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Molecular Orbital Study of the Nitrosation of Active Methyl and Methylene Groups of Pyridine and Pyrimidine Derivatives

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The reactivity of active methyl and methylene groups of nitrogen-containing heteroaromatics with alkyl nitrite in the presence of an amide ion is discussed in terms of the charge transfer ability (CTA) values according to CNDO/2 as well as PPP calculations. Intermolecular perturbation energy calculation was also applied to interpret this nitrosation. The experimental results of nitrosation can be reasonably well interpreted in terms of the CTA values in the deprotonation step of this reaction. The binding energies of methylheteroaromatics are also discussed.

Keywords——reactivity; nitrosation; deprotonation; intermolecular perturbation energy; charge transfer ability; CNDO/2; PPP; picolines; alkylpyrimidines

Since Kato and Goto[2] reported the nitrosation of alkylpyridine and quinoline derivatives in liquid ammonia, Yamanaka and Sakamoto *et al.*[3] have extensively studied the reactivity of not only pyridines and quinolines but also pyrimidine derivatives, and rationalized the chemical behavior of these compounds. Their results on the reactivity of alkyl-pyridines and pyrimidines are illustrated in Chart 1. It was shown that picolines react with alkyl nitrite in the order 4->2->3-picoline, and in the case of pyrimidine derivatives an alkyl group at the 4-position is exclusively attacked by alkyl nitrite.

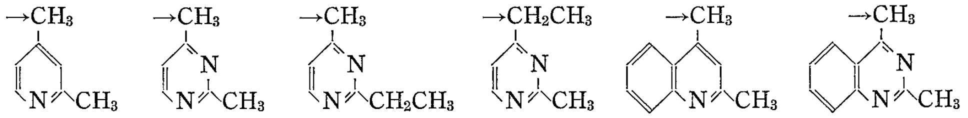

Chart 1. Methyl or methylene groups indicated by arrows are exclusively attacked by alkyl nitrite.

Here, the following sequence of steps is assumed for the nitrosation: in the first step the abstraction of a hydrogen atom occurs from the active methyl or methylene group by the negatively charged nitrogen atom of the amide ion, followed by the attack of alkyl nitrite on the carbanion thus generated as the second step. This process is indicated in the Chart 2 for picolines.

The present molecular orbital (MO) study was carried out to analyze these two steps separately.

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[2] *a*) T. Kato and Y. Goto, *Chem. Pharm. Bull.*, **11**, 461 (1963); *b*) T. Kato, Y. Goto, and M. Kondo, *Yakugaku Zasshi*, **84**, 290 (1964); *c*) T. Kato and Y. Goto, *ibid.*, **85**, 451 (1965); *d*) S.E. Forman, *J. Org. Chem.*, **29**, 3323 (1964).

[3] *a*) H. Yamanaka, H. Abe, T. Sakamoto, H. Hirayama, and A. Kamata, *Chem. Pharm. Bull.*, **25**, 1821 (1977); *b*) H. Yamanaka, H. Abe, and T. Sakamoto, *ibid.*, **25**, 3334 (1977); *c*) H. Yamanaka, H. Abe, H. Hiranuma, and T. Sakamoto, *ibid.*, **26**, 842 (1978); *d*) H. Yamanaka and T. Sakamoto, unpublished results.

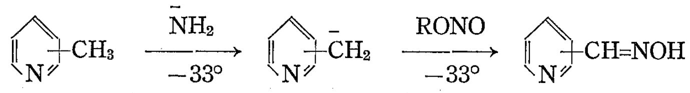

Chart 2

Methods of Calculation

The Pariser–Parr–Pople (PPP) and the complete neglect of differential overlap (CNDO/2) calculations were carried out with FACOM M-190 and ACOS 600 computers. The two-center repulsion integrals in the PPP calculation were evaluated using the Mataga and Nishimoto approximation.[4] The ionization potential (I_P),[5a] electron affinity (E_A)[5a] and core resonance integral (β_{pq}^{core})[5b] for the pyridine ring are as follows: $I_P{}^C$, $E_A{}^C$, $I_P{}^N$, $E_A{}^N$, β_{CC}^{core} and β_{CN}^{core} are 11.16, 0.03, 14.12, 1.78, −2.370 and −2.576 eV, respectively. The core resonance integral between the methyl group carbon atom and the ring carbon bonded to the methyl group was obtained by[6]

