UDC 547.94.02 : 547.833.6 : 543.422.4

# 35. Yoshio Ban, Osamu Yonemitsu, and Masanao Terashima : Preliminary Studies on the Stereochemistry of Emetine. II.[1] Ultraviolet and Infrared Absorption Spectra of 3,4-Dihydroisoquinoline and its Homologs.*1

(*Pharmaceutical Institute, Medical School, University of Hokkaido**2)

In the preceding paper,[1] it was shown that (−)-2′-acylemetines are dehydrogenated with mercuric acetate in dilute acetic acid to 2′-acyl-5,11b-dehydroemetines which are useful compounds for the stereochemical arguments of tricyclic system of emetine.

The present work is a systematic survey on ultraviolet and infrared absorption characteristics of 3,4-dihydroisoquinolines and their related compounds, which was particularly effective for the assignment of the dehydro compounds given above. These compounds were synthesized by original methods or following methods given in the literature, which are listed in Tables I, II, and III along with their ultraviolet and infrared absorption spectral data.

Considerable work was conducted in the past on the ultraviolet[2] and infrared[3] absorption spectra of 3,4-dihydroisoquinolines, which were described separately for the purpose of characterization or identification in synthetic studies and determination of chemical structure. Here they are arranged and discussed mainly from the effect of i) dimethoxyl substituent attached to the aromatic ring, ii) B-ring formation, iii) 1-alkyl substituent, iv) salt formation, and v) C-ring formation. In the infrared absorption spectra the $\nu_{C=N}$ band is particularly noted.

## Results and Discussion

In the infrared absorption spectra of (IV), (V), (V′), (V″), and (VI) series involving dimethoxyl substituents attached to the aromatic ring, four rather intense bands are observed in the region of 1700～1500 $cm^{-1}$, which are present at 1659～1624, ca. 1600, ca. 1575, and ca. 1510 $cm^{-1}$, as shown by (1) in Fig. 1.

When these compounds were hydrogenated to the corresponding 1,2,3,4-tetrahydroisoquinolines, two bands at 1659～1624 and ca. 1575 $cm^{-1}$ disappeared as shown by (2) in Fig. 1, which means that one of the two is the $\nu_{C=N}$ band, but it is impossible to decide only by this hydrogenation which represents the C=N stretching vibration. In order to obtain further information about the $\nu_{C=N}$ band, the effect of salt formation (protonation and/or quaternization) of 3,4-dihydroisoquinolines was examined. Thus, the band at 1624 $cm^{-1}$ in 6,7-dimethoxy-3,4-dihydroisoquinoline was found to shift to 1659 $cm^{-1}$ when it was converted to the corresponding methiodide, but the other three bands remained unchanged, as shown in Fig. 2, which means that the shift from 1624 to 1659 $cm^{-1}$ corresponds to the change from $-CH=N-$ to $-CH=\overset{+}{N}H-$ and the band at 1575 $cm^{-1}$, as well as

---

*1 This work was presented as a paper at the Hokkaido Local Meeting of the Pharmaceutical Society of Japan, July 20, 1958.

*2 Kita-12-jo, Nishi-5-chome, Sapporo, Hokkaido (伴 義雄, 米光 宰, 寺島正直).

1) Part I : This Bulletin, 8, 183(1960).

2) *a*) J. L. Bills, C. R. Noller : J. Am. Chem. Soc., **70**, 957(1948). *b*) C. R. Noller, M. Azima : *Ibid.*, **72**, 17(1950). *c*) H. T. Openshaw, H. C. S. Wood : J. Chem. Soc., **1952**, 39. *d*) M. Murayama: This Bulletin, **6**, 186(1958).

3) B. Witkop, J. B. Patrick : J. Am. Chem. Soc., **75**, 4474(1953); B. Witkop : J. Am. Chem. Soc., **78**, 2873(1956).

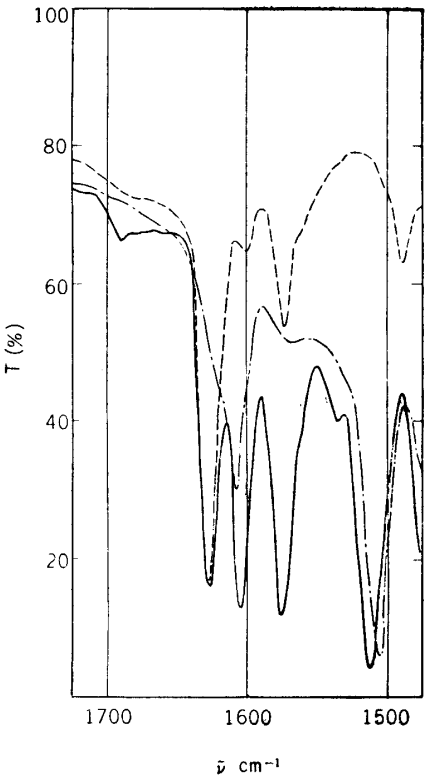



Fig. 1. Infrared Absorption Spectra

(1) ——— 1-Ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline (V c)

(2) —•—•— 1-Ethyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline

(3) ---------- 1-Ethyl-3,4-dihydroisoquinoline (II c)

