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Lutidine Buffers of Very Limited Coordination Power for the pH Range 3-8

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A series of 2,6-dimethylpyridines with substituents in the 3- and/or 4-positions has been synthesized and characterized with respect to yield upon synthesis, solubility in water, and UV absorption. pK_a values of the free bases and complex formation constants for the aquo complex ions of Mg^{2+}, Ca^{2+}, Zn^{2+}, Cu^{2+}, and Ni^{2+} as determined by potentiometric titration in aqueous solution are presented. For the pH range 3-8 a series of 2,6-lutidine type buffers is suggested with solubilities ranging from >0.5 to ≤0.03 M. The formation constants for the 1:1 complexes of divalent aquo metal cations are small (mean value $K = 1.7$ M^{-1}) and nearly independent of both the nature of the metal and the pK_a of the substituted 2,6-lutidines studied. These results are interpreted as being indicative of sterically restricted complex formation of the "outer-sphere" type. It is shown that the acids LH^+ (L = substituted 2,6-lutidine) do not act as catalysts for the dissociation of a nickel(II) triglycine complex that is known to be subject to general acid catalysis.

Introduction

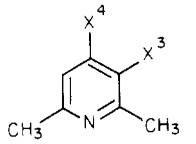
Buffer systems are of outstanding importance for solution chemistry. Depending on the field of chemistry in which a buffer is to be applied, specific properties and aspects other than pK_a and buffer capacity become important. In 1966 Good et al.[1] developed an excellent set of buffer compounds for use in biological systems. The authors put together a list of criteria for buffer compounds and buffer systems. Considering kinetic and thermodynamic studies on metal ions in aqueous solution, one might add two more criteria to this list: (i) the extent of complex formation between the buffer and metal ions should be negligibly small, and (ii) there should be no or at least only a minor catalytic effect of the buffer on systems that are subject to acid catalysis.

Most of the commonly employed buffer systems are very good complex forming agents.[2] 2,6-Lutidine and 2,4,6-collidine have often been applied as buffer compounds for the pH range 6.5-8.0 because of their restricted coordination properties due to steric hindrance through the two methyl groups neighboring the donor nitrogen. Nevertheless, there are some reports on the donor capacity of the 2,6-dimethylpyridine system toward metal ions[2-4] as well as on the isolation and characterization of complexes of the type MX_2L_2 (X = halide or pseudohalide; L = 2,6-lutidine).[5]

The complex formation constants for some of the buffers introduced by Good et al.[1] are known for the divalent cations Mg^{2+}, Ca^{2+}, Mn^{2+}, and Cu^{2+}. For other buffers accurate data are missing. Deutsch[3] synthesized pyridine derivatives carrying two tertiary butyl or trimethylammonium groups in the 2- and 6-positions; they are then no longer able to complex with metal ions. Unfortunately, however, either the solubility in water is too low or the pH range accessible is of limited interest.

The present study was initiated by the need for noncoordinating buffer systems to be applied in kinetic work involving hydrated metal ions. It is a contribution on the applicability of 2,6-lutidine type compounds L as "noncoordinating" buffer compounds in aqueous solution.

The base strength of the heterocyclic nitrogen is varied stepwise over a range of 5 pK_a units by introduction of additional substituents on the 3- and 4-positions with negligibly small donor capacity. The study presents the pK_a values of the free bases and the stability constants for their complex formation with divalent metal ions as well as data on UV absorption, on approximate solubilities, and on catalytic activity in a reaction that is subject to general acid catalysis.



L = 3-X³-4-X⁴-2,6-dimethylpyridine

Experimental Section

3-Nitro-2,6-lutidine (I) and **3-nitro-2,4,6-collidine** (III) were obtained by nitration of 2,6-lutidine and 2,4,6-collidine with potassium nitrate in fuming sulfuric acid (28% SO_3) following the method of Plazek.[6] The products were fractionated in vacuo (I, bp 125-127 °C (34 mmHg), mp 36-38 °C; III, bp 153-155 °C (65 mmHg), mp 35-37 °C). **2,6-Lutidine *N*-oxide** was obtained by a method analogous to that of Den Hertog and Combe.[7] Even after recrystallization the resultant white crystals may contain traces of hydrogen peroxide, which can cause violent explosions upon treatment with nitric acid or dimethyl sulfate. To remove residual peroxide, a chloroform solution of the crude product was stirred over anhydrous sodium carbonate at room temperature for a period of 1 week.[8] After filtration and evaporation of the solvent colorless, peroxide-free crystals were obtained.

