0.15	219	
	225	7.5	0.1425	166	0.52
	225	15	0.135	192	
	225	30	0.12	211	
	33	7.5	0.1425	22.1	
	66	7.5	0.1425	45.5	
	132	7.5	0.1425	88.0	

Kinetics of Reactions of $Ni(SA)_2$ with Amines

Methanol solutions of $Ni(SN)_2$ and basic methanol solutions of $Ni(SA)_2$ follow the Lambert–Beer law in a wide range of the U.V. spectrum. $Ni(SA)_2$ reacts with all amines used according to reation (2) and two stages were observed.

Kinetic calculations were facilitated because each stage shows a good isosbestic point at a given wavelength; thus, observed rate constants, $k'''_{obs(1)}$ (sec^{-1}), for the first stage, were determined at the wavelength of the isosbestic point of the second stage.

The wavelength of kinetic monitoring for the 1st stage of n-butylamine and ethylamine reactions was ~ 345 mμ whereas for cyclohexylamine, sec-butylamine and t-butylamine reactions it was ~ 360 mμ. Analogously the chosen wavelength for the 2nd stage of n-butylamine and ethylamine reactions was ~ 365 mμ whereas for cyclohexylamine, sec-butylamine and t-butylamine reactions it was ~ 340 mμ.

Observed rate values, $k'''_{obs(1)}$ (sec^{-1}), for the first stage of reactions between $Ni(SA)_2$ and primary amines, determined under various conditions, are

TABLE IV. Values of Kinetic Constants for the Second Stage of Reactions of $Ni(SA)_2$ with Primary Amines at 25°C; $[Ni(SA)_2] = 10^{-4}$.

Amine	$10^3[RNH_2]$	$10^3[CH_3O^-]$	$[ClO_4^-]$	$10^5k'''_{obs(2)}$ (sec^{-1})	$10^3k'''_{o(2)}$ (sec$^{-1}M^{-1}$)
n-Butylamine	2.75		0.15	48	
	3.7		0.15	60	
	4.55		0.15	74	
	5.4		0.15	87	
	13.6		0.15	215	
	4.55	10	0.14	86.5	158
	4.55	20	0.13	101	
	4.55	100	0.05	124	
	2.2	7.5	0.1425	38.9	
	5.5	7.5	0.1425	90.0	
	11.0	7.5	0.1425	190.0	
Ethylamine	10		0.15	122	
	20		0.15	230	
	52		0.15	532	
	104		0.15	1150	
	171		0.15	1960	
	171	7.5	0.1425	2180	115
	171	15	0.135	2600	
	171	37.5	0.1125	2940	
	3.9	7.5	0.1425	58	
	7.75	7.5	0.1425	114	
	15.5	7.5	0.1425	220	
Cycloexylamine	14.6		0.15	18.7	
	21.8		0.15	21.9	
	29.4		0.15	36.4	
	58.6		0.15	66	
	146		0.15	165	
	21.8	3.75	0.1462	34.5	11.2
	21.8	11.2	0.1388	48	
	21.8	30	0.12	57.5	
	5.4	3.75	0.1462	9.0	
	10.9	3.75	0.1462	17.7	
	21.8	3.75	0.1462	34.5	
s-Butylamine	5.75		0.15	4.98	
	11.4		0.15	10.7	
	22.9		0.15	18.2	
	57.5		0.15	48	9
	11.5	3.75	0.1462	12.1	
	28.7	3.75	0.1462	29.5	
	57.5	3.75	0.1462	58	
t-Butylamine	201		0.15	28.8	
	403		0.15	54.6	
	705		0.15	95.5	
	225	7.5	0.1425	50	
	225	15	0.135	53	1.36
	225	30	0.12	63	
	33	7.5	0.1425	6.1	
	66	7.5	0.1425	12.2	
	132	7.5	0.1425	26	

reported in Table III. These values depend linearly on the amine concentration.