$$\beta_{pq}^{core} = \frac{k}{d_{pq}^{6}} \qquad (1)$$

where d_{pq} is the distance between the atoms p and q, and $k=-17.617$, *i.e.* $\beta_{CC}^{core}=-1.428$ eV. I_P and E_A for the methyl group carbon atom were taken as 11.16 and 0.03 eV, respectively. The values (eV) of I_P and E_A for the atoms of alkyl nitrite are: 14.12 and 1.78 for –N=;[5a] 32.90 and 10.00 for –O–;[5c] and 17.28 and 2.01 for =O,[5a] respectively. The $-\beta_{pq}^{core}$ values (eV) and the bond lengths (Å) are: 3.30[5d] and 1.22 for N=O; and 3.25 (Calcd using the Eq. 1 ($k=-21.459$)) and 1.37 for N–O, respectively. The values of the parameters included in the CNDO/2 calculation are the same as those used in the original papers.[7] The molecular geometries of picolines, pyrimidines, toluene, methyl nitrite, and so on were taken from appropriate references.[8] The CH_3 conformation suitable for proton abstraction from heteroaromatics by an amide ion is shown in Fig. 1a, where we see that the CH_3 group is most efficiently hyperconjugated with the $p\pi$ orbitals of the heteroaromatic nucleus. The adoption of this conformation is based on the following results. For neutral picolines, *e.g.* 2-picoline, as shown in Fig. 2, there are no significant differences among the CNDO/2 total energies of the all conformations pertinent to the methyl group, while in the case of the anions, the conformation shown in Fig. 1-c is the most stable. Based on CNDO/2 total energy calculations for neutral ethylpyrimidines, the conformation shown in Fig. 3-a is the most stable, whereas in the case of the anions the conformation shown in Fig. 3-c is the most stable. It may be assumed that hydrogen abstraction occurs in such a conformation, as the anions produced are then most effectively stabilized. Charge transfer ability (CTA) calculations (*vide infra*) relating to the ethyl group were therefore performed using the conformation shown in Fig. 3-b. When the deprotonation step was calculated using the intermolecular perturbation energy program,[9] the conformation depicted in Fig. 1-b was adopted. In the case of calculation on the nitrosation of the carbanion of alkylheteroaromatics with methyl nitrite using the intermolecular perturbation energy program, the sp^2 type conformation of the pyridomethide anion was adopted, because carbanions are generally planar when they are generated next to a group capable of conjugative stabilization.[10] The geometrical orientation of the pyridomethide anion with respect to methyl nitrite was considered to be as shown in Fig. 4. This is energetically most stable on the basis of CNDO/2 calculation when the methyl nitrite molecule rotates around the z axis.

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4) N. Mataga and K. Nishimoto, *Z. Phys. Chem.*, **13**, 140 (1957).

5) *a*) J. Hinze and H.H. Jaffé, *J. Am. Chem. Soc.*, **84**, 540 (1962); *b*) S. Kobinata and S. Nagakura, *Theor. Chim. Acta*, **14**, 415 (1969); *c*) M. Yamakawa, K. Ezumi, Y. Mizuno, and T. Kubota, *Bull. Chem. Soc. Jpn.*, **47**, 2982 (1974); *d*) J. Tanaka, *Nippon Kagaku Zasshi*, **78**, 1647 (1957).

6) H. Kon, *Bull. Chem. Soc. Jpn.*, **28**, 275 (1955).

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9) This program was kindly made available by Professor T. Fueno and Dr. S. Nagase. T. Fueno, S. Nagase, K. Tatsumi, and K. Yamaguchi, *Theor. Chim. Acta*, **26**, 43 (1972); S. Nagase and T. Fueno, *ibid.*, **35**, 217 (1974).