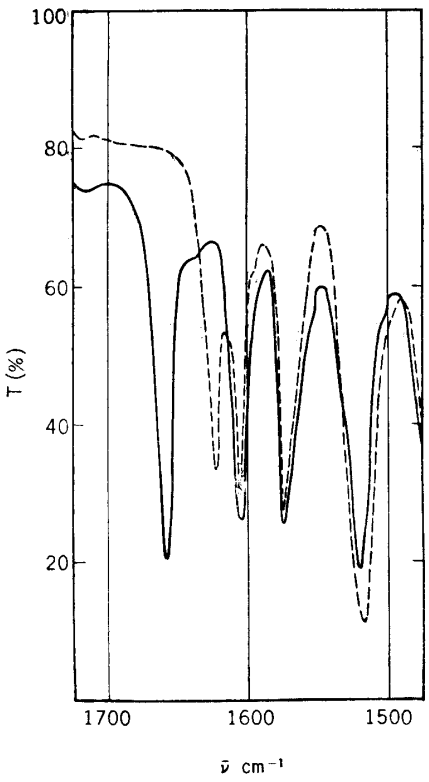



Fig. 2. Infrared Absorption Spectra

(1) ------ 6,7-Dimethoxy-3,4-dihydroisoquinoline (V a)

(2) —— 6,7-Dimethoxy-3,4-dihydroisoquinoline methiodide(V″a)

Table I. Ultraviolet Absorption Maxima

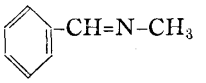
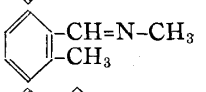
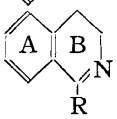
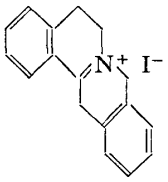
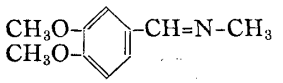
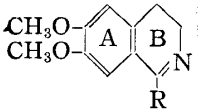
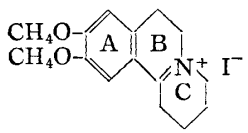
| Compound | Free base No. | Free base K-band $\lambda_{max}^{EtOH}$ mμ (log ε) | Hydrochloride No. | Hydrochloride K-band $\lambda_{max}^{EtOH}$ mμ (log ε) | Methiodide No. | Methiodide K-band $\lambda_{max}^{EtOH}$ mμ (log ε) |
|---|---|---|---|---|---|---|
|  | (Ia) | 245(4.21) | | | | |
|  | (Ib) | 249(4.08) | | | | |
|  (II) | | | | | | |
| R=H- | (IIa) | 254(3.95) | | | (II″a) | 284(4.16) |
| R=$CH_3$- | (IIb) | 249(3.90) | (II′b) | 274(4.02) | | |
| R=$C_2H_5$- | (IIc) | 249(3.90) | | | | |
| R=$n$-$C_3H_7$- | (IId) | 250(3.91) | | | | |
| R=$C_6H_5CH_2$- | (IIe)[1] | 254(4.02) | (II′e) | 273(3.90) | (II″e)[1] | 282(4.09) |
|  | | | | | (III)[1] | 286(4.07) |

Table II. Ultraviolet Absorption Maxima

| Compound | Free base No. | Free base $\lambda_{max}^{EtOH}$ mμ (log ε) E-band | Free base K-band | Hydrochloride No. | Hydrochloride E-band | Hydrochloride K-band | Methiodide No. | Methiodide E-band | Methiodide K-band |
|---|---|---|---|---|---|---|---|---|---|
|  | (IV) | 226(4.24) | 267(4.07)<br>300(3.97) | | | | | | |
|  (V) | | | | | | | | | |
| R=H | (Va) | 230(4.39) | 278(3.85)<br>310(3.85) | (V′a) | 237(4.07)<br>245(4.05) | 308(3.84)<br>360(3.70) | (V″a) | 248(4.33) | 308(4.05)<br>360(4.05) |
| R=$CH_3$ | (Vb) | 227(4.41) | 272(3.89)<br>308(3.84) | | | | | | |
| R=$C_2H_5$ | (Vc)[1] | 228(4.36) | 272(3.84)<br>308(3.77) | | | | | | |
| R=$n$-$C_3H_7$ | (Vd)[1] | 228(4.37) | 271(3.86)<br>307(3.82) | (V′d) | 232(4.14)<br>243(4.10) | 304(3.89)<br>352(3.77) | (V″d)[1] | 247(4.29) | 306(4.01)<br>356(4.04) |
|  | | | | | | | (VI)[1] | 244(4.26) | 302(3.96)<br>349(4.00) |

the other two, is due to the C=C skeletal in-plane vibration.