Table IV lists observed rate constants, $k'''_{obs(2)}$ (sec^{-1}), for the second stage of $Ni(SA)_2$ reactions. A linear dependence of these values on the amine concentration is always observed. Values of second-order rate constants, k_o''' ($sec^{-1}M^{-1}$), determined as slopes of plots, relative to the first and the second stage, are included in Table III and in Table IV respectively.

Both the first and the second stage undergo base catalysis; Figure 1 and Figure 2 show the linear dependence of $1/k'''_{obs}$ (sec) against $1/[CH_3O^-]$ at constant amine concentration, whereas plots of k'''_{obs} values against the amine concentration in the presence of a constant methoxide concentration are always linear. These results indicate, for both stages, an overall kinetic law of the form:

$$k'''_{obs} = \frac{a[RNH_2][CH_3O^-]}{b + c[CH_3O^-]} \qquad (3)$$

Discussion

The U.V. spectrum of $Ni(SA)_2$ in methanol shows an intense band at about 380 mμ and a weak one, centered at about 330 mμ. Addition of a base causes the disappearance of the second band, as shown in Figure 3. According to the literature[10] we attribute the band at 380 mμ to the coordinated salicylaldehydato group whereas the other one, centered at 330 mμ, can be attributed to the presence of free salicylaldehyde in solution. Spectral results may then be explained by the following sequence of equilibria:

$$\begin{array}{lll} Ni(SA)_2 \rightleftarrows & Ni(SA)^+ + SA^- & \qquad (4) \\ & \quad CH_3OH \downarrow\uparrow & \\ & \qquad SAH + CH_3O^- & \end{array}$$

In basic media the concentration of free salicylaldehyde is deeply reduced, allowing the disappearance of the band centered at 330 mμ. Interestingly the