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11) L. Pauling, "The Nature of The Chemical Bond," 3rd. ed., Cornell University Press, Ithaca, N.Y., 1960, p. 263.

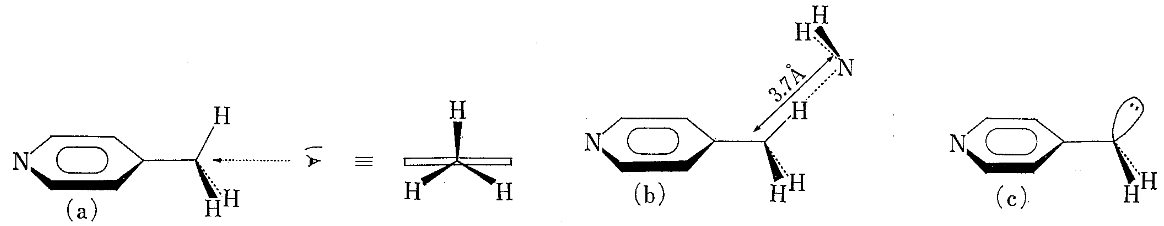


Fig. 1. (a) The conformation of 4-picoline for CTA calculation using the CNDO/2 method.
(b) The coordinate system assumed for hydrogen abstraction by the amide ion from 4-picoline. This was used for the intermolecular perturbation energy calculation.
(c) The most stable conformation of sp^3 type 4-pyridomethide anion.

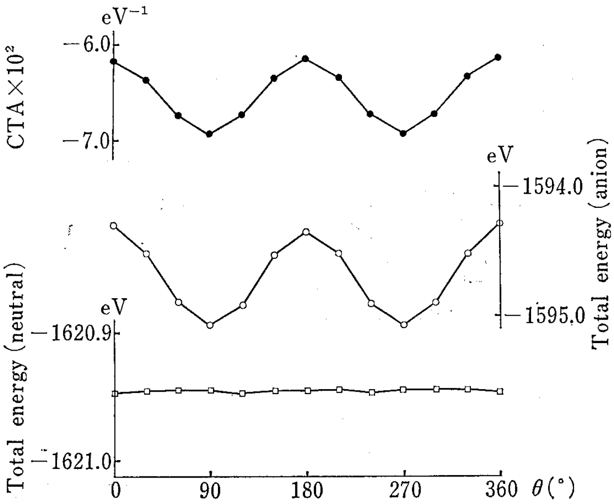


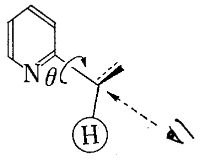
Fig. 2. Total Energies of the Neutral Molecule and the Anion of 2-Picoline, and Its CTA Values in the Deprotonation Step for Various Conformations of the Methyl Group (CNDO/2)

a) The diagram below shows the initial structure of 2-picoline ($\theta=0°$). The methyl group was rotated clockwise.

b) The CTA values were calculated with respect to the circled hydrogen.

c) The total energies of the anions were calculated using the anion molecule without the circled hydrogen.

d) —●—: CTA,
—○—: anion (sp^3),
—□—: neutral.