4-Nitro-2,6-lutidine *N*-oxide was prepared by the reaction of fuming nitric acid in concentrated sulfuric acid with 2,6-lutidine *N*-oxide according to the nitration of pyridine *N*-oxide:[7] yield 94%; mp 56 °C (acetone/hexane). The reduction of 4-nitro-2,6-lutidine *N*-oxide with trimethyl phosphite in dichloromethane under irradiation with a 500-W mercury light source according to a procedure described in the literature[9] yielded **4-nitro-2,6-lutidine** (II). The product was purified by column chromatography (silica gel, dichloromethane/hexane = 9/1) followed by crystallization from hexane (yield 80%, mp 37 °C).

4-Cyano-2,6-lutidine (IV) was synthesized from 2,6-lutidine *N*-oxide by a method similar to one described in the literature.[10a] For the sake of security the methylation with dimethyl sulfate was carried out in boiling carbon tetrachloride. When the addition of dimethyl sulfate was complete, the solution was kept boiling for another 2 h. The 1-methoxy-2,6-dimethylpyridinium methyl sulfate separates as an oil, which solidifies upon cooling to room temperature. It is converted to IV by reaction with potassium cyanide. Purification by

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(1) Good, N. E.; Winget, G. D.; Winter, W.; Conolly, Th. N.; Izawa, S.; Singh, R. M. M. *Biochemistry* **1966**, *5*, 467.

(2) Smith, R. M.; Martell, A. E. "Critical Stability Constants"; Plenum Press: New York, 1975; Vol. 2.

(3) Deutsch, E.; Cheung, N. K. V. *J. Org. Chem.* **1973**, *38*, 1123.

(4) Raycheba, J. M. T.; Margerum, D. W. *Inorg. Chem.* **1980**, *19*, 837.

(5) See for example: (a) Goldstein, M.; Mooney, E. F.; Anderson, A.; Gebbie, H. A. *Spectrochim. Acta* **1965**, *21*, 105. (b) Ludwig, W.; Gasser, F. *Helv. Chim. Acta* **1969**, *52*, 107. (c) Campbell, J. A.; Raston, C. L.; Varghese, J. N.; White, A. H. *Aust. J. Chem.* **1977**, *30*, 1947. (d) Darby, W. L.; Vallarino, L. M. *Inorg. Chim. Acta* **1979**, *36*, 253.

(6) Plazek, E. *Ber. Dtsch. Chem. Ges.* **1939**, *72*, 577.

(7) Den Hertog, H. J.; Combe, W. P. *Recl. Trav. Chim. Pays-Bas* **1951**, *70*, 581.

(8) Kreher, R., Medizinische Hochschule Lübeck, private communication.

(9) Kaneko, C.; Yamamoto, A.; Gomi, M. *Heterocycles* **1979**, *12*, 227.

(10) (a) Feely, W. F.; Beavers, E. M. *J. Am. Chem. Soc.* **1959**, *81*, 4004. (b) La Montagne, M. P. *J. Med. Chem.* **1973**, *16*, 68.

column chromatography (Al_2O_3, low-boiling petroleum ether (eluent)) yielded IV in the form of long colorless needles (mp 83 °C).