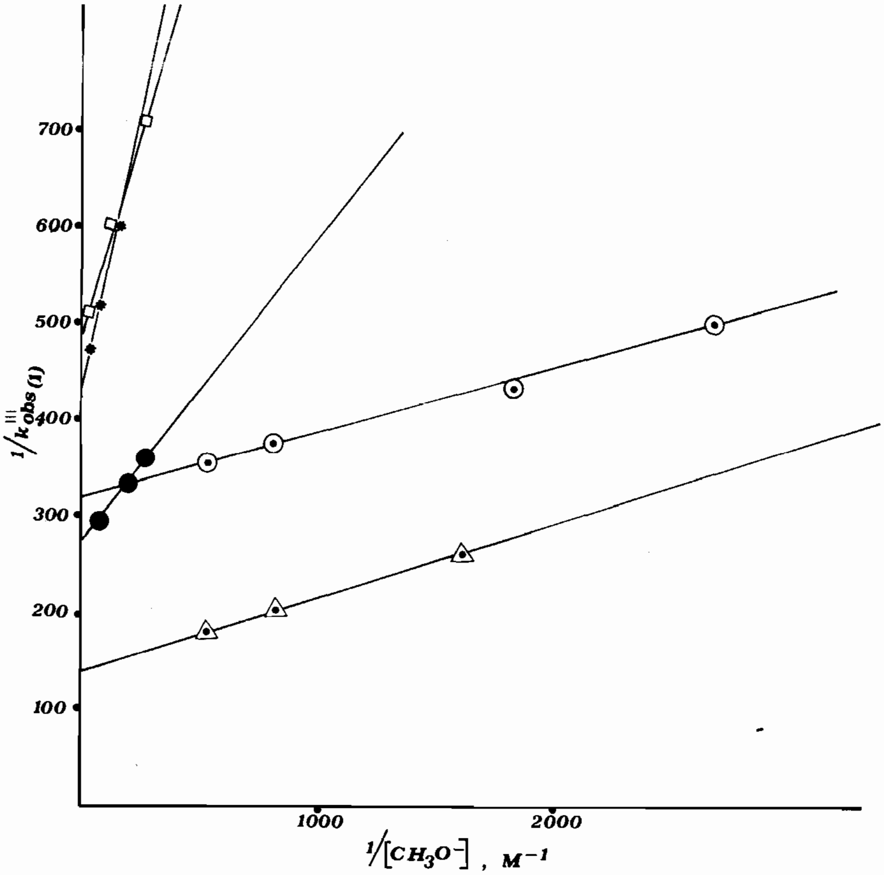


Figure 1. Plots of $1/k'''_{obs(1)}$(sec) values against $1/[CH_3O^-]$ at constant $[RNH_2]$ in the first stage of the reaction of $Ni(SA)_2$ with primary amines. ◬, [ethylamine] = 5.1×10^{-3}; ⊙, [n-butylamine] = 2.2×10^{-3}; ●, [sec-butylamine] = 4.32×10^{-2} *, [t-butylamine] = 2.25×10^{-1}; □, [cyclohexylamine] = 2.18×10^{-2}.

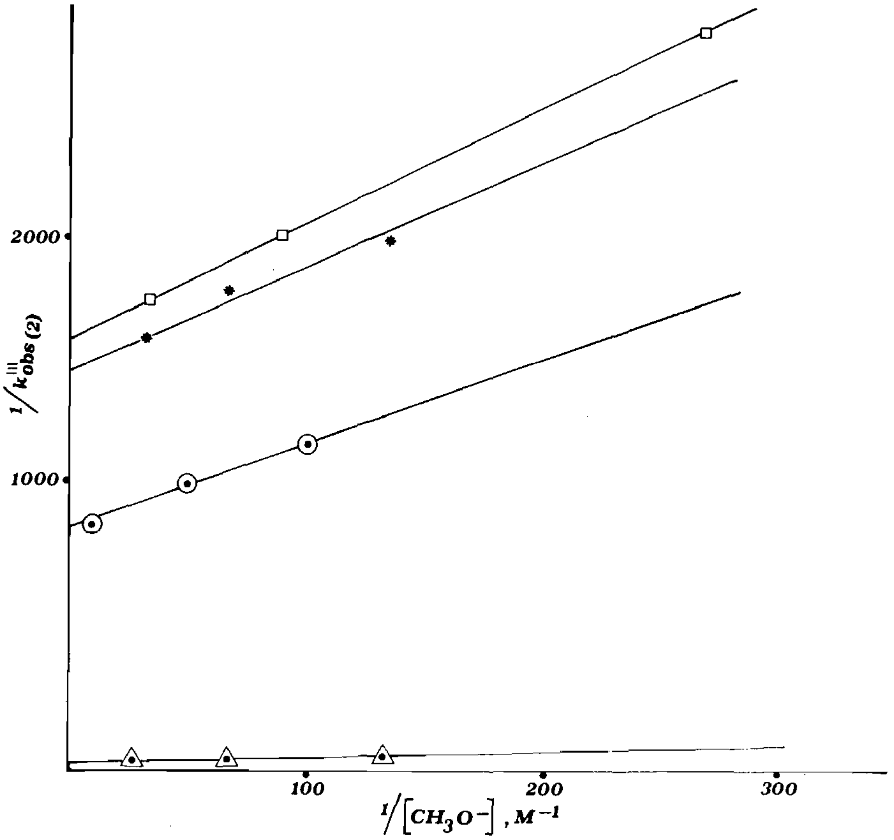


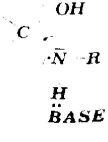
Figure 2. Plots of $1/k_{obs(2)}'''$ values against $1/[CH_3O^-]$ at constant $[RNH_2]$ in the second stage of the reaction of $Ni(SA)_2$ with primary amines. △, [ethylamine] = 1.71×10^{-1}; ⊙, [n-butylamine] = 4.55×10^{-3}; *, [t-butylamine] = 2.25×10^{-1}; □, [cyclohexylamine] = 2.18×10^{-2}.

spectrum of the complex in basic methanol resembles that of $Ni(SA)_2$ in the solid state,[10] suggesting that this compound is the main species in solution.