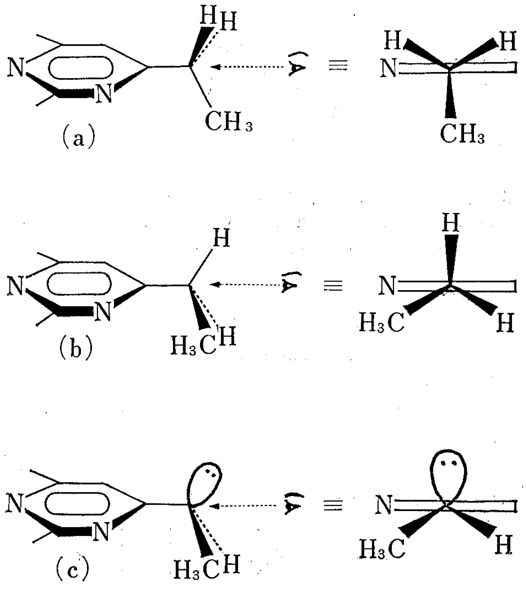


Fig. 3. The Conformation of the Ethyl Group in 4-Ethylpyrimidine and Its Anion

Recently Kubota (one of the authors) *et al.* reported an interpretation of the reactivity of heteroaromatic nitriles with the enolate anion in terms of CTA calculated by the PPP SCFMO method of π-electron approximation.[12] Here we have attempted to apply this technique to the present problems, *i.e.* the reactivity of alkylheteroaromatics with the amide ion and that of the anions with alkyl nitrite, by employing the CNDO/2 and PPP methods. The stabilization energies due to the charge transfer (CT) interaction between two molecules can be written approximately as[13]

$$\Delta E_{\mathrm{AB}} = 2\left\{\sum_{i}^{\mathrm{OCC}}\sum_{l}^{\mathrm{VAC}}\frac{\left(\sum_{r}^{\mathrm{A}}\sum_{s}^{\mathrm{B}}C_{\mathrm{R}.l}^{r}C_{\mathrm{M}.i}^{s}H_{rs}\right)^2}{(\varepsilon_{\mathrm{M}.i}-\varepsilon_{\mathrm{R}.l}+V_{\mathrm{R}.l}^{\mathrm{M}.i})}+\sum_{k}^{\mathrm{OCC}}\sum_{j}^{\mathrm{VAC}}\frac{\left(\sum_{r}^{\mathrm{A}}\sum_{s}^{\mathrm{B}}C_{\mathrm{R}.k}^{r}C_{\mathrm{M}.j}^{s}H_{rs}\right)^2}{(\varepsilon_{\mathrm{R}.k}-\varepsilon_{\mathrm{M}.j}+V_{\mathrm{M}.j}^{\mathrm{R}.k})}\right\} \tag{2}$$

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12) M. Yamakawa, T. Kubota, Y. Terui, T. Honma, and Y. Tada, *Bull. Chem. Soc. Jpn.*, **51**, 3059 (1978).

13) N. Mataga and T. Kubota, "Molecular Interactions and Electronic Spectra," Marcel Dekker, New York, 1970, Chapter 6; H. Fujimoto and K. Fukui, "Advances in Quantum Chemistry," Vol. 6, ed. by P.-O. Löwdin, Academic Press, New York, 1972, pp. 177—201.

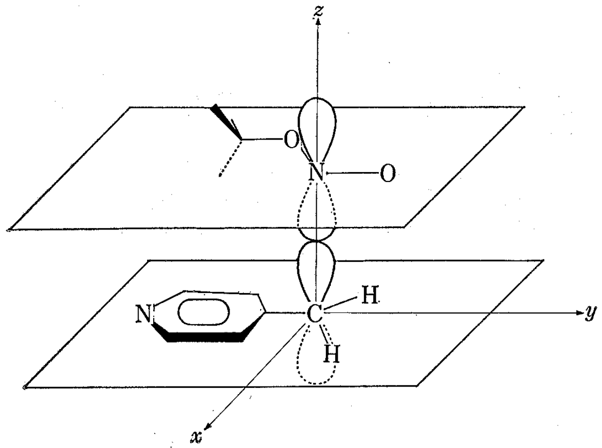
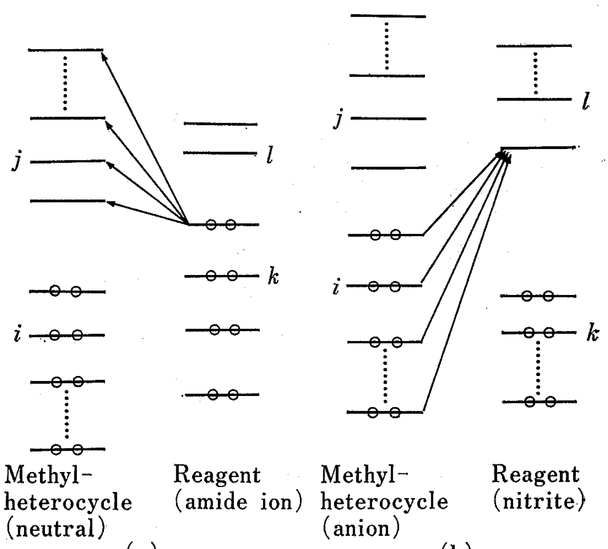