2,6-Dimethylisonicotinic acid ethyl ester (IX) is obtained from IV according to the literature[10b] (bp 116–118 °C (5–6 mmHg), mp 35–36 °C). Reduction of 4-nitro-2,6-lutidine *N*-oxide with iron powder in acetic acid[11] gave 4-amino-2,6-lutidine (XVI; mp 186–188 °C, from toluene). 2,6-Lutidine *N*-oxide is converted into its hydrochloride and then treated with phosphorus oxychloride to yield **4-chloro-2,6-lutidine**[12] (XI). The partially formed side chain chlorinated byproducts can only be separated by fractionated distillation after hydrolysis with aqueous potassium hydroxide (XI; bp 75–78 °C (20 mmHg)). **4-Bromo-2,6-lutidine** (X) was obtained from 4-nitro-2,6-lutidine *N*-oxide by the reaction with 30% HBr in glacial acetic acid[7] at 120 °C during 4.5 h in a sealed iron tube (bp 110 °C (20 mmHg)). **4-Methoxy-2,6-lutidine** (XV) was prepared according to the literature[13] (bp 100 °C (27 mmHg)). **3-Acetyl-2,4,6-collidine** (XII), as prepared according to a published procedure,[14] was purified by fractionation under an argon atmosphere (bp 114 °C (12 mmHg)). **3-Bromo-2,4,6-collidine** (VI) was obtained according to the literature[15] and purified by distillation in vacuo (bp 104–106 °C (10 mmHg)). **3-Chloro-2,6-lutidine** (VII) was synthesized according to the literature[16] (bp 23 °C (5–6 mmHg)). **2,6-Lutidine-3-sulfonic acid** (VIII) was obtained by sulfonation,[17] decolorized by treatment with charcoal, and recrystallized from water. **2,6-Lutidine** (XIII) as obtained from EGA-Chemie was dried with potassium hydroxide and fractionated over a Vigreux column. **Tetramethylpyrazine** (V; Fluka) and 2,4,6-collidine (XIV; reagent grade, Fluka) were used without further purification.

Spectrophotometric Measurements. The absorption spectra were recorded with a Perkin-Elmer spectrophotometer (Model PE554) in 1-cm quartz cells.

Kinetic Measurements. Solutions of the doubly deprotonated nickel(II) triglycine complex were prepared by mixing appropriate solutions of nickel(II) perchlorate and triglycine (Sigma) using a slight excess of the ligand and by adjusting the pH with sodium hydroxide to 9–10. Buffer solutions were made from the corresponding lutidine compounds, and the pH was adjusted with perchloric acid or sodium hydroxide. The ionic strength was maintained at I = 0.3 M with sodium perchlorate in both solutions. The kinetic measurements were done with a modified[18] Durrum D110 stopped-flow apparatus at 25 °C. The rate of disappearance of the nickel complex was followed at 430 nm. The pH in the solutions of the reaction partners was measured with a glass electrode.

Potentiometric Measurements. The potentiometric measurements were made with a Metrohm E536 titration apparatus at 25 °C in a thermostated glass vessel with a glass electrode. A set of four titrations with 0.1 M sodium hydroxide was carried out for each buffer compounds: (i) 0.1 mmol HNO_3; (ii) 0.6 mmol HNO_3 + 0.5 mmol base; (iii) 0.1 mmol HNO_3 + 8.13 mmol metal(II) nitrate; (iv) 0.6 mmol HNO_3 + 0.5 mmol base + 8.13 mmol metal(II) nitrate. The ionic strength was adjusted to I = 0.5 M with $NaNO_3$. From the differences between the titration curves (i) and (ii) the pK_a values were determined with a computer program based on a literature procedure.[19] The experimental error for the pK_a values thus obtained is ±0.05 pK_a unit.

The difference between the titration curves (iv) and (ii) is used to determine the complex formation constant, the hydrolysis of the metal ion as described by curve (iii) being taken into account. The evaluation of the equilibrium constant for the formation of the 1:1 complex was done with a computer program based on published procedures.[19] Since the complex formation constants obtained by this subtraction procedure are small, the limits of error can be as large as ±40%.

Results and Discussion

In Table I the substituted lutidines chosen as potential buffer compounds are listed together with those commercially available (V, XIII, and XIV) and those obtained as intermediate products upon synthesis of others (XVI). The yields given in the table are based on the commercially available starting material (in most cases 2,6-lutidine). Although compounds IV and XII were obtained in rather poor yields, their synthesis is very simple and convenient whereas the synthesis of others (XI) is more different yet leads to the product in a higher yield.

Table I. pK_a Value, Solubility, and Yield upon Synthesis of 3-X^3-4-X^4-2,6-Dimethylpyridines

no.	X^3	X^4	% yield	solubility in water, M	pK_a[g]
I	NO_2	H	61	0.045	2.87
II	H	NO_2	70	0.01	3.15
III	NO_2	CH_3	86	0.03	3.47
IV	H	CN	21	0.03	3.68
V	Me_4pyr		*a*	0.05	4.0[f]
VI	Br	CH_3	41	0.01	4.82[b,f]
VII	Cl	H	45	0.05	4.87[f]
VIII	SO_3H	H	45	0.5	4.80 (4.89[c])
IX	H	COOEt	28	0.05	5.27
X	H	Br	31	<0.01	5.41
XI	H	Cl	69	0.05	5.46
XII	$COCH_3$	CH_3	22	>0.5	5.91
XIII	H	H	*a*	>0.5	6.96 (6.75[d])
XIV	H	CH_3	*a*	>0.5	7.55[f] (7.59[d])
XV	H	OCH_3	72	>0.5	8.04 (7.86[e])
XVI	H	NH_2	31	0.07	10.21[f]

