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Characteristic Coloration in Formation of *N*-1-Pyridinio Amidate and Enhancing Effect of Benzaldehydes

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N-Aminopyridinium iodide (NAPI) turned a bluish purple color upon the addition of NaOH. The NMR spectral data of the NAPI–NaOH system indicate that N-1-pyridinio amidate (NPA) is the species responsible for the coloration, which is probably due to intramolecular charge transfer transition. The intensity of the coloration increased remarkably with addition of benzaldehyde derivatives, especially p-nitrobenzaldehyde, to the NAPI–NaOH system. NAPI reacted with the benzaldehyde derivatives to form the corresponding Schiff bases. The mechanism of the coloration in the NAPI–NaOH–benzaldehyde derivative system is proposed to involve the formation of betaines, which can also be formed by adding NaOH to the isolated Schiff bases. Furthermore, there was a good correlation between the enhancing effects on the coloration and the redox potentials of the benzaldehyde derivatives. This indicates that benzaldehyde derivatives with an electron-withdrawing substituent group can enhance the coloration intensity much more effectively.

Keywords pyridine-*N*-imine; coloration; aldehyde; *N*-aminopyridinium iodide; redox potential

We have reported[1)] that *N*-aminopyridinium iodide (NAPI) acts as a 1,3-dipolar compound under basic reaction conditions, and is useful for syntheses of novel hetero aromatic compounds[1a)] which contain nitrogen at a bridgehead position, such as pyrazolopyridines,[2)] triazolopyridines[3)] and others,[4)] as well as for the preparation of 4-cyanopyridine.[1a)]

In all of these reactions, addition of alkali to CH_3OH solution of NAPI caused a remarkable color change of the reaction solution from pale yellow to bluish purple. The coloration was also observed when CH_3OH solution of NAPI was passed through a strong anion exchange resin column treated with alkali. In addition, the intensity of the coloration was greatly enhanced by addition of benzaldehyde derivatives to the NAPI–alkali system. The coloration mechanism has not previously been investigated.

In this paper, we propose a mechanism of the coloration and describe the enhancing effects of various benzaldehyde derivatives on the coloration.

Experimental

Materials All chemicals and solvents used were of analytical grade, obtained from Wako Pure Chemicals, Tokyo Kasei Kogyo Co., Ltd. and Daiichi Kasei Kogyo Co., Ltd. NAPI was prepared according to the method of Goesl and Meuwsen.[5)]

Measurement of Nuclear Magnetic Resonance (NMR) NMR spectra were measured after adding NaOH to NAPI dissolved in CH_3OH or CD_3OD. The apparatus used was a JEOL JNM-GX-400. Tetramethylsilane (TMS) was used as an internal standard.

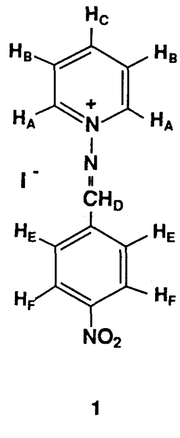

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Fig. 1. *N*-(4-Nitrobenzylideneamino)pyridinium Iodide (**1**)

Typical Procedure for Coloration of NAPI–NaOH–Benzaldehyde Derivatives System p-Nitrobenzaldehyde (0.02—0.2 μmol) in CH_3OH was added to NAPI (2 μmol) dissolved in CH_3OH (3 ml), and then NaOH (20 μmol) in H_2O was added to the mixture. The color of the mixture changed from pale yellow to bluish purple, and the visible absorption spectrum was measured at 25 °C. When NAPI was used at high concentrations the NAPI–NaOH system turned a bluish purple color by itself. However, at NAPI concentrations below 0.67 mM (<2 μmol in 3 ml of CH_3OH) and in the absence of benzaldehyde derivatives, the system turned only a faint yellow.

Measurement of Redox Potentials of Benzaldehyde Derivatives Redox potentials of benzaldehyde derivatives (3 mM) were measured in dimethyl formamide containing tetraethylammonium perchlorate as the supporting electrolyte and a saturated calomel electrode (SCE) as the reference electrode, using a Yanaco model P-1000 voltammetric analyzer, an NF circuit design block model FG-121B function generator and a Nikko Keisoku rotating ring-disk electrode RRDE-1. The sweep speed was 50 mV/s.

