Isolation of Enammonium Salt and Its Rearrangement to the Corresponding Iminium Salt

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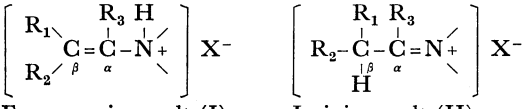
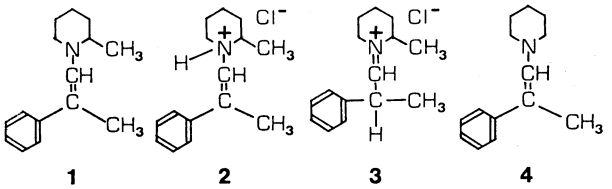
Enammonium salt of 2-methyl-1-(β-methylstyryl)piperidine (**1**) was isolated for the first time and characterized. The enammonium salt, 2-methyl-1-(β-methylstyryl)piperidinium chloride (**2**), was found to change easily to the corresponding iminium salt, 2-methyl-1-(2-phenylpropylidene)piperidinium chloride (**3**), at room temperature. The structure of the salts derived from 1-(β-methylstyryl)piperidine (**4**), 2-methyl-1-(β-methylstyryl)pyrrolidine (**5**), 1-(β-methylstyryl)pyrrolidine (**6**), 1-(2-methyl-1-propenyl)pyrrolidine (**7**), and 2-methyl-1-(2-methyl-1-propenyl)piperidine (**8**) were also examined.

Enamines are useful as a starting material for various organic syntheses, and their reactivities have been investigated by many workers.[1] One of the reactions is the formation of salts with acids. Protonation on the nitrogen or the β-carbon of the enamine to give the salt (I) or (II) is possible.

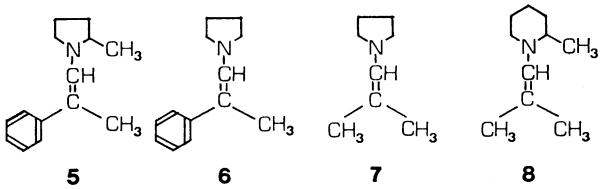


Enammonium salt (I) Iminium salt (II)

It has been shown that the protonation takes place rapidly on nitrogen and is followed by a transfer of the proton to the carbon. The evidence for *N*-protonation has been based on the reaction of ozone, diazomethane or lithium aluminum hydride with *N*-protonated salts under cooling.[2] Existence of the enammonium salt and its rearrangement to the corresponding iminium salt were also suggested kinetically.[3] However, the enamine salts so far isolated have the iminium salt structure (II).[4] This paper deals with the isolation and identification of *N*-protonated salt derived from 2-methyl-1-(β-methylstyryl)piperidine (**1**), 2-methyl-1-(β-methylstyryl)piperidinium chloride (**2**), and its rearrangement to the corresponding iminium salt (**3**). Structures of the salts derived from 1-(β-methylstyryl)piperidine (**4**),[5] 2-methyl-1-(β-methylstyryl)pyrrolidine (**5**),[6] 1-(β-methylstyryl)pyrrolidine (**6**),[5] 1-(2-methyl-1-propenyl)-pyrrolidine (**7**)[3] and 2-methyl-1-(2-methyl-1-propenyl)piperidine (**8**) were also examined.



1 **2** **3** **4**



5 **6** **7** **8**

Experimental

Proton magnetic resonance spectra were obtained with a JNM-PS-100 Spectrometer. Chemical shifts are indicated in δ value using TMS as an internal standard. The IR spectra were recorded with a JASCO IR-S Spectrometer. Gas chromatographic analyses were carried out on a 2 m column of 20% Carbowax 20 M on Cromosorb W with a Hitachi Gas Chromatograph, Model K 53.

Materials. Enamines, **1**, **4**, **5**, **6**, **7**, and **8** were prepared by the usual azeotropic procedures with benzene as a solvent. **8**; bp 66.5—67 °C (17 Torr).