[a] Commercially available; pyr = pyrazine. [b] $MeOH/H_2O$ (1/1). [c] Evans, R. F.; Brown, H. C. *J. Org. Chem.* 1962, *27*, 3127. [d] Brown, H. C.; Gintis, D.; Domash, L. *J. Am. Chem. Soc.* **1956**, *78*, 5387. [e] Bellingham, P.; Johnson, C. D.; Katritzky, A. R. *J. Chem. Soc. B* 1968, 866. [f] Determined by manual titration at ambient temperature (16–20 °C) at I = 0.1 M (KCl). [g] Conditions (unless otherwise noted): I = 0.5 M ($NaNO_3$); T = 25 °C.

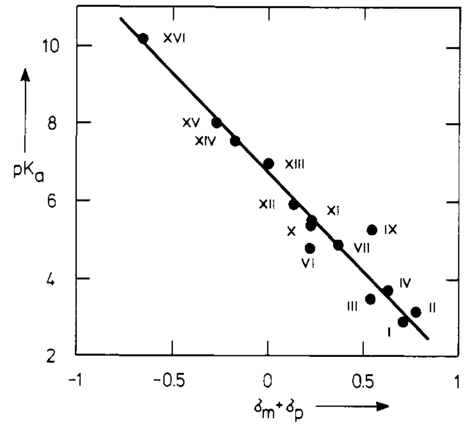

Figure 1. Plot of the pK_a values vs. the sum of Hammett's substituent constants for meta and para substituents (the numbers correspond to those in Table I).

The data on the approximate solubility (see Table I) show that compounds VIII and XII–XV are well suited as buffer compounds from the point of solubility (≥0.5 M), compounds II, VI, and X are not suited (≤0.01 M), and the remaining compounds (0.03–0.05 M) are acceptable as buffers although better solubility and hence greater buffer capacity would be desirable.

The pK_a values of the compounds were determined either in the presence of 0.1 M KCl at room temperature or in the presence of 0.5 M $NaNO_3$ at 25.0 °C (see Table I). The pK_a values of the potential buffer compounds I–IV and VI–XV span more than 5 pK units, thus indicating that the electron density at the heterocyclic nitrogen atom strongly depends on the type of substituents introduced. In Figure 1 the pK_a values

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(12) Kato, T.; Ohta, M. *J. Pharm. Soc. Jpn.* **1951**, *71*, 218.
(13) Baeyer, A. *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 2337.
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(16) De Angelis, F.; Gambacorta, A.; Nicoletti, R. *Synthesis* **1976**, 798.
(17) McElvain, S. M.; Goese, M. A. *J. Am. Chem. Soc.* **1943**, *65*, 2233.
(18) Elias, H.; Fröhn, U.; von Irmer, A.; Wannowius, K. J. *Inorg. Chem.* **1980**, *19*, 869.
(19) (a) Irving, H. M.; Rossotti, H. S. *J. Chem. Soc.* **1954**, 2904. (b) See also: Gaizer, F.; Puskas, A. *Talanta* **1981**, *28*, 565.

Table II. Stability Constants for Mono Complex Formation between 3-X^3-4-X^4-2,6-Dimethylpyridines and Some Aquo Metal Ions ($T = 25$ °C)

no.	X^3	X^4	λ_{lim},[a] nm	pK_a[b]	K,[d] M^{-1} Mg^{2+}	Ca^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}
I	NO_2	H	410	2.87	0.3	<0.2	1.7	1.3	0.3
II	H	NO_2	500	3.15			1.6		
III	NO_2	CH_3	410	3.47			2.8	1.4	
IV	H	CN	320	3.68			1.2		
VIII	SO_3H	H	295	4.80	1.3	<0.2	2.3	1.6	1.4
IX	H	COOEt		5.27			1.3	...[c]	...
XI	H	Cl	392	5.46			1.3	...	...
XII	$COCH_3$	CH_3	335	5.91			1.8	...	...
XIII	H	H	295	6.96			1.6	...	...
XV	H	OCH_3	300	8.04	1.1	0.8	1.4	...	...