Reaction of NAPI with Benzaldehyde Derivatives[6)] A typical procedure is described below. p-Nitrobenzaldehyde (5 mmol) was added to NAPI (5 mmol) dissolved in CH_3OH (25 ml). The mixture was stirred for 30 min at 80 °C, then the precipitate was collected by filtration. The product was recrystallized from CH_3OH. Yield of the Schiff base **1** (Fig. 1): 38.2%, mp, 222—223 °C. IR (KBr): 1625 (C=N), 1587, 1515 (NO_2), 1465, 1373, 1346 (NO_2) cm^{-1}: *Anal.* Calcd for $C_{12}H_{10}IN_3O_2$: C, 40.56; H, 2.82; I, 35.77; N, 11.83; O, 9.01. Found: C, 40.97; H, 2.76; N, 11.82. ^1H-NMR ($CDCl_3$/TMS) δ: 8.29 (2H, dd, J=7.1, 7.7 Hz, H_B), 8.32 (2H, d, J=8.8 Hz, H_E), 8.48 (2H, d, J=8.8 Hz, H_F), 8.72 (1H, t, J=7.7 Hz, H_C), 9.30 (2H, d, J=7.1 Hz, H_A), 9.35 (1H, s, H_D).

Results and Discussion

Coloration upon Formation of NPA NAPI turned a bluish purple color with the addition of NaOH, showing its absorption spectra (λ_{max} = 516 nm, ε = 31).

The mechanism of the coloration was examined using NMR spectroscopy. Figure 2 shows the NMR spectral change of NAPI with various concentrations of NaOH in CH_3OH. All signals shifted to a higher magnetic field, and those assigned to the proton (H_C) at the 4-position of NAPI showed a particularly large shift from 8.37 to 6.99 (δ value/TMS). NMR spectra of NAPI were also measured in CD_3OD solution with or without NaOH (Fig. 3). The signals assigned to the proton (H_A) at the 2-position disappeared with addition of NaOH (Fig. 3b). These phenomena were not observed in CH_3OH solution, and indicate that the hydrogen atoms (H_A) at the 2-position can be exchanged for the deuterium atoms of the NMR solvent.

We have found[7)] that a pyridine ring of a betaine can be attacked by electrophiles as shown in the nitration by HNO_3–H_2SO_4.

We have also reported[1a)] that NAPI reacts with dienophiles such as olefins, acetylenes and cyanides under basic conditions to form novel heteroaromatic compounds containing nitrogen at a bridgehead position *via* 1,3-dipolar cycloaddition.

The results presented above suggest the formation of *N*-1-pyridinio amidate (NPA) in the NAPI–NaOH system. That is, the shift to higher magnetic field of the signal of