In a similar way, the band between 1661 and 1620 $cm^{-1}$ in (I), (II), (II′), (II″), and (III), possessing no substituent in the aromatic ring, can be interpreted as the C=N stretching vibration, one example of which is shown in Fig. 3. These data give support to the position for the C=N stretching vibration as listed in Table III.

i) Effect of Dimethoxyl Substituents in the Aromatic Ring (Table IV)—The ultraviolet absorption spectra of (Ia, b) and (IIa, b, c) are given in Figs. 4 and 5. In this series, there is only one maximum (log ε 3.90~4.21) at 245~254 mμ, which is perhaps the K-band due

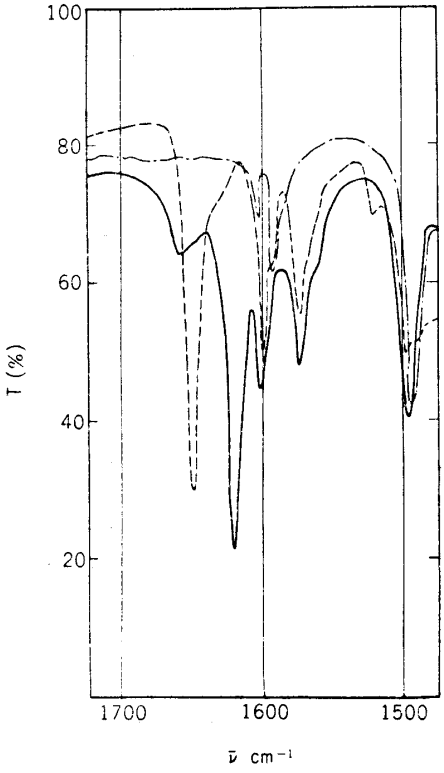



Fig. 3. Infrared Absorption Spectra

(1) ———— 1-Benzyl-3,4-dihydroisoquinoline (IIe)

(2) ---------- 1-Benzyl-3,4-dihydroisoquinoline hydrochloride (II'e)

(3) —•—•— 1-Benzyl-1,2,3,4-tetrahydroisoquinoline

TABLE III. $\nu_{C=N}$ Bands in the Infrared Absorption Spectra[a)]

| Free base | | Hydrochloride | | Methiodide | |
|---|---|---|---|---|---|
| No. | $cm^{-1}$ | No. | $cm^{-1}$ | No. | $cm^{-1}$ |
| (Ia) | 1647[b)] | | | | |
| (Ib) | 1643[b)] | | | | |
| (IIa) | 1622[b)] | | | (II''a) | 1661 |
| (IIb) | 1628[b)] | (II'b) | 1659 | (II''b) | 1638 |
| (IIc) | 1627[b)] | | | (II''c) | 1633 |
| (IId) | 1625[b)] | | | (II''d) | 1630 |
| (IIe)[1)] | 1620[b)] | (II'e) | 1650 | (II''e)[1)] | 1629 |
| | | | | (III)[1)] | 1639 |
| (IV) | 1644 | | | | |
| (Va) | 1624 | (V'a) | 1644 | (V''a) | 1659 |
| (Vb) | 1626 | | | (V''b) | 1630 |
| (Vc)[1)] | 1626 | | | (V''c) | 1628 |
| (Vd)[1)] | 1627 | (V'd) | 1644 | (V''d)[1)] | 1626 |
| | | | | (VI)[1)] | 1641 |

*a*) As Nujol mull unless otherwise stated.
*b*) Obtained on a thin film of the analytically pure liquid.

to the conjugation of C=N bond with the aromatic ring, and the E-band presumably lies below 220 mμ. When dimethoxyl groups are present in the aromatic ring of 3,4-dihydroisoquinolines, there are characteristic maxima at 226~230 (log ε 4.24~4.41), 267~278 (log ε 3.84~4.07), and 300~310 mμ (log ε 3.77~3.99) as shown in Fig. 6.

The very intense maximum at 226~230 mμ is not observed in the spectra of (I) and (II) series, and this is perhaps the E-band shifted bathochromically due to the presence of the dimethoxyl groups. Also the K-band seems to be divided into two maxima, at 267~278 and 300~310 mμ, due to the effect of the dimethoxyls, which means that they have made a bathochromic shift by 21~24 and 55~76 mμ, respectively, from $\lambda_{max}$ ca. 250 mμ, the K-band for compounds of (I) and (II) series. In infrared absorption spectra, the

Table IV. Effect of Dimethoxyl Substituted in the Aromatic Ring

| | UV $\Delta\lambda$(mμ) K-band | IR $\Delta\bar{\nu}$(cm$^{-1}$) ($\nu_{C=N}$ band) |
|---|---|---|
| ( IV )—( Ia ) | 22<br>55 | −3 |
| (V a)—(II a) | 24<br>56 | 2 |
| (V b)—(II b) | 23<br>59 | −2 |
| (V c)—(II c) | 23<br>59 | −1 |
| (V d)—(II d) | 21<br>57 | 2 |
| (V″a)—(II″a) | 24<br>76 | −2 |
| (V″b)—(II″b) | | −8 |
| (V″c)—(II″c) | | −5 |
| (V″d)—(II″d) | | −4 |

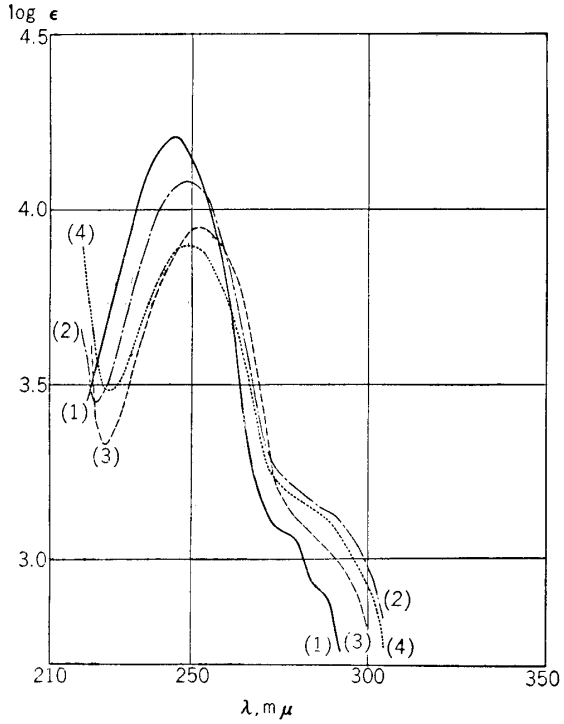



Fig. 4.