During the course of reaction (2) there is always a change from the typical spectrum of $Ni(SA)_2$, in basic methanol, to that of $Ni(SN)_2$. This is quite understandable since the amines used are basic enough to provide an appreciable concentration of CH_3O^- in solution.

The possibility that $Ni(SA)^+$ or SA^- could be reactive species in reactions with amines can be ruled out because we should expect, is this case, different kinetic patterns than thos experimentally observed.

A comparison of all experimental data concerning reactions of benzaldehyde, salicylaldehyde and $Ni(SA)_2$ with amines shows a remarkable difference. Whereas, in fact, the nickel(II) complex undergoes basic catalysis, the rate of both benzaldehyde and salicylaldehyde is not affected by the presence of methoxide. These findings are in agreement with previous results[11], already reported, which indicate complete absence of basic catalysis in reactions of n-butylamine with substituted benzaldehydes. Base catalysis is not very common in reactions of aldehydes with primary amines although several cases of base catalyzed reactions have been reported. Rate constants, for example, concerning reactions of *p*-nitro, *m*-nitro and *p*-clorobenzaldehydes with semicarbazide or hydroxylamine were found to increase with the pH and an interaction between an intermediate hydroxyalkylamine and a molecule of a base was postulated to be responsible for the removal of a proton from a nitrogen atom[12]:



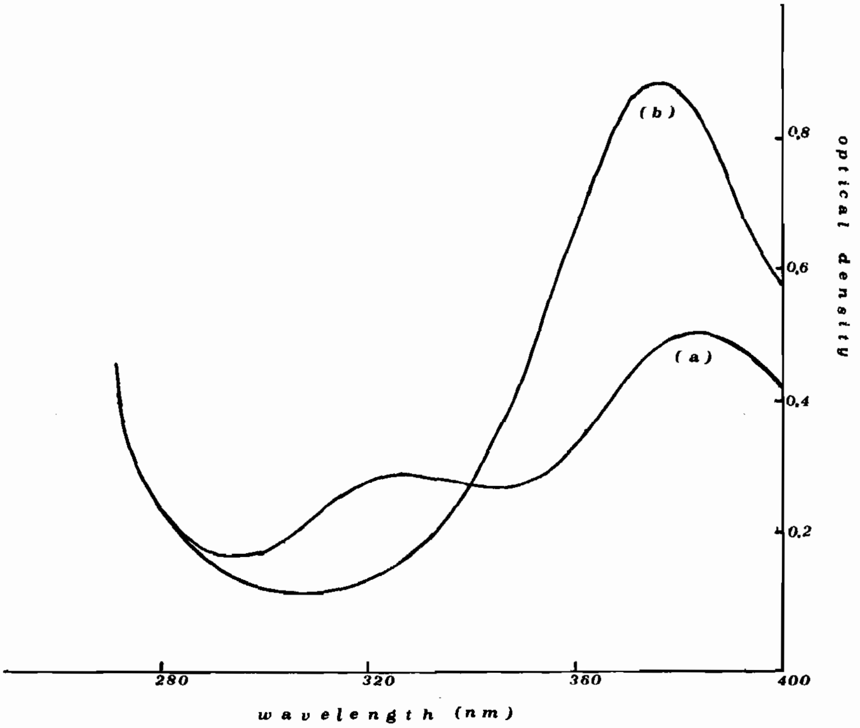


Figure 3. U.V. spectra of (a) $Ni(SA)_2$ in methanol and (b) $Ni(SA)_2$ in basic methanol. $[CH_3O^-] = 2.5 \times 10^{-3}$–$3.75 \times 10^{-2}$; $[Ni(SA)_2] = 1 \times 10^{-4}$.