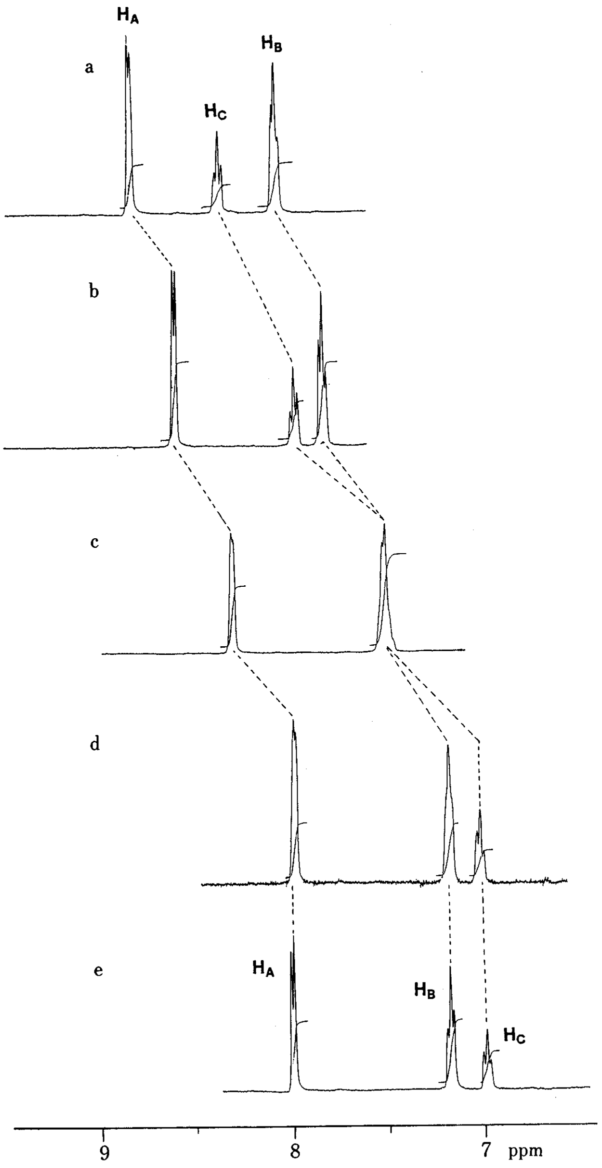

Fig. 2. NMR Spectra of NAPI with Various Concentrations of NaOH in CH_3OH

NAPI 0.2 mmol; and NaOH, a) 0 mmol, b) 0.1 mmol, c) 0.3 mmol, d) 1 mmol, e) 2 mmol.

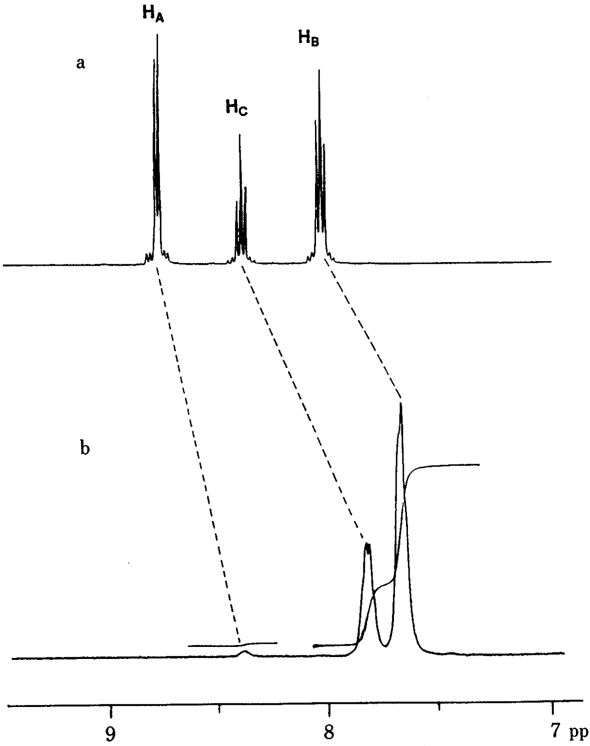

Fig. 3. NMR Spectra of NAPI with or without NaOH in CD_3OD

a) NAPI, 0.2 mmol; NaOH, 0 mmol; b) NAPI, 0.2 mmol; NaOH, 0.2 mmol.