Ultraviolet Absorption Spectra

(1) ———— N-Benzylidene-methylamine (Ia)

(2) —•—•— N-(*o*-Methylbenzylidene)-methylamine (Ib)

(3) -------- 3,4-Dihydroisoquinoline (IIa)

(4) ..... 1-Ethyl-3,4-dihydroisoquinoline (IIc)

C=N stretching absorption band appears at a slightly lower frequency, as shown in Table III, than the position of ordinary one (1690~1640 cm$^{-1}$).[4]

In compounds (I), (II), (II′), (II″), and (III), the $\nu_{C=N}$ band appears as the most intense of all absorption bands in each of them. With the dimethoxyl derivatives (IV, V, V′, V″, and VI), these substituents cause an intensification not only in the $\nu_{C=N}$ absorption band, but also to a much greater extent in the aromatic bands at ca. 1600, 1575, and 1510 cm$^{-1}$. Additionally, as the strong absorption bands of aralkyl ether occur at ca. 1250, 1150, and 1030 cm$^{-1}$,[5] the relative intensity of C=N absorption is median of all of the bands, one example of which is seen in Fig. 1.

4) L.J. Bellamy, "The Infra-red Spectra of Complex Molecules," 263 (1958). Methuen & Co., London.
5) L.H. Briggs, L.D. Colebrook, H.M. Fales, W.C. Wildman : Anal. Chem., **29**, 904(1957).

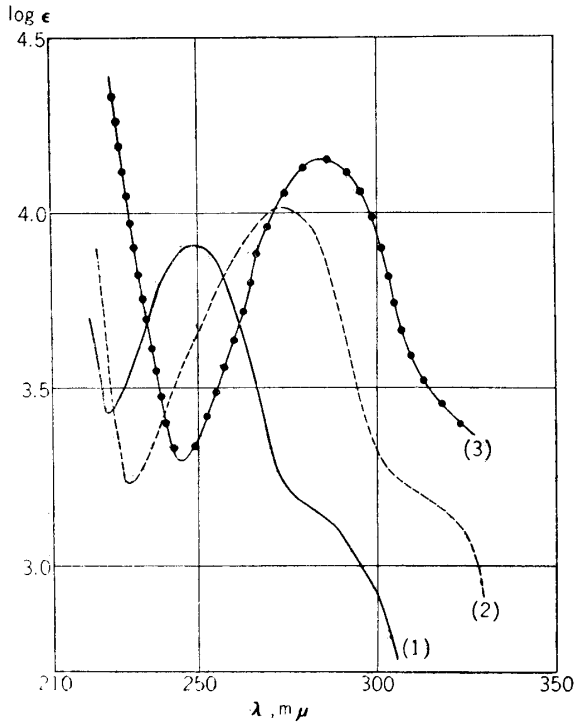



Fig. 5.
Ultraviolet Absorption Spectra

(1) ———— 1-Methyl-3,4-dihydroisoquinoline (IIb)
(2) -------- (IIb) Hydrochloride (II'b)
(3) —•—•— 3,4-Dihydroisoquinoline methiodide (II"a)