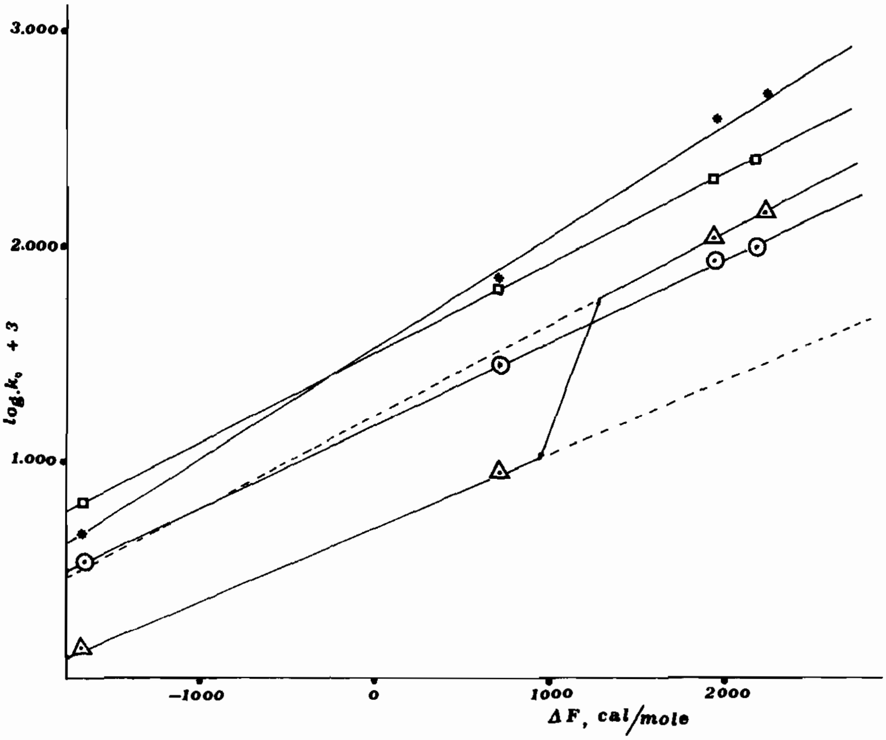


Figure 4. Plots of $\lg k_0$ against $\Delta F°$ (cal/M) values of $RNH_2 \cdot B(CH_3)_3$ addition compounds; □, salicylaldehyde; ⊙, benzaldehyde; *, 1st stage of $Ni(SA)_2$; ◬, 2nd stage of $Ni(SA)_2$.

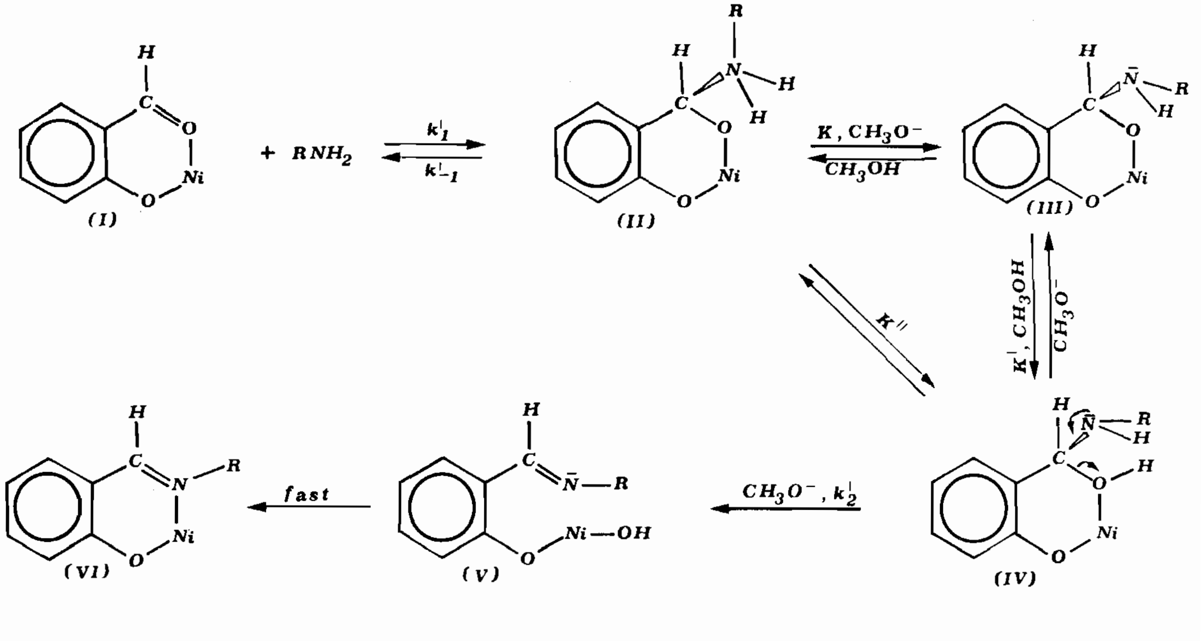
Accordingly electron withdrawing substituents on the aromatic ring and on the amine could aid proton removal by bases.