Preparation of the Salts. The preparation of the salts was carried out as follows. Dry hydrogen chloride gas was bubbled into a benzene solution (60 ml) of each enamine (0.1 mol) under cooling in an ice–salt bath. White very fine needles precipitated out gradually. The needles were separated from the solution by filtration, washed with benzene completely in a dry box, and dried under vacuum. The data of PMR spectra and IR spectra are summarized in Tables 1 and 2, respectively.

PMR Spectra of Enamines and Their Salts. The solutions for PMR spectral measurements were prepared by dissolving about 30 mg of the enamines or their salts in 0.5 ml CD_3OD or $CDCl_3$ in a dry box. They are easily soluble in both solvents. The spectra of the salts were obtained immediately after preparation of the samples.

Results and Discussion

The salts derived from **1**, **4**, **5**, and **6** are highly hydroscopic and decompose into 2-phenylpropanal and the amine hydrochlorides on exposure to air. No elemental analyses of these salts could be carried out. The salts were hydrolyzed and the resulting 2-phenylpropanal was estimated gas-chromatographically. (The 2-phenylpropanal obtained from the hydrolyzates of the salts: 0.93 mol/1 mol salt of **1**, 0.91 mol/1 mol salt of **4**, 0.97 mol/1 mol salt of **5**, 0.95 mol/1 mol salt of **6**). The results show that one mol of 2-phenylpropanal is obtained from one mol of each salt within experimental error.

PMR spectra of **1**, **2**, and **3** in CD_3OD and those of **2** and **3** in $CDCl_3$ are shown in Fig. 1. The spectrum of **1** in $CDCl_3$ was essentially the same as that of **1** in CD_3OD.

Two olefin proton signals (5.75 and 5.99 ppm) and

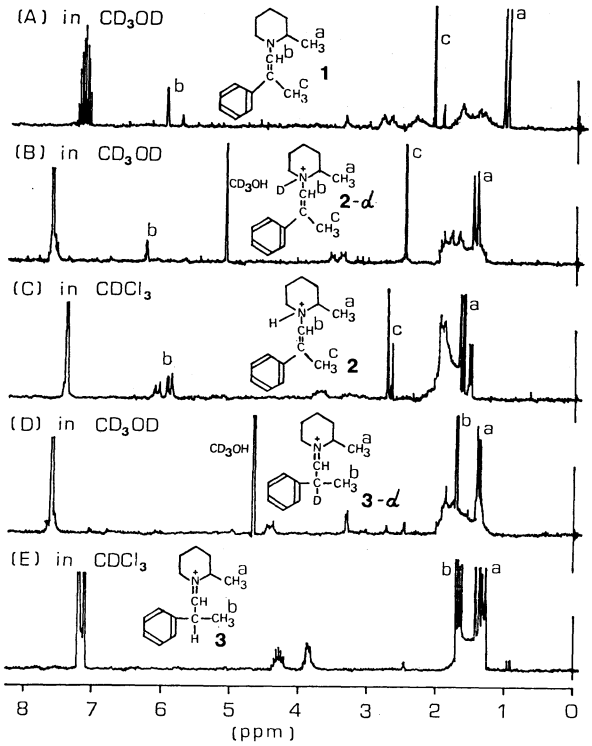
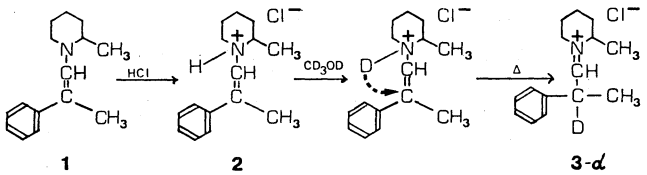


Fig. 1. 100 MHz PMR spectra of **1**, **2**, and **3** in CD_3OD or $CDCl_3$.