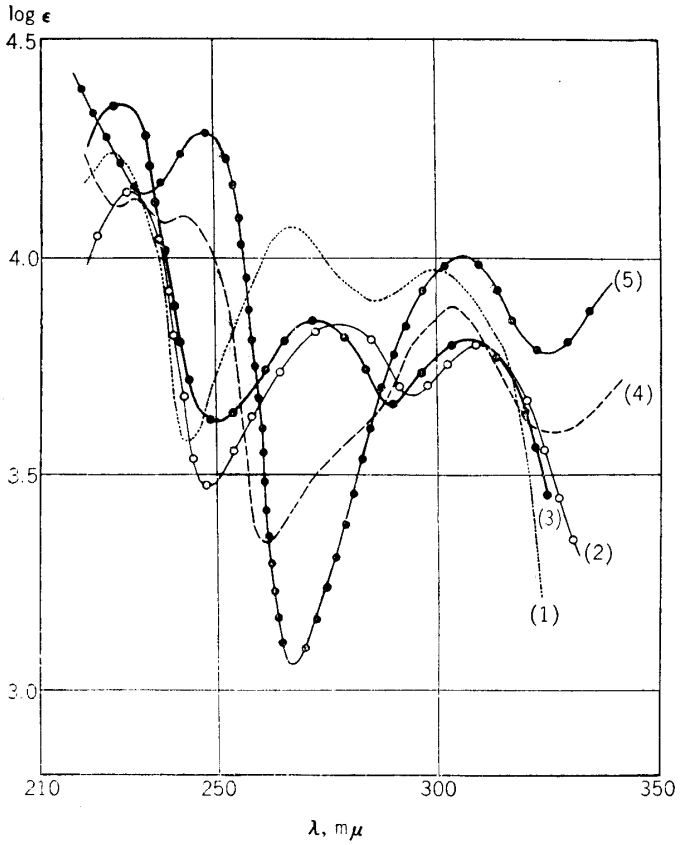



Fig. 6.
Ultraviolet Absorption Spectra

(1) ..... N-(3,4-Dimethoxybenzylidene)methylamine (IV)
(2) -o-o-o-o 6,7-Dimethoxy-3,4-dihydroisoquinoline (Va)
(3) -•-•-•-• 1-Propyl-6,7-dimethoxy-3,4-dihydroisoquinoline (Vd)
(4) -------- (Vd) Hydrochloride (V'd)
(5) —•—•— (Vd) Methiodide (V"d)

The effect of dimethoxyl groups in the aromatic ring on the position of the $\nu_{C=N}$ bands is shown in Table IV. According to the calculation of $\Delta\bar{\nu}$ $cm^{-1}$, the bands have a tendency to lie at a slightly lower frequencies, but there are some exceptions (i.e. Va and Vd). Thus, it is very difficult to find the rule of shift in these cases, and this suggests that vinylogy is more complicated in the infrared than in the ultraviolet absorption spectra.

Table V. Effect of B-Ring Formation

| | UV $\Delta\lambda$(mμ) | | IR $\Delta\bar{\nu}$($cm^{-1}$) ($\nu_{C=N}$ band) |
|---|---|---|---|
| | E-band | K-band | |
| (IIa)—(Ia) | | 9 | −25 |
| (Va)—(IV) | 4 | 11 | −20 |
| | | 10 | |

ii) Effect of B-Ring Formation (Table V)—On comparing the ultraviolet absorption spectra of (Ia) and (IV) with those of (IIa) and (Va), $\lambda_{max}$ for K-band of the latter shows bathochromic shift by about 9~11 mμ from those of the former as seen in Table V. As for the effect on the infrared absorption spectra, Table V shows that the position of the $\nu_{C=N}$ bands shifts by about 20~25 $cm^{-1}$ towards lower frequencies.

Table VI. Effect of 1-Alkyl Substituent

| | UV $\lambda\Delta$(mμ) | | IR $\Delta\bar{\nu}$($cm^{-1}$) ($\nu_{C=N}$ band) |
|---|---|---|---|
| | E-band | K-band | |
| (IIb)—(IIa) | | −5 | 6 |
| (IIc)—(IIa) | | −5 | 7 |
| (IId)—(IIa) | | −4 | 3 |
| (IIe)—(IIa) | | 0 | −2 |
| (Vb)—(Va) | −3 | −6 | 2 |
| | | −2 | |
| (Vc)—(Va) | −2 | −6 | 2 |
| | | −2 | |
| (Vd)—(Va) | −2 | −7 | 3 |
| | | −3 | |
| (V'd)—(V'a) | −5 | −4 | 0 |
| | −2 | −8 | |
| (II''b)—(II''a) | | | −23 |
| (II''c)—(II''a) | | | −28 |
| (II''d)—(II''a) | | | −31 |
| (II''e)—(II''a) | | | −32 |
| (V''b)—(V''a) | | | −29 |
| (V''c)—(V''a) | | | −31 |
| (V''d)—(V''a) | −1 | −2 | −33 |
| | | −4 | |

iii) Effect of 1-Alkyl Substituent (Table VI)—The effect on the absorption spectra when alkyl group is introduced into 1-position is shown in Table VI.

In the ultraviolet region, the maxima for the E- and K-bands of alkyl derivatives show hypsochromic shift by about 1~5 mμ and 2~8 mμ, respectively, from those of the corresponding compound having no substituent at 1-position, and the shift is independent of the kind of alkyls, with the only exception of 1-benzyl compound.

As for the position of the $\nu_{C=N}$ band in the infrared absorption spectra of 1-alkyl derivatives (free bases), a slight shift (2~6 $cm^{-1}$) towards higher frequencies than the 1-nonsubstituted compounds is generally observed, except in 1-benzyl compound. In the corresponding quaternary salts, however, rather a marked shift of 23~33 $cm^{-1}$ towards lower frequencies is observed in 1-alkylated salts from those of non-substituted quater-

nary compounds (II″a and V″a). As will be mentioned in the section on the effect of salt formation, derivation of (IIa) and (Va) to their corresponding quaternary salts (II″a and V″a) produces shift of 35~39 $cm^{-1}$ towards higher frequencies (cf. Fig. 2). In compounds having 1-alkyl substituent, no such remarkable shift occurs on salt formation. The foregoing facts suggest that the presence of alkyl group in 1-position in the series of quaternary salts (II″b, c, d, e, and V″b, c, d) appears as a great shift towards lower frequencies.