Accounting for these assumptions we could attribute the basic catalysis in both stages of $Ni(SA)_2$ reactions with primary amines to a methoxide attack on nitrogen bonded protons during the course of the reaction. Furthermore since two stages were observed for reaction (2), having the same kinetic law (3), the same mechanism can be formulated for both of them. The stages, therefore, refer to the partial reactions:

$Ni(SA)_2 + RNH_2 \rightarrow Ni(SA)(SN) + H_2O$

and $Ni(SA)(SN) + RNH_2 \rightarrow Ni(SN)_2 + H_2O$

A mechanism consistent with the observed kinetic law is proposed in the following scheme in which all charges on the groups have been omitted and only one coordinated aldehyde has been considered for simplicity:



Scheme 1

Since the spectral variations during the course of each stage of the reactions show a good isosbestic point, no intermediate can be detected and the steady state approximation can be applied to the species (II); the following kinetic expression may then be deduced from the reaction scheme 1:

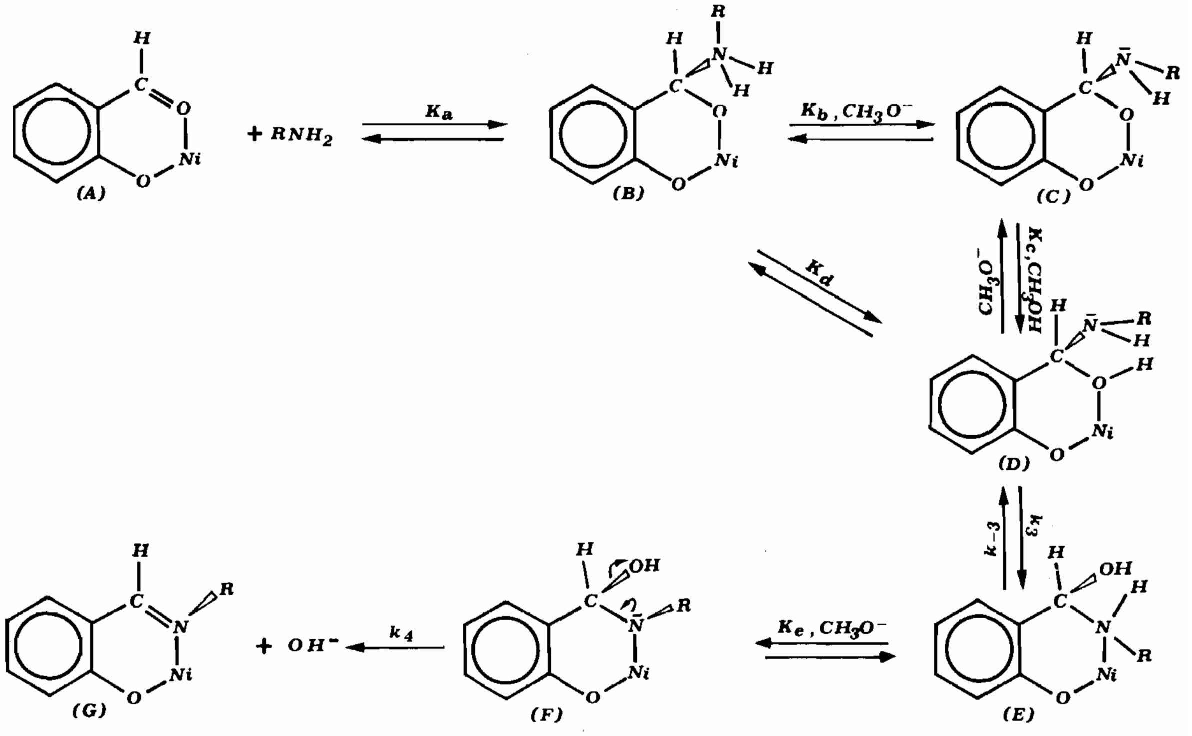
$$k_{obs} = \frac{k_1'k_2'\,KK'[RNH_2][CH_3O^-]}{k'_{-1} + k_2'\,KK'[CH_3O^-]} \qquad (5)$$