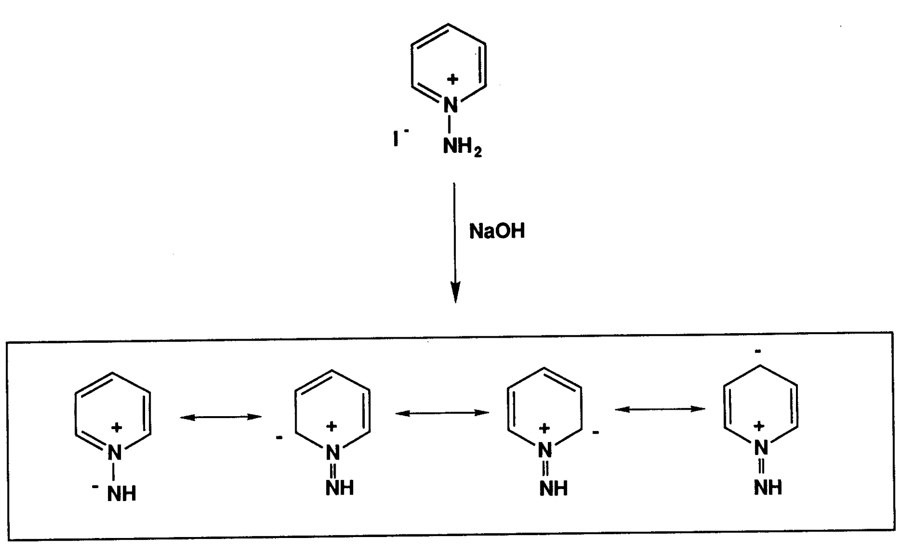

Fig. 4. Resonance Forms of the Betaine, NPA

the proton at the 4-position of NAPI can be explained by back-donation of the *N*-imine group. The betaine, NPA, has some resonance forms as shown in Fig. 4. The NMR signals assigned to the protons on the pyridine ring of NPA would be shifted to higher magnetic field than those assigned to protons on the ring of NAPI. The shift is due to the electron density of the pyridine ring of NPA being richer than that of NAPI. The substitution reactions and 1,3-dipolar cycloaddition can also support the formation of NPA in the NAPI–NaOH system. NPA appears to react readily with electrophiles in the same manner as pyridine-*N*-oxide.[8)]

In conclusion, the betaine, NPA, was suggested to be formed in the NAPI–NaOH system and to be responsible for the coloration.

Ingold and Jessop[9)] also have reported a strong purple color of a solution of 9-fluorenyltrimethylammonium hydroxide which they attributed to the ylide structure **2** (Fig. 5). Kosower and Kawsey[10)] reported the coloration behavior of the ylide, pyridinium cyclopentadienylide **3** (Fig. 5), and concluded the coloration to be due to intramolecular charge transfer transition. These results are consistent with the hypothesis that an electronic transition of the betaine, NPA, is responsible for the coloration.

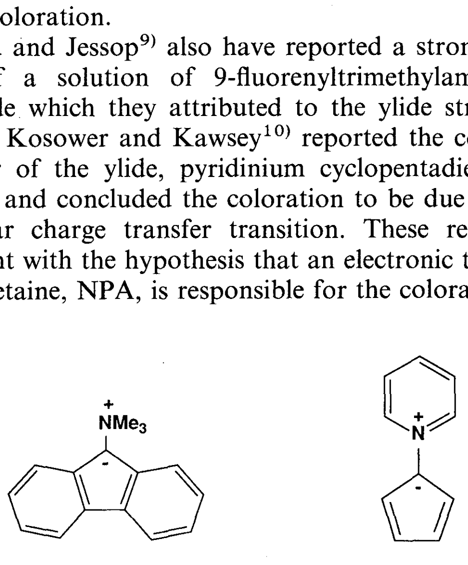
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Fig. 5. Structures of 9-Fluorenyl Trimethylammonium Hydroxide (**2**), and Pyridinium Cyclopentadienylide (**3**)

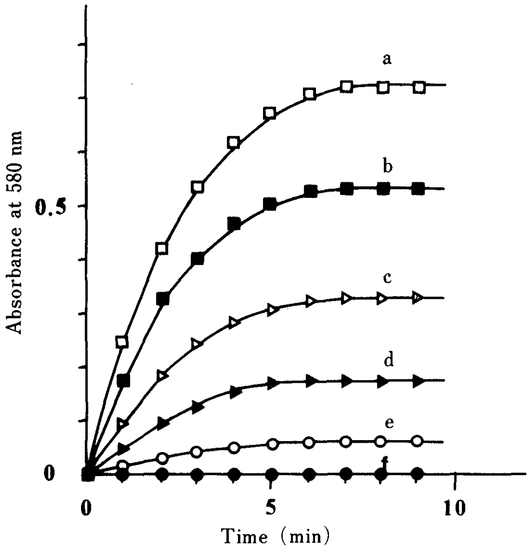

Fig. 6. Time-Course of Absorbance Change in the NAPI–NaOH–*p*-Nitrobenzaldehyde System in CH_3OH

a) NAPI, 0.67 mM; NaOH, 6.7 mM; *p*-nitrobenzaldehyde, 67 μM; b) NAPI, 0.67 mM; NaOH, 6.7 mM; *p*-nitrobenzaldehyde, 50 μM; c) NAPI, 0.67 mM; NaOH, 6.7 mM; *p*-nitrobenzaldehyde, 33 μM; d) NAPI, 0.67 mM; NaOH, 6.7 mM; *p*-nitrobenzaldehyde, 17 μM; e) NAPI, 0.67 mM; NaOH, 6.7 mM; *p*-nitrobenzaldehyde, 7 μM; f) NAPI, 0.67 mM; NaOH, 6.7 mM; *p*-nitrobenzaldehyde, 0 μM.