Table VII. Effect of Salt Formation

| | UV $\Delta\lambda$(mμ) | | IR $\Delta\bar{\nu}$($cm^{-1}$) |
|---|---|---|---|
| | E-band | K-band | ($\nu_{C=N}$ band) |
| (II′b)—(IIb) | | 25 | 31 |
| (II′e)—(IIe) | | 19 | 30 |
| (V′a)—(Va) | 7 | 30 | 20 |
| | 15 | 50 | |
| (V′d)—(Vd) | 4 | 33 | 17 |
| | 15 | 45 | |
| (II″a)—(IIa) | | 30 | 39 |
| (II″b)—(IIb) | | | 10 |
| (II″c)—(IIc) | | | 6 |
| (II″d)—(IId) | | | 5 |
| (II″e)—(IIe) | | 28 | 9 |
| (V″a)—(Va) | 18 | 30 | 35 |
| | | 50 | |
| (V″b)—(Vb) | | | 4 |
| (V″c)—(Vc) | | | 2 |
| (V″d)—(Vd) | 19 | 35 | −1 |
| | | 49 | |

iv) Effect of salt formation (Table VII).

a) Protonation (Hydrochloride) : It is generally known that with an open chain or cyclic base of the Schiff type, salt formation (–CH=N– → –CH=$\overset{+}{N}$H–) causes a bathochromic shift in the ultraviolet absorption spectra,[2a,6] and the frequency of the $\nu_{C=N}$ bands in the infrared absorption spectra[7] shifts to a slightly higher positions.

With 3,4-dihydroisoquinolines, as shown in Table VII, bathochromic shift is observed (respectively by 7~19 and 19~50 mμ) in the E- and K-bands of ultraviolet absorptions of the hydrochlorides from those of the free bases, which are particularly marked in the K-band (Figs. 5 and 6). In the infrared absorption spectra, the $\nu_{C=N}$ bands shift by 17~31 $cm^{-1}$ towards higher frequencies.

b) Quaternization (Methiodides) : With the formation of a methiodide from the free base as shown in Table VII, a marked bathochromic shift is also observed in the K-band of ultraviolet absorption spectra (Fig. 6), which is quite similar to those of the hydrochlorides. In compounds(II″a) and (V″a) with no substituent at 1-position, the effect of quaternization on the $\nu_{C=N}$ band in infrared absorption spectra is rather remarkable, as has already been described. These bands shifted by 35~39 $cm^{-1}$ towards higher frequencies, which are similar to the quaternization of Schiff type of compounds.

With 1-alkyl-3,4-dihydroisoquinolines, the magnitude of shift is comparatively small being only 2~10 $cm^{-1}$ towards higher frequencies. Furthermore, with 1-propyl-3,4-dihydroisoquinoline (Vd), the effect of quaternization is, even if to a very small extent, reverse of the others and the band shifted by 1 $cm^{-1}$ towards lower frequencies. These facts show that there are substantial differences between 1-nonsubstituted and 1-alkyl-

6) *a*) B. Witkop, J. B. Patrick, H. M. Kissman : Ber., **85**, 949(1952). *b*) B. Witkop : Experientia, **10**, 420(1954). *c*) E. D. Bergmann : Chem. Revs., **53**, 309(1953).

7) B. Witkop : J. Am. Chem. Soc., **76**, 5597(1954).

ated compounds on quaternization. An alkyl group at 1-position seems to depress the shift toward higher frequencies when an open-chain or cyclic Schiff bases of the type $-\overset{1}{C}=\overset{2}{N}-$ is quaternized.

Table VIII. Effect of C-Ring Formation

| | UV $\lambda\Delta$(mμ) | | IR $\Delta\bar{\nu}$(cm$^{-1}$) |
|---|---|---|---|
| | E-band | K-band | ($\nu_{C=N}$ band) |
| (III)—(II″e) | | 4 | 10 |
| (VI)—(V″d) | −3 | −4<br>−7 | 15 |

v) Effect of C-ring formation (Table VIII): As will be seen from Table VIII, the hypsochromic shift in the K-band of the ultraviolet absorption spectrum and a similar shift in the $\nu_{C=N}$ band between (VI) and (Vb) are contrary to the case of B-ring formation. On conversion of (IIe) to (III), however, a bathochromic shift is observed in the K-band of ultraviolet absorption spectrum. Based upon these results, the infrared absorption spectra of 2′-acyl-5,11b-dehydroemetine perchlorate (Figs. 7 and 8) were interpreted as