Fig. 4. Orientation of Methyl Nitrite towards the 4-Pyridomethide Anion (sp^2) in Cartesian Coordinates for the Intermolecular Perturbation Energy Calculation

The distance between the N atom of nitrite and the C atom of methylene is 3.1 Å. The separation $d=3.1$ Å is approximately equal to the sum of the van der Waals radius of the carbon and the nitrogen $p\pi$ orbitals.[11)]



(a) (b)

Fig. 5. Schematic Model of Charge Transfer Processes (a) from HOMO of the Amide Ion to All Vacant Orbitals of the Neutral Molecule of a Methylheterocyle, and (b) from All Occupied Orbitals of the Anion of the Methyl-heterocycle to LUMO of Nitrite

where it is assumed that the interaction occurs only through atom A in one molecule and B in the other. The symbols $C^{r}_{\mathrm{R}.l}$, $C^{r}_{\mathrm{R}.k}$, $\varepsilon_{\mathrm{R}.l}$ and $\varepsilon_{\mathrm{R}.k}$ are the coefficients of the r-th atomic orbital (AO) contributed by atom A in the l-th and k-th MO's, and the l-th and k-th MO energies of the reagent, respectively, and $C^{s}_{\mathrm{M}.i}$, $C^{s}_{\mathrm{M}.j}$, $\varepsilon_{\mathrm{M}.i}$ and $\varepsilon_{\mathrm{M}.j}$ are the coefficients of the s-th AO contributed by atom B in the i-th and j-th MO's, and the i-th and j-th MO energies of the methylheterocyclic compound, respectively. H_{rs} is the resonance energy between the corresponding two AO's. The $V^{\mathrm{M}.i}_{\mathrm{R}.l}$ and $V^{\mathrm{R}.k}_{\mathrm{M}.j}$ are the electrostatic interaction energies between the MO's $\phi_{\mathrm{R}.l}$ and $\phi_{\mathrm{M}.i}$, and between $\phi_{\mathrm{M}.j}$ and $\phi_{\mathrm{R}.k}$, respectively, which are expressed by

$$V^{\mathrm{M}.i}_{\mathrm{R}.l} = \left\langle \phi^{*}_{\mathrm{M}.i}\phi^{*}_{\mathrm{R}.l} \left| \frac{\mathrm{e}^2}{\mathrm{r}} \right| \phi_{\mathrm{M}.i}\phi_{\mathrm{R}.l} \right\rangle \tag{3}$$

and

$$V^{\mathrm{R}.k}_{\mathrm{M}.j} = \left\langle \phi^{*}_{\mathrm{R}.k}\phi^{*}_{\mathrm{M}.j} \left| \frac{\mathrm{e}^2}{\mathrm{r}} \right| \phi_{\mathrm{R}.k}\phi_{\mathrm{M}.j} \right\rangle \tag{4}$$

The contribution from these electrostatic interaction terms may be considered constant and disregarded in the present calculation (see discussions in Refs. 12 and 13). The total contribution from the terms H_{rs} to the A–B interaction can also be assumed to be constant. We can now simplify Eq. 2 to evaluate the CTA's. In the case of the calculation for the deprotonation of a methylheterocycle by the amide ion, the CTA values, which contribute predominantly to the system, are given by

$$(\mathrm{CTA})_{\mathrm{H}} = \sum_{j}^{\mathrm{VAC}} \frac{(C^{\mathrm{H}}_{\mathrm{M}.j})^2}{(\varepsilon_{\mathrm{R.HO}} - \varepsilon_{\mathrm{M}.j})} \tag{5}$$