[a] λ_{lim} is the limiting wavelength below which the buffer (0.01 M, 1-cm path length) absorbs more than 10% of the incident light. [b] $I = 0.5$ M ($NaNO_3$); limits of error ±0.05 pK_a unit. [c] Due to hydrolysis no accurate data for K could be obtained. [d] For the reaction $M^{2+}(aq) + L \rightleftharpoons [ML]^{2+}$. Conditions: $I = 0.5$ M ($NaNO_3$); maximum limits of error ±40% (see Experimental Section).

are plotted vs. the sum of Hammett's substituent constants ($\sigma_m + \sigma_p$). Omitting systems V, VI, VIII, and IX,[20] one obtains through regression analysis the relationship

$$pK_a(X^3,X^4) = \rho(\sigma_m + \sigma_p) + pK_a(H,H)$$

with $\rho = -5.15 \pm 0.17$ and $pK_a(H,H) = 6.71 \pm 0.08$.

The size of the reaction constant ρ demonstrates that the pyridine ring system is more susceptibile to substituent effects than the isocyclic aromatic ring system of benzoic acid. The advantage of the plot shown in Figure 1 is that quite reliable predictions can be made concerning the acid strength of any lutidinium cation LH^+ with a given set of substituents.

If it is assumed that a given buffer is able to cover a pH range of approximately pH = $pK_a \pm 0.3$, the following series of buffers with increasing pH can be suggested:

I-III/IV-V-VIII-XI-XII-XIII-XIV-XV

The obvious gap existing between pH 5.9 and pH 6.9 can be filled—at least for certain applications—with buffers such as MES and PIPES introduced by Good et al.[1]

For buffer systems to be applied in kinetic studies involving metal ions, the question of complex formation is very important. For a series of divalent metal ions potentiometric titrations were therefore carried out. Under the excess condition $[M^{2+}]_T >> [L]_T$ only mono complex formation has to be considered:

$$M^{2+}(aq) + L \rightleftharpoons [ML]^{2+} \quad K \qquad (1)$$

The data that were obtained for Mg^{2+}, Ca^{2+}, Zn^{2+}, Cu^{2+}, and Ni^{2+} at 25 °C and $I = 0.5$ M ($NaNO_3$) are compiled in Table II. The results can briefly be summarized as follows (see also Figure 2): (i) the complex formation constants are very small; (ii) the differences in pK_a are not at all reflected in the K values obtained for (1); (iii) for the various divalent metal ions studied, there is no significant metal effect to be observed.

The complex formation constants listed in Table II are based on the potentiometric titration of the various lutidinium species and describe metal–nitrogen interaction only.[21a] In principle, additional complex formation through the substituents X^3 and X^4 is possible and has to be considered. Looking at the various groups introduced, one could argue that especially the sulfonate group of buffer compound XIII might be coordinated to an appreciable extent. A spectroscopic study shows however that the strong absorptions of XIII at 272 and 215 nm are not at all shifted upon addition of a 2500-fold excess of nickel(II) perchlorate to XIII. So, the UV spectroscopic experiment fails to detect the complex formation to be expected for the sulfonate group. The information available on the complexing properties of sulfonates in general is very scarce. Ahrland et al.[21b] report that complex formation between benzenesulfonic acid and its *p*-methoxy derivative and silver(I) ions is very weak, with $K_1 = 0.91$ M^{-1} and $K_1 = 0.76$ M^{-1}, respectively. This is in line with the general experience with "noncoordinating" buffer compounds such as MES and PIPES,[1] namely that complex formation through the sulfonate group is very weak and is hard to detect.

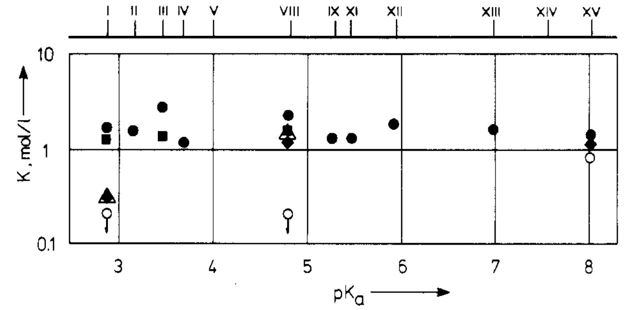

Figure 2. Plot of the equilibrium constant K for mono complex formation according to eq 1 vs. the pK_a values of the buffer compounds: (●) Ni^{2+}; (○) Ca^{2+}; (■) Cu^{2+}; (♦) Mg^{2+}; (▲) Zn^{2+}.