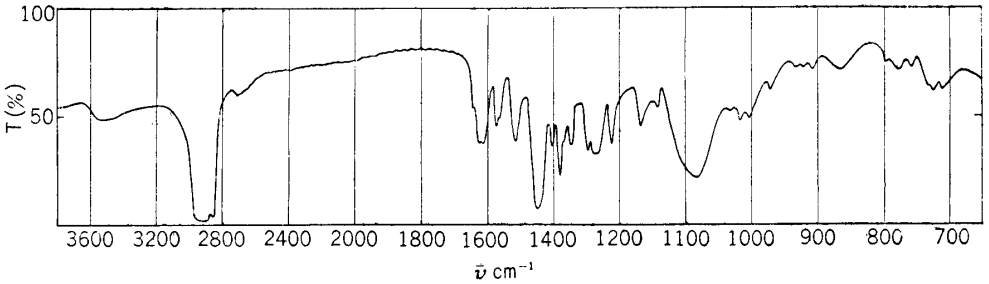



Fig. 7. 2′-Benzoyl-5,11b-dehydroemetinium Perchlorate Monohydrate

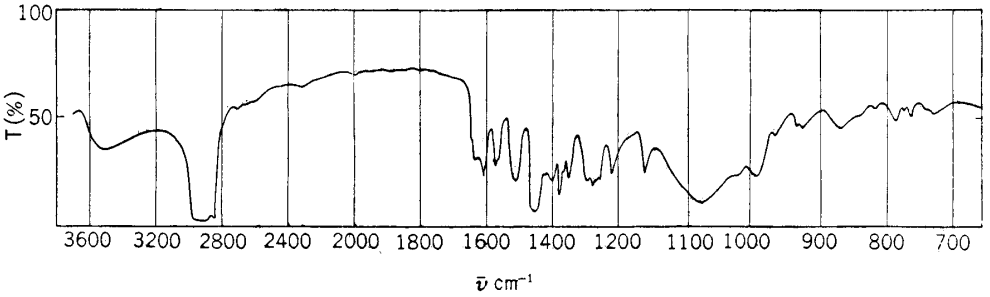



Fig. 8. 2′-Acetyl-5,11b-dehydroemetinium Perchlorate Tetrahydrate

follows: In the 1700~1500 cm$^{-1}$ region of 2′-benzoyl-5,11b-dehydroemetinium perchlorate monohydrate, the bands at 1644 and 1619 cm$^{-1}$ may be interpreted as C=N and C=O stretching vibrations, respectively, and the three bands at 1605, 1575 and 1515 cm$^{-1}$ will be the benzene ring vibrations.*3

In a similar manner 2′-acetyl-5,11b-dehydroemetinium perchlorate tetrahydrate absorbs at 1645 cm$^{-1}$(-C=N-), 1635 cm$^{-1}$(C=O), 1605, 1570, and 1510 cm$^{-1}$(benzene vibrations).

Thus, the assignments for the structures of these compounds are also supported by the interpretation of their infrared absorption spectra, combined with the evidence of their ultraviolet absorption spectra which were already given in the preceding paper.[1]

*3 The $\nu_{C=O}$ bands of 1-ethyl-2-benzoyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline and 1-ethyl-2-acetyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline are present at 1624 and 1637 cm$^{-1}$, respectively. As shown in Figs. 7 and 8, the $\nu_{C=O}$ bands are comparatively weak, which are presumably interpreted as being due to crystal water and other unknown effects.

## Experimental*4

**N-Benzylidenemethylamine (Ia)**—Prepared according to the method of Cromwell[8] and purified by distillation to a colorless oil, b.p. 182~185° (reported[8] b.p. 183~185°).

**N-(*o*-Methylbenzylidene)methylamine (Ib)**—This was also prepared in the usual way[8] and purified by distillation to a pale yellow, viscous oil, $b.p_{14}$ 89~92°.

**3,4-Dihydroisoquinoline and Its Homologs (II-Series)**—3,4-Dihydroisoquinoline (IIa) was prepared by the method of Snyder;[9] 1-methyl- (IIb), 1-ethyl- (IIc), 1-propyl- (IId), and 1-benzyl-3,4-dihydroisoquinolines (IIe) were obtained by the procedures given by Späth.[10] The physical properties of these compounds, their picrates, and hydrochlorides[11] are shown in Table IX.

Table IX.

| Compound | Free base b.p. (°C/mm. Hg) | Picrate m.p. (°C) | Hydrochloride m.p. (°C) |
|---|---|---|---|
| 3,4-Dihydroisoquinoline (IIa) | 106~108/30 | 175~177 (lit.[11] 176~177) | |
| 1-Methyl-3,4-dihydroisoquinoline (IIb) | 128~132/26 | 188~190 (lit.[12] 188~190) | 191~193 (reported[13] 196~198) |
| 1-Ethyl-3,4-dihydroisoquinoline (IIc) | 128~135/16 | 189~191 (lit.[12] 190~192) | |
| 1-Propyl-3,4-dihydroisoquinoline (IId) | 130~134/15 | 171~173 (lit.[12] 173~174) | |
| 1-Benzyl-3,4-dihydroisoquinoline (IIe) | 165~171/2.5 (reported 220/12) | 174~176 (lit.[12] 173~175) | 223~225 (reported[13] 227~229) |

**3,4-Dihydroisoquinoline Methiodide and Its Homologs (II″-Series)**—An excess of MeI was added to 3,4-dihydroisoquinoline (II) and the whole was heated under reflux for 3 hr. After the excess MeI was evaporated *in vacuo*, the residue was recrystallized from EtOH-$Me_2CO$ to the corresponding methiodide in a good yield. The physical properties of these methiodides and analytical data for new ones are shown in Table X.

