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Studies on Tertiary Amine Oxides. LV.*,[1] Reactions of N-Alkoxyquinolinium Salts with Enamines of Ketones. (1)

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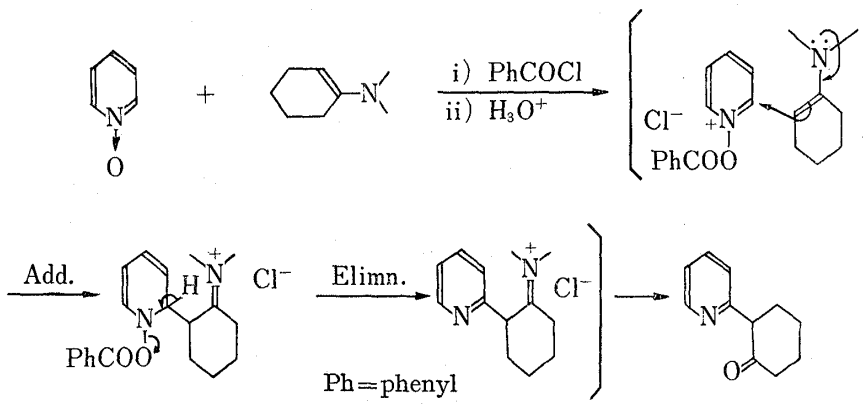
Reactions of N-alkoxyquinolinium salts (**1**) with enamines of cyclohexanone (**2**) gave not the expected 2-(2-quinolyl)cyclohexanone but instead products of a novel tricyclic system (**3**); for example, 3-ethoxy-14-(2-quinolyl)-3-azabenzo[*d*]tricyclo[5,3,1,$1^{2,8}$]dodecan-13-ylidenemorpholinium iodide (**3a**) was obtained from N-ethoxyquinolinium iodide (**1a**) and the morpholine enamine (**2a**). The stereochemistry of **3a** was finally established by X-ray diffraction study as **C**, but interesting informations supporting its structure were obtained by its chemical reactions which involed thermolysis to 2,3′-biquinolyl (**4a**), stereoselective addition to the azomethinium moiety, alkaline hydrolysis to the corresponding ketone (**7**), pyrolytic elimination of ethylene oxide from some derivatives (**5a**, **7** and **8**) and others. Spectral examinations of **3a** and its transformed compounds also agreeded with its structure. The reaction mechanism was discussed.

Aromatic N-oxides react very readily with enamines in the presence of an acylating agent, and it has been well established that the reaction is nucleophilic substitution of the initially formed acyl-adduct of N-oxide and proceeds by the addition-elimination mechanism as illustrated below.[3]



This type of reaction has widespread applicability and it has been recently disclosed that the reaction occurs also with 1(10)-dehydroquinolizidine[4] and enamines of N-acyl-4-piperidones[5] besides enamines of cyclohexanone[3a-c] and isobutyraldehyde.[3d]

* Dedicated to the memory of Prof. Eiji Ochiai.

1) Part LIV; M. Hamana and S. Kumadaki, *Chem. Pharm. Bull.* (Tokyo), **23**, 2284 (1975).
2) Location: *a*) *Maidashi, Higashi-ku, Fukuoka*; *b*) *Ropponmatsu, Chuo-ku, Fukuoka.*
3) *a*) M. Hamana and H. Noda, *Chem. Pharm. Bull.* (Tokyo), **13**, 912 (1965); *b*) *Idem, ibid.*, **14**, 762 (1966); *c*) *Idem, ibid.*, **15**, 474 (1967); *d*) *Idem, Yakugaku Zasshi*, **89**, 641 (1969).
4) S. Saeki, A. Yamashita, Y. Matsukura, and M. Hamana, *Chem. Pharm. Bull.* (Tokyo), **22**, 2341 (1974).
5) M. Nakanishi, M. Yatabe, and M. Hamana, *Heterocycles*, **3**, 287 (1975).

On the other hand, the reaction of N-ethoxyquinolinium iodide (**1a**) with 1-morpholinocyclohexene (**2a**) was found to give not the expected 2-(2-quinolyl)cyclohexanone but instead an interesting product (**3a**) seemingly comprising two quinoline rings and one enamine in a good yield. We previously suggested that its structure would be closely related with structure A or B from some preliminary examinations as well as a mechanistic viewpoint.[6]