Although 2,6-lutidine and 2,4,6-collidine have often been applied in kinetics studies as so-called noncoordinating buffers,[22] there are several reports in the literature concerning their complex formation capacity.[3,4] Appreciable formation of ternary complexes is reported for nickel complexes with certain deprotonated oligopeptides in aqueous solution.[23] For aquo ions, however, there are no data on complex formation.[2] In aqueous solution obviously only mono complexes are formed although four-coordinate complexes of the type $[M^{II}X_2L_2]$ can be synthesized[5] under appropriate conditions (M^{II} = Ni, Co, Cu; X = halide or pseudohalide; L = 2,6-lutidine or 2,4,6-collidine). Once formed, however, these complexes are of extreme kinetic inertness as has been shown for M^{II} = Ni.[5d]

The most interesting result is undoubtedly that variation of the electron density at the donor nitrogen of the pyridine

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[20] The lutidine compounds VI, VIII, and IX were not considered because the pK_a of VI refers to $MeOH/H_2O$ instead of water and because the data for the σ_m or σ_p value are not known (see VIII) or fluctuate (see IX).

[21] (a) One of the reviewers has pointed out correctly that complex formation through substituents such as the sulfonate group could increase the acidity of the nitrogen and hence release hydrogen ions. As an example the pK_a of singly coordinated ethylenediamine in the species *cis*-$[Co(en)_2Cl(enH)]^{3+}$ is 7.1 instead of $pK_a > 10$ in the noncoordinated state (Alexander, M. D.; Spillert, C. A. *Inorg. Chem.* **1970**, *9*, 2344). It is to be expected, however, that this effect is much less pronounced in the case of outer-sphere complexation. (b) Ahrland, S.; Chatt, J.; Davies, N. R.; Williams, A. A. *J. Chem. Soc.* **1958**, 276.

[22] See for example: (a) Kodama, M.; Yatsunami, T.; Kimura, E. *J. Chem. Soc., Dalton* **1979**, 1783. (b) Zuberbühler, A. D.; Kaden, Th. A. *Helv. Chim. Acta* **1982**, *65*, 753.

[23] Bannister, C. E.; Margerum, D. W. *Inorg. Chem.* **1981**, *20*, 3149.

ring (as reflected by widespread pK_a values) does not affect the extent of complex formation: for Ni^{2+} ions a mean of $\bar{K} = 1.7 \pm 0.16\ M^{-1}$ is obtained. It is concluded from this rather unexpected finding that the two methyl groups neighboring the nitrogen prevent normal inner-sphere complex formation. What is observed upon potentiometric titration might be more adequately described as a restricted complexation of the outer-sphere type due to shielding of the basic nitrogen through the methyl groups.

The size of an outer-sphere complex formation constant K_{os} can be estimated according to (2).[24] In this equation a is the

$$K_{os} = \frac{4}{3000}\pi a^3 N_A e^{-U/k_BT} \qquad (2)$$

distance of closest approach of the aquo metal ion and lutidine; the potential energy U should reflect variations in electron density at the donor nitrogen. The fact that the complex formation constant K does not depend on the pK_a value of the buffer compound (i.e., on the electron density of the nitrogen) indicates that the exponential term in (2) is close to unity:

$$\exp\left(-\frac{U}{k_BT}\right) \approx 1 - \frac{U}{k_BT} \approx 1$$

On the basis of $\bar{K} = 1.7\ M^{-1}$ for Ni^{2+} ions a distance of ~8.7 Å results, which is not unreasonable if one considers that the Stokes radius of a hydrated divalent metal ion such as nickel(II) is about 5.0 Å[24a] and that an appreciable steric hindrance is brought about by the two methyl groups in the 2- and 6-positions of the buffer compounds L.