where $\varepsilon_{\mathrm{R\cdot HO}}$ is the energy of the highest occupied MO (HOMO) of the reagent amide ion, considered constant in all the calculations on the deprotonation (Fig. 5-a). When the reagent alkyl nitrite attacks the carbanion of the methylheterocycle, the most important term contributing to the CTA values is

$$(\mathrm{CTA})_{\mathrm{B}} = \sum_{i}^{\mathrm{OCC}} \frac{\left(\sum_{s}^{\mathrm{B}} C^{s}_{\mathrm{M}.i}\right)^2}{(\varepsilon_{\mathrm{M}.i} - \varepsilon_{\mathrm{R.LU}})} \tag{6}$$

where $\varepsilon_{\mathrm{R.LU}}$ is the energy of the lowest unoccupied MO (LUMO) of the reagent nitrite (Fig. 5-b). In using Eq. 6 with the CNDO/2 technique, it should be noted that when the CNDO/2 calculation of methyl nitrite is performed using the conformation shown in Fig. 4, the coefficients of the $2s$, $2p_x$ and $2p_y$ orbitals at the nitrogen atom of methyl nitrite in the LUMO are all zero, and that of the $2p_z$ orbital is 0.7456. This $2p_z$ orbital is orthogonalized to the $2p_x$ and $2p_y$ orbitals at the carbons of the benzyl and pyridomethide carbanions, so the CTA calculations are performed using Eq. 6 with only the coefficients of the $2s$ and $2p_z$ orbitals at the corresponding carbons of these anions.[14]

Results and Discussion

Calculation of CTA Values

The CTA values in the deprotonation step obtained by the CNDO/2 calculations are shown in Table I. It can be said that when the methylheterocycle has a CTA value at the hydrogen atom of an active methyl or methylene group larger than an absolute value of *ca.*$|6.90\times10^{-2}|$, the oxime may be obtained in reasonable yield. For a heterocycle that has two or more alkyl groups at different positions in the same nucleus, if there is a difference between two CTA values of alkyl groups larger than *ca.*$|0.2\times10^{-2}|$, the alkyl group having the larger CTA value is exclusively deprotonated by amide ions, even if the CTA value of the other alkyl group is larger than $|6.90\times10^{-2}|$. As is evident from Table I, especially for 2,4-disubstituted heteroaromatics, the reactivity is affected by the position of the substituents more strongly than by the molecular species or conformation. These results show a strikingly good parallelism between the reactivity of hydrogen atoms and their CTA values for deprotonation with the amide ion. The experimental results for nitrosation can be quite reasonably interpreted in terms of the CTA values in the deprotonation step. These results suggest that the CT process plays an important role in such intermolecular hydrogen bonding-type activated complexes.[15]

TABLE I. CTA Values in the Deprotonation Step using the CNDO/2 Method[a]

Compound		CTA × 10^2 (eV^{-1})	Yield of oxime (%)	Ref. No.
Toluene		−6.78	0[b]	
2-Picoline		−6.94	23	2*a*)
3-Picoline		−6.83	1	2*d*)
4-Picoline		−7.13	71	2*a*)
2,4-Di-Me-pyridine	4-Me	−7.08	37	3*a*)
	2-Me	−6.89	0	
2,4-Di-Me-pyrimidine	4-Me	−7.43	79	3*a*)
	2-Me	−6.90	0	
2-Et-4-Me-pyrimidine	4-Me	−7.42	53	3*d*)
	2-Et	−7.06	0	
4-Et-2-Me-pyrimidine	4-Et	−7.51	70	3*d*)
	2-Me	−6.95	0	
Quinaldine		−7.24	57	2*b*)
Lepidine		−7.83	69	2*b*)
2,4-Di-Me-quinoline	4-Me	−7.80	59	3*a*)
	2-Me	−7.16	0	
2-Me-quinazoline		−7.20	[c]	
4-Me-quinazoline		−8.70	[c]	
2,4-Di-Me-quinazoline	4-Me	−8.74	71	3*a*)
	2-Me	−7.08	0	

a) When the MO's obtained by the CNDO/S-EKJ technique[16] are employed instead of those obtained by the CNDO/2 method, the absolute values of CTA are different from the values given here. However, the order of CTA values is the same in both cases.
b) Y. Goto and M. Matsuda, unpublished result.
c) No experimental results available.
d) Me=CH_3, Et=C_2H_5.