two propenyl methyl proton signals (1.95 and 2.10 ppm) were observed (Fig. 1-(A)). The area ratio of the former signals 5.75 ppm: 5.99 ppm is 8: 92, coinciding with that of the latter 1.95 ppm: 2.10 ppm (10: 90). This shows that **1** is a mixture of two geometrical isomers, one of which predominantes over the other. The existence ratio of the isomers in $CDCl_3$ is essentially the same as that in CD_3OD. The predominant one seems to have a structure where the phenyl and the 2-methylpiperidino groups are situated in trans position to each other judging from the steric models of the two geometrical isomers. Allyl couplings (1.5 Hz) are observed between the corresponding olefin and methyl protons. The allyl coupling constant, 1.5 Hz, was also observed between the olefin proton (6.27 ppm) and the propenyl methyl protons (2.48 ppm) (Fig. 1-(B)). This shows that **2** has the same partial structure, N–CH=C–CH_3, as enamine, **1**. The propenyl methyl signals at 2.10 ppm in spectrum (A) shift toward lower field, 2.48 ppm, in spectrum (B). This also supports the partial structure of the enammonium salt, N^+H–CH=C–CH_3. The occurrence of the proton exchange between CD_3OD and N^+H–CH=C–CH_3 or HCl is shown by the appearance of the signal at 5.10 ppm assignable to CD_3OH in spectrum (B). The hydrochloric acid might be derived from that of crystallization. The PMR signals of the two geometrical isomers in CD_3OD are considered to completely overlap each other, because of the existence of the isomers as shown in Fig. 1-(C). The existence ratio of the geometrical isomers was determined as 2: 3 based on the area ratio of the respective signals. This suggests that the formation of the enammonium salt is accompanied by geometrical isomerization. The isomerization was also observed in the case of **4**.[5] The signal of the olefin proton seems to be the A part of a nearly pure first-order AMX_3 pattern; major isomer (J=8.0, 1.2 Hz), minor isomer (J=9.1, 1.5 Hz). The coupling constant, 1.2 or 1.5 Hz, is due to the allyl coupling between the olefin proton and the propenyl methyl protons. The coupling constant, 8.0 or 9.1 Hz, may be due to the coupling between this olefin proton and the proton attached to the nitrogen atom. The major one seems to have a structure in which the phenyl and the 2-methylpiperidino groups are situated in trans position to each other. The smaller allyl coupling constant of the major isomer (1.2 Hz) suggests that the propenyl methyl group is situated in trans position of the olefin proton, because J_{cisoid} is usually larger than $J_{transoid}$.[7]

When the CD_3OD solution of **2** was heated up to 50 °C, the signals of the PMR spectrum of **2** (spectrum B) changed to those of **3** in a CD_3OD solution (Fig. 1-(D)). The methyl proton signal at 2.48 ppm in spectrum B is shifted to the higher field (at 1.70 ppm) in spectrum D. This suggests that the enammonium structure, CH_3–C=C–$\overset{+}{N}$–, was converted in solution into the iminium structure, CH_3–C–C=$\overset{+}{N}$. The signal at 1.70 ppm was singlet, and no allyl coupling could be observed, indicating that **3** in CD_3OD had been deuterated at the β-carbon. This shows that **2** is easily deuterated in CD_3OD to the N-deuterated salt which is subsequently rearranged to the corresponding iminium salt. The sequence of the reactions (Scheme 1) is in line with the generally accepted mechanism of the iminium salt formation.



Scheme 1.

In the case of a $CDCl_3$ solution, the signals of the PMR spectrum of **2** (Fig. 1-(C)) also changed to those of **3** (Fig. 1-(E)).[8] Addition of CD_3OD to the $CDCl_3$ solution of **2** is recognized to accelerate the rearrangement, giving **3-d** (Fig. 1-(D)). Possibility of the existence of two geometrical isomers of **3** can be neglected by consideration of the steric interaction using models (Corey-Pauling-Kaltum type and Dreiding type).[6] PMR spectra of the salts derived from **4** and **5** were also obtained. As shown in Table 1, the produced salts have the iminium salt structures. Bubbling of dry hydrogen chloride gas into the solution of **4** or **5** under cooling also gave the corresponding enammonium salts although their amounts were much smaller in comparison with those of the iminium salts.