Equation (5) reduced to the observed rate law of equation (3) where $a = k_1'k_2'KK'$, $b = k'_{-1}$ and $c = k_2'KK'$.

The mechanism in scheme 1 involves a stepwise sequence of reactions beginning with a nucleophilic attack of a primary amine on the aldehydic carbon of the nickel(II) complex, leading to the intermediate (II). A proton transfer from the nitrogen atom in (II) to the nickel coordinated oxygen may then occur, in a fast equilibrium, either through a participation of methoxide involving the intermediate (III), or *via* an intramolecular transfer (II) $\rightleftarrows$ (IV). Since the C–OH bond in (IV) is weakened by coordination of oxygen to nickel, a carbon–nitrogen double bond formation may occur at this stage and can be favoured by an attack of CH_3O^- on the nitrogen bonded proton. A fast chelation of nitrogen to nickel leads finally to the salicylaldiminato complex (VI).

According to the mechanism the basic catalysis is due to an interaction of CH_3O^- with the nitrogen bonded proton in (IV) and is favoured by the inductive effect exerted by the $\gt$OH coordinated group. Therefore the proposed mechanism resembles that generally accepted for uncoordinated aldehydes, where electron withdrawing substituents on the aromatic ring can aid proton removal by bases[12].

However, on the wake of our results, we cannot exclude an alternative mechanism indicated in scheme 2.



Scheme 2

On applying the steady state approximation to the intermediate (E) the following kinetic expression may be derived:

$$k_{obs} = \frac{K_aK_bK_cK_ek_3k_4[RNH_2][CH_3O^-]}{k_4K_e[CH_3O^-] + k_{-3}} \qquad (6)$$

equation (6) reduces to the observed rate law of equation (3) where $a = K_aK_bK_cK_ek_3k_4$; $b = k_{-3}$ and $c = k_4K_e$.

The mechanism in scheme 2 shows a stepwise sequence of fast equilibria leading from (A) to (D). A rearrangement of this intermediate, involving breaking of the Ni–O bond and formation of a Ni–N bond, leads in a slow step to (E). Since coordination of nitrogen to nickel makes the hydrogen bonded to it more acidic, an interaction of CH_3O^- with the proton may occur in a fast equilibrium at this stage leading to the intermediate (F). An electron rearrangement, involving a concerted double bond formation between carbon and nitrogen and expulsion of the OH^- group, leads finally to the salicylaldiminato complex. According to the mechanism the basic catalysis is only due to a shift of the equilibrium (E) $\rightleftarrows$ (F) by methoxide.