For the case of approach of methyl nitrite to the corresponding carbanion (sp^2 type), the circumstances may be just the reverse of the situation described above. The CTA values calculated using the PPP and CNDO/2 methods are shown in Table II. The finding that

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14) The CTA calculations with Eqs. 5 and 6 correspond to the CT processes shown by the arrows in Fig. 5. Of course, there are many other CT terms in addition to those given by the above equations. However the contribution from these terms is small compared with the values obtained from Eq. 5 or 6, so even if we take account of the contribution from other CT processes, the conclusions described in the discussion (*vide post*) should not be affected.

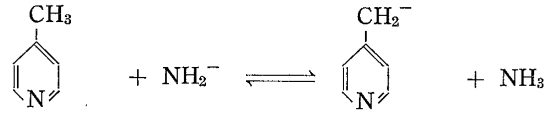
15) *a*) K. Nukazawa, J. Tanaka, and S. Nagakura, *J. Phys. Soc. Jpn.*, **8**, 792 (1953); *b*) H. Nakanishi, H. Morita, and S. Nagakura, *Bull. Chem. Soc. Jpn.*, **51**, 1723 (1978), and references cited therein; *c*) K. Morokuma, *Acc. Chem. Res.*, **10**, 294 (1977); *d*) H. Umeyama and K. Morokuma, *J. Am. Chem. Soc.*, **99**, 1316 (1977).

Table II. CTA Values in the Nitrosation of the Anions with Methyl Nitrite using the PPP and CNDO/2[a] Methods

Compound	CTA × 10 (eV^{-1}) (PPP)	CTA × 10 (eV^{-1}) (CNDO/2)
Toluene	−1.20	−1.77
2-Picoline	−1.09	−1.70
3-Picoline	−1.18	−1.78
4-Picoline	−1.05	−1.66

a) The calculations were performed using the planar conformation of the carbanions.

the absolute CTA value of the apparently less reactive 3-picoline is the largest can be interpreted by assuming that the electron tends to remain on the methylene carbon of the 3-pyridomethide anion more than on the other carbons, *i.e.* the electron migration from the carbanion derived from 3-picoline to the pyridine nucleus is small compared with that of 4- or 2-picoline. In other words, the 4-pyridomethide anion is the most stabilized among the three anions because of the large delocalization of the electron on the carbanion into the ring π electron system. Moreover, in the case of 4-picoline the equilibrium between the neutral molecule and the anion is pushed considerably to the right. The equilibrium of 3-picoline is moved relatively to the left compared with that of 4-picoline.[17] This is one of the reasons why the CTA values in the second step were inconsistent with the experimental results.



(7)

(8)

Calculation of the Intermolecular Perturbation Energy

The intermolecular perturbation energy was calculated for the deprotonation step with an amide ion. This calculation explicitly took account of the reaction coordinate: an amide ion approaches the hydrogen of the methyl group along the axis of the carbon-hydrogen bond shown in Fig. 1-b. The results are shown in Table III, where E_Q, E_K, E_I, E_D, and E_{CT} are the coulombic, exchange repulsion, induction, dispersion, and charge transfer energies, respectively. No significant differences exist among the values of all four compounds with respect to E_K, E_I, and E_D. The E_{CT} values are consistent with the experimental reactivity order 4->2->3-picoline>toluene, while the E_Q value of 2-picoline shows lower stabilization than the other compounds. This lower stabilization may be mainly due to electron repulsion between the electrons in the nitrogen p orbital of the amide ion and those of the nitrogen lone pair orbital of the pyridine nucleus at the *ortho* position to the methyl group.