Enhancing Effects of Benzaldehyde Derivatives on the Coloration The intensity of the coloration was enhanced by adding certain compounds to the NAPI–NaOH system. We examined whether approximately 400 organic compounds have enhancing effects. All the aldehyde compounds examined except formaldehyde markedly enhanced the coloration intensity of the NAPI–NaOH system. The mechanism was examined in detail using benzaldehyde derivatives.

The NAPI–NaOH system turns the bluish purple color by itself. However, when NAPI was used at <0.67 mM, the absorbance at 516 nm (λ_{max}) was <0.01. Thus, the enhancing effects of compounds were examined under the following conditions: NAPI, 0.67 mM; NaOH, 6.70 mM; methanol, 3 ml; benzaldehyde derivative, various concentrations. Figure 6 shows the time–course of absorbance ($\lambda_{max}=580$ nm) at various concentrations (0—67 μM) of *p*-nitrobenzaldehyde after NaOH was added. The time required to reach the maximum absorbance was within 7 min. The absorbance increased linearly with the increase of the concentration of *p*-nitrobenzaldehyde. Table I shows the values of molar absorption coefficient (ε) and the wavelength of the maximum absorption (λ_{max}) obtained using various aldehydes. The coefficients were in the following order: $p\text{-NO}_2 > m\text{-NO}_2 > o\text{-Cl} > p\text{-Cl} > o\text{-OCH}_3 > p\text{-CH}_3 > p\text{-OCH}_3$. The absorption coefficient ($\varepsilon=10600$) with *p*-nitrobenzaldehyde was about 342 times as high as that ($\varepsilon=31$) without any aldehyde. The wavelength of the maximum absorption became shorter in the order shown above. *p*-Hydroxybenzaldehyde did not show significant absorbance (<0.01) within 2 h after mixing.

Reactions of NAPI with Benzaldehyde Derivatives NAPI reacted with benzaldehyde derivatives to form the corresponding Schiff bases with no bluish purple color (Fig. 7). Structures of the Schiff bases were determined by NMR, IR and elemental analysis. The reaction times were in the following order: $p\text{-NO}_2 < m\text{-NO}_2 < o\text{-Cl} < p\text{-Cl} < o\text{-OCH}_3 < p\text{-CH}_3 < p\text{-OCH}_3$, which is the same as that of the times required to reach the maximum absorbance. The Schiff bases turned the bluish purple color upon addition of NaOH. The molar absorptivity and the wavelength of the maximum absorption of the Schiff base **1**–NaOH system were identical with those in the NAPI–NaOH–*p*-nitrobenzaldehyde system. These results show that the

Table I. Molar Absorptivity and Wavelength of Maximum Absorption of the NAPI–NaOH–Benzaldehyde Derivatives System, and Redox Potentials of Benzaldehyde Derivatives

Benzaldehyde deriv. $C_6H_4(R)CHO$	ε value (λ_{max}, nm)	$E_{1/2}$ *vs.* SCE (mV)
$p\text{-NO}_2$	10600 (580)	−780
$m\text{-NO}_2$	7280 (550)	−953
o-Cl	7200 (550)	−1526
p-Cl	4960 (545)	−1607
$o\text{-OCH}_3$	3750 (540)	−1820
$p\text{-CH}_3$	2280 (540)	−1870
$p\text{-OCH}_3$	1870 (539)	−1950
p-OH	Not detectable	> −2000

The absorption spectra were measured under the following conditions: NAPI, 0.67 mM; NaOH, 6.7 mM; benzaldehyde derivative, various concentrations; CH_3OH 3 ml. The redox potentials were measured in dimethyl formamide. The sweep speed was 50 mV/s.