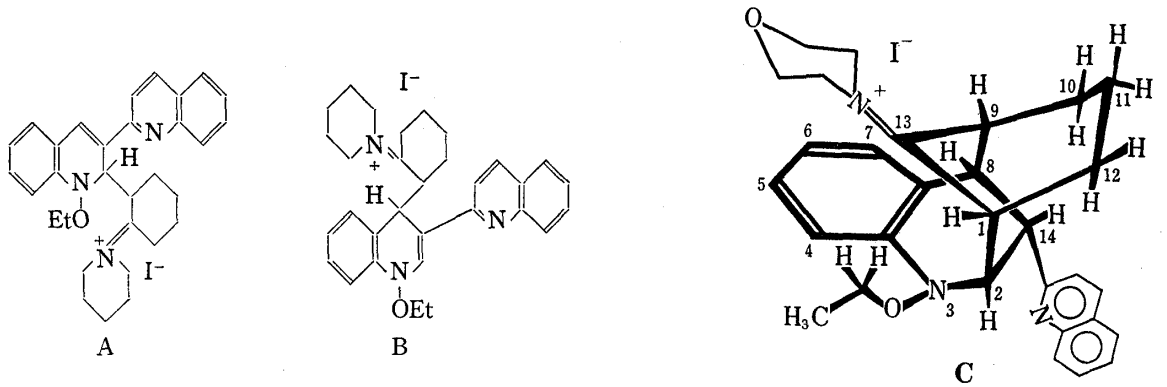


Fig. 1

This paper describes the chemical and spectral examinations carried out in connection with the structure elucidation of **3a**. Although its structure could not be elucidated by these means alone and finally established by X-ray diffraction study as 3-ethoxy-14-(2-quinolyl)-3-azabenzo[*d*]tricyclo[5,3,1,$1^{2,8}$]dodecan-13-ylidenemorpholinium iodide (C, Fig. 1),[7] interesting informations supporting the structure were obtained. The chemical reactions examined are illustrated in Chart 1.

When 1-morpholinocyclohexene (**2a**) was added with stirring to a water-cooled chloroform solution of N-ethoxyquinolinium iodide (**1a**), colorless morpholine hydroiodide began to precipitate after a while. After the reactants were allowed to stand at room temperature for 5 days, the chloroform solution freed of precipitates was shaken with 20% hydrochloric acid,[8] and the acidic solution was made alkaline with potassium carbonate to deposit crystals which were extracted with chloroform. The extract residue was solidified by triturating with ether and recrystallized from ethanol to give **3a**, almost colorless pillars,[9] mp 216—217° (decomp.), in a good yield of 61%.[10]

Product **3a** is a fairly stable compound with an empirical formula $C_{30}H_{34}O_2N_3I$, and is insoluble in water and sparingly soluble in usual organic solvents. Its nuclear magnetic resonance (NMR) spectrum gave no clear-cut chart partly because of sparing solubility of **3a** in deuteriochloroform. Accordingly, the detailed analysis could not be made, but integrated area of peaks at aromatic region suggested the presence of two quinoline rings and a very complicated resonance signals resulting from approximate twenty-four aliphatic protons which involved a triplet due to the methyl protons of an ethoxy group appeared at higher field.

6) *a*) M. Hamana, *J. Heterocycl. Chem.*, **9**, S-51 (1972); *b*) H. Noda, M. Minemoto, K. Narimatsu, and M. Hamana, *Yakugaku Zasshi*, **95**, 1078 (1975).
7) I. Ueda, H. Noda, and M. Hamana, *Acta Crystllographica*, 1976 32.
8) The product could not be extracted with 10% hydrochloric acid.
9) Besides these crystals of the orthorhombic system, those of the triclinic system, mp 208—209° (decomp.), were obtained in some cases depending upon the condition of recrystallization. They are interconvertible and they showed slightly different infrared (IR) spectra in solid state but the same one in chloroform solution. See ref. 7 and also the experimental section.
10) When the reaction mixture was stirred with 10% hydrochloric acid at room temperature for 1 hr instead of extracting with 20% hydrochloric acid and then made alkaline with potassium carbonate followed by extracting with chloroform, the crude **3a** was isolated in practically quantitative yield.