For the so-called second step, *i.e.* for the approach of methyl nitrite to the carbanion (sp^2 type), calculation of the intermolecular perturbation energy was also performed. The conformation used for the calculation and the results are shown in Fig. 4 and Table IV, respectively. As was seen in the calculation results for the deprotonation step, no significant differences are apparent among the energy values of all four compounds with respect to E_Q, E_K, E_I, and E_D. On the other hand, the order of stabilization is as follows, 3-picoline>toluene>2->4-picoline,

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16) R.L. Ellis, G. Kuehnlenz, and H.H. Jaffé, *Theor. Chim. Acta*, **26**, 131 (1972).
17) M.J.S. Dewar and R.C. Dougherty, "The PMO Theory of Organic Chemistry," Plenum Press, New York, 1975, p. 161.

Table III. Energies of Interaction between Amide Ion and Methyl Compounds (kcal/mol)

Energies	Toluene	2-Picoline	3-Picoline	4-Picoline
E_Q	−1.084	−0.987	−1.548	−2.102
E_K	0.339	0.337	0.338	0.335
E_I	−2.798	−2.787	−2.755	−2.768
E_D	−0.062	−0.061	−0.062	−0.061
E_{CT}	−0.564	−0.645	−0.576	−1.453
E_{total}	−4.169	−4.143	−4.603	−6.049

Table IV. Energies of Interaction between Methyl Nitrite and Anions (kcal/mol)

Energies	Toluene	2-Picoline	3-Picoline	4-Picoline
E_Q	−3.462	−3.519	−3.468	−3.563
E_K	5.714	5.558	5.638	5.617
E_I	−0.625	−0.648	−0.630	−0.634
E_D	−1.260	−1.215	−1.236	−1.229
E_{CT}	−3.938	−3.507	−4.151	−3.051
E_{total}	−3.571	−3.331	−3.847	−2.860

with respect to E_{CT}. This order is inconsistent with the experimental results, but is the same as that of the CTA calculation for the step of the attack of methyl nitrite on the carbanion. The explanation discussed in connection with the CTA calculation results can also be applied to the above case.

The Binding Energies as a Measure of the Reactivity and the Acidity of Picolines and Methylpyrimidines

As shown in Table V for the binding energies, the order of stabilization of the pyridomethide anions has the following sequence, 4->2->3-picoline. In other words, 4-picoline tends to transform more easily into the 4-pyridomethide anion than the others, so its acidity is the highest.[18] The hydrogen of the methyl group of 4-picoline may therefore be most easily

Table V. Binding Energies (eV) (CNDO/2)

Compound	Neutral (A)		Anion (sp^3) (B)	Difference (B) − (A)	Anion (sp^2) (C)	Difference (C) − (A)
Toluene	−204.91		−196.29	8.62	−196.26	8.65
2-Picoline	−191.39		−182.89	8.50	−182.90	8.49
3-Picoline	−191.35		−182.75	8.60	−182.70	8.65
4-Picoline	−191.37		−183.01	8.36	−183.04	8.33
2,4-Di-Me-pyridine	−225.52	$4\text{-}CH_2^-$	−217.17	8.35	−217.20	8.32
		$2\text{-}CH_2^-$	−217.03	8.49	−217.05	8.47
2,4-Di-Me-pyrimidine	−212.09	$4\text{-}CH_2^-$	−203.97	8.12	−204.08	8.01
		$2\text{-}CH_2^-$	−203.65	8.44	−203.67	8.42

Me=CH_3.

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18) P. Birner, H.-J. Köhler, and C. Weiss, *Z. Chem.*, **11**, 117 (1971); *idem*, *ibid.*, **13**, 354 (1973); *idem*, *Chem. Phys. Lett.*, **27**, 347 (1974).

abstracted by the amide ion. When the difference of the binding energies between the neutral picoline and its anion is larger than 8.60 eV, nitrosation does not take place. In the case of a heterocycle having two different types of active methyl groups, the methyl group having the smaller difference is predominantly attacked by nitrite.

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