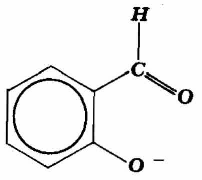
The experimental results do not permit a choice between the reaction paths reported in scheme 1 and in scheme 2. In fact both have the same dependence on the amine and on the methoxide concentration and a discrimination is not possible. It is interesting to note, however, that the initial steps are substantially common for both schemes and the differences concern the final steps leading to $Ni(SN)_2$.

The second order dependence of the rate on the concentration of amines is general in Schiff base formation reactions[11] and the second-order rate constants, k_o ($sec^{-1}M^{-1}$), include different kinetic terms allowing interesting considerations about the factors controlling the mechanism. For a given substrate the order of reactivity is always as follows: n-butylamine>ethylamine > cyclohexylamine ≃ sec-butylamine > t-butylamine. The proton basicity of the amines is clearly not a good index of the observed rates. Whereas in fact proton basicities of n-butylamine and t-butylamine are about the same[13], their reactivities are at the top and at the bottom respectively. A correlation appears, however, when a different reference acid is used. A linear dependence is found, in fact, between $\lg k_o$ and the standard free energy of the corresponding amine–borontrimethyl addition compound[14, 15].

These quantities ($\lg k_o$ and ΔF°) are plotted in Figure 4 for benzaldehyde, salicylaldehyde and both stages of $Ni(SA)_2$. A similar correlation indicates that the change in the various structural parameters produces similar effects on the rate of Schiff base formation and on the extent of association of the $RNH_2 \cdot B(CH_3)_3$ compounds. Since these effects are mainly steric in nature we can conclude that the steric hindrance of amines is a very important factor in these reactions. The plot in Figure 4 relative to the second stage of $Ni(SA)_2$ appears, however, anomalous. There is in fact a break between the reactivity of n-butylamine and ethylamine and that of sec-butylamine and t-butylamine. We recall that the second stage refers to the reaction of a Ni(SA)(SN) compound and we suggest that a distorsion from the planar configuration may be promoted by the sec-butylamine and the t-butylamine.

A similar suggestion is supported by some structural data which indicate for bis(N-n-butylsalicylaldiminato) Ni(II) and bis(N-ethylsalicylaldiminato)Ni(II) a planar configuration[6,16] whereas analogous bis(N-sec-butylsalicylaldiminato)Ni(II) and bis(N-t-butylsalicylaldiminato)Ni(II) have a tetrahedral structure[6,16].

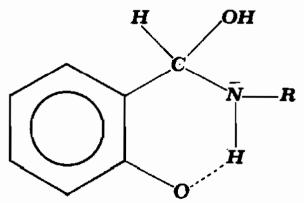
Plots in Figure 4 show also that the reactivity of salicylaldehyde is always higher than that of benzaldehyde. We have a kinetic evidence that the reactive species is the salicylaldehydato ion:



because values of k''_{obs} (sec^{-1}) are not affected by the presence of methoxide in solution. The equilibrium

$$SAH + RNH_2 \rightleftarrows SA^- + RNH_3^+$$

is, in fact, shifted towards the right and a nucleophilic attack of an amine on the aldehydic carbon of the salicylaldehydato ion should be disfavoured. In our opinion the increased reactivity of such a negative anion may be attributed to an anchimeric assistance effect of the negative oxygen through a N–H····O bridge during the dehydration path:



This interaction contributes to stabilize the hydroxyalkylamine intermediate disfavouring also the back reaction *via* k_{-1} in scheme (1).

Intramolecular general base catalysis has been reported to occur in reactions of aspirine with weakly basic amines[17,18] and it is expected from the stepwise mechanism acting in these reactions.

Finally the high reactivity observed in the first stage of reactions of $Ni(SA)_2$ can be attributed to an increase of the rate of amine attack on the aldehydic carbon as a consequence of an enhanced electrophilicity of such carbon center promoted by coordination of salicylaldehyde to nickel(II) and to a stabilization of the transition state, during the attack, caused by a discharge of the incipient negative charge on the oxygen bonded to nickel(II).

Acknowledgments

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