From the PMR spectral data of the enamines and their salts, **1**—**8** (Table 1), we see that the salts except for **2** have an iminium salt structure.

The complex bands observed in 2350—2600 cm^{-1} in the IR spectrum of **2** were assignable to the ammonium

Table 1. PMR Spectral data of enamines, enammonium and iminium salts (in $CDCl_3$)

1	major: 1.03 (d, J=6.70 Hz, N-CH-C$\underline{H}_3$), 2.10 (d, J=1.5 Hz, CH=C-C$\underline{H}_3$), 5.99 (d, J=1.5 Hz, C$\underline{H}$=C-CH_3), minor: 1.09 (d, J=6.70 Hz, N-CH-C$\underline{H}_3$), 1.95 (d, J=1.5 Hz, CH=C-C$\underline{H}_3$), 5.75 (d, J=1.5 Hz, C$\underline{H}$=C-CH_3).
2	major: 1.63 (d, J=6.0 Hz, $\overset{+}{N}$H-CH-C$\underline{H}_3$), 2.72 (d, J=1.2 Hz, CH=C-C$\underline{H}_3$), 5.90 (dq, J=8.0, 1.2 Hz, C$\underline{H}$=C-CH_3), minor: 1.51 (d, J=6.0 Hz, $\overset{+}{N}$H-CH-C$\underline{H}_3$), 2.66 (d, J=1.5 Hz, CH=C-C$\underline{H}_3$), 6.09 (dq, J=9.1, 1.5 Hz, C$\underline{H}$=C-CH_3).
3	major: 1.40 (d, J=7.0 Hz, $\overset{+}{N}$-CH-C$\underline{H}_3$), 1.69 (d, J=7.5 Hz, CH-CH-C$\underline{H}_3$), 9.00 (m, $\overset{+}{N}$=C$\underline{H}$-C), minor: 1.29 (d, J=6.5 Hz, $\overset{+}{N}$-CH-C$\underline{H}_3$), 1.66 (d, J=7.5 Hz, CH-CH-C$\underline{H}_3$), 9.08 (m, $\overset{+}{N}$=C$\underline{H}$-C).
4	major: 2.09 (d, J=1.2 Hz, CH=C-C$\underline{H}_3$), 6.11 (d, J=1.2 Hz, C$\underline{H}$=C-CH_3), minor: 1.97 (d, J=1.6 Hz, CH=C-C$\underline{H}_3$), 5.82 (d, J=1.6 Hz, C$\underline{H}$=C-CH_3).
Salt of **4**	1.46 (d, J=7.0 Hz, CH-CH-C$\underline{H}_3$), 9.65 (m, $\overset{+}{N}$=C$\underline{H}$-C).
5	major: 1.17 (d, J=6.3 Hz, N-CH-C$\underline{H}_3$), 2.15 (d, J=1.3 Hz, CH=C-C$\underline{H}_3$), 6.40 (d, J=1.3 Hz, C$\underline{H}$=C-CH_3), minor: 1.17 (d, J=6.3 Hz, N-CH-C$\underline{H}_3$), 2.04 (d, J=1.5 Hz, CH= C-C$\underline{H}_3$), 6.11 (d, J=1.5 Hz, C$\underline{H}$=C-CH_3).
Salt of **5**	major: 1.55 (d, J=7.0 Hz, $\overset{+}{N}$-CH-C$\underline{H}_3$), 1.80 (d, J=7.5 Hz, -CH-C$\underline{H}_3$), 8.86 (m, $\overset{+}{N}$=C$\underline{H}$-C), minor: 1.55 (d, J=7.0 Hz, $\overset{+}{N}$-CH-C$\underline{H}_3$), 1.78 (d, J=6.5 Hz, -CH-C$\underline{H}_3$), 8.86 (m, $\overset{+}{N}$=C$\underline{H}$-C).
6	major: 2.07 (d, J=1.2 Hz, CH=C-C$\underline{H}_3$), 6.38 (d, J=1.2 Hz, C$\underline{H}$=C-CH_3), minor: 1.95 (d, J=1.6 Hz, CH=C-C$\underline{H}_3$), 6.07 (d, J=1.6 Hz, C$\underline{H}$=C-CH_3).
Salt of **6**	1.80 (d, J=7.5 Hz, -CH-C$\underline{H}_3$), 9.76 (m, $\overset{+}{N}$=C$\underline{H}$-C).
7	major: 1.75 (s, -C$\underline{H}_3$), 5.67 (m, C$\underline{H}$=C-CH_3), minor: 1.68 (s, -C$\underline{H}_3$), 5.67 (m, C$\underline{H}$=C-CH_3).
Salt of **7**	1.32 (C-C$\underline{H}_3$), 8.15 (d, J=9.0 Hz, $\overset{+}{N}$=C$\underline{H}$-).
8	mixture of two geometrical isomers (1: 1) 0.97 (d, J=6.2 Hz, N-C-C$\underline{H}_3$), 1.67 (d, J=1.6 Hz, C=C-C$\underline{H}_3$), 1.72 (d, J=1.4 Hz, C= C-C$\underline{H}_3$), 5.24 (m, N-C$\underline{H}$=C).
Salt of **8**	1.37 (d, J=6.8 Hz, $\overset{+}{N}$-C-C$\underline{H}_3$), 1.61 (d, J=7.2 Hz, $\overset{+}{N}$=C-C-C$\underline{H}_3$), 9.14 (d, J=8.0 Hz, $\overset{+}{N}$=C$\underline{H}$).