There are no data in the literature on the complexation of metal ions with 2,6-lutidine or substituted 2,6-lutidines except for the system Ag^+/2,6-lutidine. The complex formation constant obtained for the mono complex is reported to be 480 M^{-1},[2] which is surprisingly high. It may well be that this has to do with the softness of the silver cation and/or with the low solvation number of silver(I) ions.[24a]

As compared to the buffers introduced by Good et al.,[1] the lutidine type buffers L show only a weak tendency to complex with aquo metal ions. With respect to their absorption properties the disadvantage is that they are not suited for studies requiring spectrophotometric monitoring below 350–400 nm (cf. Table II) because of strong self-absorption.

Another important point of interest to be looked at is the catalytic activity of the conjugate acids LH^+ of the lutidine type compounds L. The well-characterized acid dissociation of the nickel(II) triglycine complex was chosen as a model reaction for such a study. It has been shown[23] that this reaction is subject to general acid catalysis. The acid dissociation was therefore reinvestigated in the presence of lutidine buffers. In Figure 3 the kinetic results obtained are summarized. In the upper part the data are shown for measurements at pH 4.05 with a pair of buffer compounds having almost the same pK_a value, 4-cyano-2,6-lutidine ($pK_a = 3.68$) and 4-chloropyridine ($pK_a = 3.84$[25]). The observed rate constant k_{obsd} clearly depends on the concentration of 4-chloropyridine (slope = 124 $M^{-1}\ s^{-1}$), whereas k_{obsd} appears to be independent of the concentration of 4-cyano-2,6-lutidine; i.e., there is no catalytic activity (the concentration range accessible for the latter buffer is unfortunately limited by solubility). The rate constant obtained is in satisfactory agreement with the value calculated from data found in the literature[23] (for the uncatalyzed reaction).

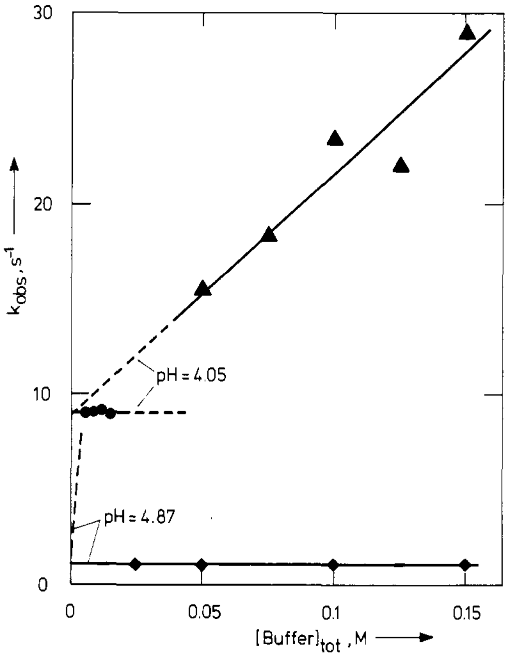

Figure 3. Plot of k_{obsd} for the acid dissociation of the anion $[Ni(H_{-2}G_3)]^-$ (25 °C; I = 0.3 M ($NaClO_4$); cf. ref 23) vs. buffer concentration. At pH 4.05 (upper part), the buffers are 4-chloropyridine (▲) and 4-cyano-2,6-lutidine (●). At pH 4.87 (lower part), the buffers are 2,6-lutidine-3-sulfonic acid (♦) and acetic acid (dashed line; calculated from ref 23).

More instructive are the results obtained with another pair of buffers at pH 4.87, namely acetic acid ($pK_a = 4.64$) and 2,6-lutidine-3-sulfonic acid ($pK_a = 4.85$). The dependence of k_{obsd} on the total buffer concentration as shown in the lower part of Figure 3 clearly proves that the acetic acid buffer does catalyze (dashed line; data from ref 23), whereas the lutidine buffer does not, which is in contrast to the case for α-picoline.[23] The mean value for k_{obsd} for the uncatalyzed reaction of 1.1 s^{-1} is even lower than that obtained by extrapolation from the acetate-buffered system ($k_{obsd} = 1.3\ s^{-1}$ at pH 4.87, calculated from ref 23).

It has been pointed out[23] that the nickel triglycine complex studied forms ternary complexes with α-picoline and 2,6-lutidine. It has been claimed[23] that these complexes are not subject to general acid catalysis. We find,[26] however, that the catalytic effect exerted by acetic acid is the same in solutions buffered either with MES or with 3-acetyl-2,4,6-collidine.

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