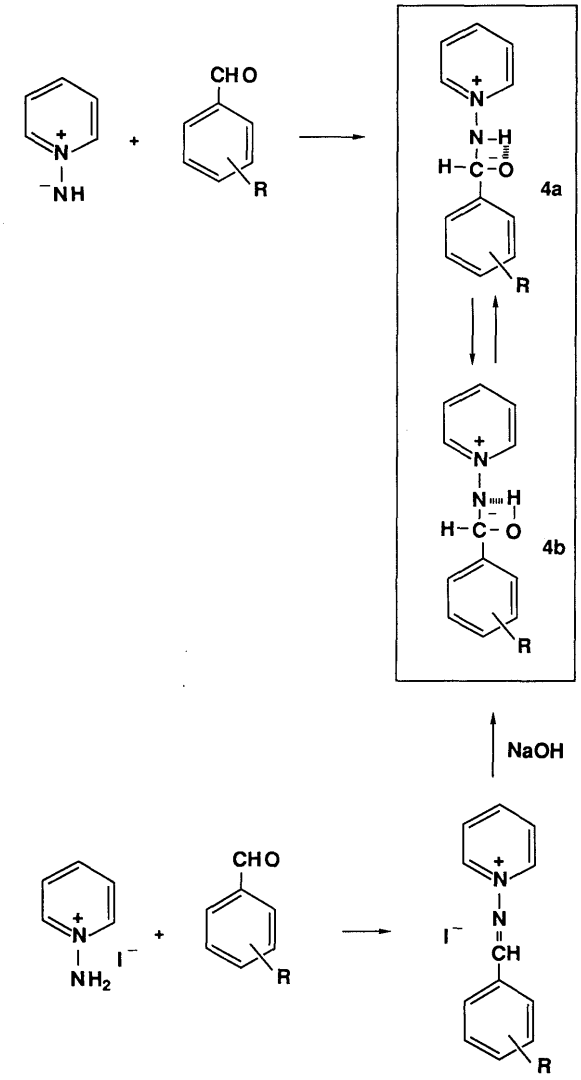

Fig. 7. Reaction of NAPI with Benzaldehyde Derivatives and Proposed Mechanism of the Coloration of the NAPI–NaOH–Benzaldehyde Derivatives System

ultimate species responsible for the coloration is the betaine **4a** or **4b**, which could also be formed *via* the Schiff base (Fig. 7).

Redox Potentials of Benzaldehydes The redox potentials of benzaldehyde derivatives were measured in dimethyl formamide. The values related well with the molar absorptivity coefficients of the benzaldehyde derivatives (Table I). The higher the redox potential, the stronger the colorlation-enhancing effect. That is, aldehydes with an electron-withdrawing substituent showed the greatest enhancement of the intensity.

NAPI turned a bluish purple color with NaOH addition, and the betaine, NPA, was suggested to be responsible for this. Aldehyde compounds enhanced the intensity of the coloration. Benzaldehyde derivatives readily reacted with NAPI to form the corresponding Schiff bases, which turned the bluish purple with NaOH. The species generated by addition of NaOH to the Schiff base was too unstable to isolate, but the molar absorptivity and the wavelength of the maximum absorption were the same as those of the compound formed in the NAPI–NaOH–benzaldehyde derivatives system. These results suggest that the betaine (**4a** or **4b** in Fig. 7) was responsible for the coloration. A nitro substituent will contribute to the stabilization of the betaine (**4**), because the nitro-substituted benzene ring is electron-deficient and allows delocalization of the anion species. Consequently, the betaine (**4**) will have a stable resonance structure and an intense absorbance at the λ_{max}. This was supported by the good correlation between the redox potentials and the coloration-enhancing effects of the benzaldehyde derivatives.

Benzylidenemalononitrile is widely used, sometimes by criminals, as a potent lachrymatory gas. Its reactivity is similar to that of benzaldehyde. The selective colorlation described above will be useful for detection of benzaldehyde analogues such as benzylidenemalononitrile. Further studies on applications of the coloration are in progress.

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