structure, N^+–H. In the case of nicotine hydrochloride, it was reported that the band attributable to the ammonium structure was observed in the region of 2350—2440 cm^{-1}.[9] The IR spectrum of **3** was obtained after concentration of its $CDCl_3$ solution. The absorption band, 1637 cm^{-1}, due to the double bond stretching of the enamine shifts by 21 and 34 cm^{-1} toward higher frequencies in those of **2** and **3**, respectively. Leonard and Gash reported a shift of 20—50 cm^{-1} toward higher frequencies when an enamine was converted into its iminium salt.[4] The salts derived from enamines except for **2** have an iminium salt structure, since the band due to ν_{NH} connot be observed in the spectra of these salts (Table 2).

Table 2. Infrared frequencies of enamines, enammonium and iminium salts

	$\nu_{C=C}$	$\nu_{C=N}$	ν_{N-H}	Lit
1	1637			
2	1658		2350—2600	
3		1671		
4	1637			
Salt of **4**		1677		
5	1631			6
6	1633			
Salt of **6**		1679		
7	1672			2
Salt of **7**		1715		10
8	1675			
Salt of **8**		1690		
Nicotine HCl			2353—2439	9
Nicotine 2HCl			2353—2439	9

It seems that the enammonium salt is too labile to be isolated. Salt **2** seems to be the first case of the isolation of the enammonium salt. Preparation of the salts of **4**, **5**, and **6** under cooling also gave the enammonium salts although their contents were low. This shows that **4**, **5**, and **6** as well as **1** have a possibility of giving their corresponding enammonium salt. No enammonium salts could be detected in the salts derived from **7** and **8**. The stability of the enammonium salt can be attributed to the conjugation of the C=C double bond with benzene ring. The salt isolated as crystals derived from **1** was enammonium salt **2**, and iminium salt **3** could be obtained as the product of the rearrangement of **2**. On the other hand, the salts of **4**, **5**, and **6** isolated as crystals were iminium salts. It seems that enammonium salt of **1** is sparingly soluble in benzene, but those of **4**—**5** are readily soluble and subsequently converted into the corresponding less soluble iminium salts. Thus, it is concluded that in the case of the salt of **1**, rearrangement from **2** to **3** would be interfered by the immediate precipitation of **2** out of the solution. This may be the reason why the salt derived from **1** has the enammonium salt structure.

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