Table X.

| Compound | m.p. (°C) | Formula | Analyses (%) Calcd. C | H | N | Found C | H | N |
|---|---|---|---|---|---|---|---|---|
| 3,4-Dihydroisoquinoline methiodide (II″a) | 124~126[a] | | | | | | | |
| 1-Methyl-3,4-dihydroisoquinoline methiodide (II″b) | 191~193 | $C_{11}H_{14}NI$ | 46.01 | 4.92 | 4.88 | 45.48 | 4.62 | 4.95 |
| 1-Ethyl-3,4-dihydroisoquinoline methiodide (II″c) | 107~109 | $C_{12}H_{16}NI$ | 47.85 | 5.36 | 4.65 | 48.24 | 5.83 | 4.89 |
| 1-Propyl-3,4-dihydroisoquinoline methiodide (II″d) | 131~133 | $C_{13}H_{18}NI$ | 49.54 | 5.76 | 4.44 | 49.00 | 5.61 | 4.57 |
| 1-Benzyl-3,4-dihydroisoquinoline methiodide (II″e) | 197~199[b] | | | | | | | |

*a*) Reported m.p. 124~125° (N. J. Leonard, G. W. Leubner: J. Am. Chem. Soc., **71**, 3408(1949)).
*b*) Reported m.p. 197~199° (A. Dobrowsky: Monatsh., **82**, 122(1949)).

**N-(3,4-Dimethoxybenzylidene)methylamine (IV)**—Obtained as colorless liquid, $b.p_{14}$ 148~150° (reported[12] $b.p_{11}$ 145°).

*4 A Koken model DS-301 double-beam spectrophotometer equipped with NaCl prism was used for the determination of infrared spectra. A Beckman Model DK-2 spectrophotometer was used for the determination of ultraviolet spectra and samples were run as 85% EtOH solution.

8) N. H. Cromwell, R. D. Babson, C. E. Harris: J. Am. Chem. Soc., **65**, 312(1943).
9) H. R. Snyder, F. X. Werber: *Ibid.*, **72**, 2962(1950).
10) E. Späth, F. Berger, W. Kuntara: Ber., **63**, 134(1930).
11) W. M. Whaley, W. H. Hartung: J. Org. Chem., **14**, 650(1949).
12) R. B. Moffett, W. H. Hoehn: J. Am. Chem. Soc., **69**, 1792(1947).
13) E. Späth, N. Polgar: Monatsh., **51**, 190(1929).

**6,7-Dimethoxy-3,4-dihydroisoquinolines (V-Series)**—Prepared by following details given by Späth.[17] The physical properties of these compounds, their picrates, and hydrochlorides are given in Table XI.

Table XI.

| Compound | Free base b.p. (°C/mm.Hg) or m.p. (°C) | Picrate m.p. (°C) | Hydrochloride m.p. (°C) |
|---|---|---|---|
| 6,7-Dimethoxy-3,4-dihydroisoquinoline (V a) | 146~148/2[a] | 201~202 (201~203)[13] | 201~205 (decomp.) |
| 1-Methyl-6,7-dimethoxy-3,4-dihydroisoquinoline (V b) | m.p. 97~99[b] | 205~207 (210~212)[13] | |
| 1-Ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline (V c) | 146~150/2[c] | 190~192 (195~196)[13] | |
| 1-Propyl-6,7-dimethoxy-3,4-dihydroisoquinoline (V d) | 153~157/2[d] | 174~176 (180~181)[13] | 179~182 (decomp.) |

*a*) Reported b.p. 155~160° (air bath) (W. H. Whaley, M. Meadow : J. Chem. Soc., **1953**, 1067).
*b*) Reported m.p. 106~107°.[13]
*c*) Reported b.p. 170°.[13]
*d*) Reported b.p. 170~175°.[13]

**6,7-Dimethoxy-3,4-dihydroisoquinoline Methiodides (V″-Series)**—Prepared in a similar way as for preparation of (II″) series described above. The m.p. of these compounds and the analytical data for the new ones are given in Table XII.

Table XII.

| Compound | m.p. (°C) | Formula | Analyses (%) Calcd. C | H | N | Found C | H | N |
|---|---|---|---|---|---|---|---|---|
| 6,7-Dimethoxy-3,4-dihydroisoquinoline methiodide (V″a) | 199~201[a] | | | | | | | |
| 1-Methyl-6,7-dimethoxy-3,4-dihydroisoquinoline methiodide (V″b) | 173~176[b] | | | | | | | |
| 1-Ethyl-6,7-dimethoxy-3,4-dihydroisoquinoline methiodide (V″c) | 147 | $C_{14}H_{20}O_2NI$ | 46.55 | 5.58 | 3.38 | 46.81 | 5.77 | 3.97 |
| 1-Propyl-6,7-dimethoxy-3,4-dihydroisoquinoline methiodide (V″d) | 167~169[1] | | | | | | | |

*a*) Reported m.p. 201~202° (W. H. Whaley, M. Meadow : J. Chem. Soc., **1953**, 1067.
*b*) Reported m.p. 176~178°.[13]

The authors wish to express their gratitude to Professor Emeritus S. Sugasawa, University of Tokyo, for his interest and encouragement throughout this work. Thanks are also due to Mr. K. Narita of the Central Analysis Room of this Institute, and to Mrs. F. Hisamichi and Messrs. T. Yoda and T. Kono of Tokyo Research Laboratories, Tanabe Seiyaku Co., Ltd., for elemental analysis. They are also grateful to the Ministry of Education for Grant-in-Aid for Developmental Scientific Research for 1958 in aid of this work.

## Summary

The ultraviolet and infrared absorption spectra of 3,4-dihydroisoquinoline and its homologs are described which have been very useful in the interpretation of the absorptions of 2′-acyl-5,11b-dehydroemetines.

(Received July, 31, 1959)