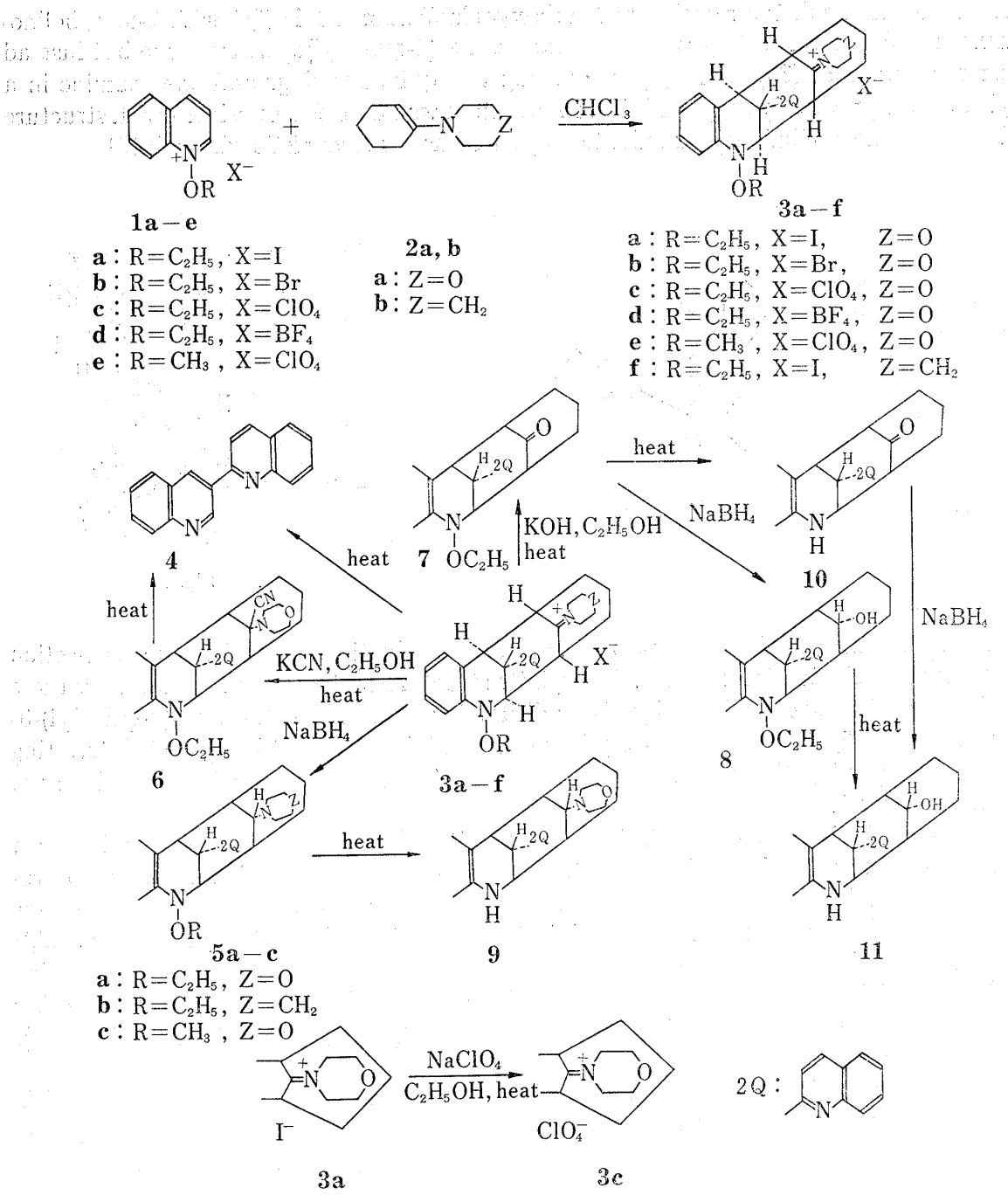


Chart 1

Dissolution of **3a** in concentrated sulfuric acid or nitric acid deposited crystals of iodine. Whereas no visible sign of change was noticed when **3a** was dissolved in cold hydrochloric acid, the initial light yellow solution became yellow green through brown upon heating to yield morpholine hydroiodide accompanied with respectively small amounts of several products which could not be characterized.

In the similar way, N-ethoxyquinolinium bromide (**1b**), perchlorate (**1c**) and tetrafluoroborate (**1d**) as well as N-methoxyquinolinium perchlorate (**1e**) reacted with **2a** to produce the corresponding products (**3b**, **3c**, **3d** and **3e**) in moderate to good yields, and application of 1-piperidinocyclohexene (**2b**) to **1a** gave the piperidium analog of **3a** (**3f**) in 59% yield (Table I). These products evidently have structures of the same type with that of **3a** and showed practically the same chemical reactivities.

Table I. Reactions of N-Alkoxyquinolinium Salts (1) with Enamines of Cyclohexanone (2)

N-Alkoxyquinolinium salt 1			Enamine 2		Product 3		
	R	X		Z		Yield (%)	mp (decomp.) (°C)
1a	C_2H_5	I	2a	0	3a	99(61)[a]	217
1b	C_2H_5	Br	2a	0	3b	50	199
1c	C_2H_5	ClO_4	2a	0	3c	30	216
1d	C_2H_5	BF_4	2a	0	3d	72	199
1e	CH_3	ClO_4	2a	0	3e	44	215
1a	C_2H_5	I	2b	CH_2	3f	59	217

a) See footnote 10.

Heating **3a** or **3f** in an oil bath maintained at 230° immediately caused decomposition accompanied by evolution of gas. The cooled reaction mixture was treated with potassium carbonate solution followed by extracting with chloroform to give 2,3′-biquinolyl (**4**), mp 171°, which was identified by comparison with an authentic sample prepared by the known method.[11] Hence, **3a** and **3f** apparently contain 2,3′-biquinolyl linkage as a partial structure.

Upon heating with ethanolic sodium perchlorate, **3a** was converted into **3c**, which fact apparently indicates that an iodine anion was contained in **3a**. However curiously, this anion exchange was not observed at low temperatures.

The presence of an azomethinium moiety in **3a** was verified by sodium borohydride reduction, addition of cyanide anion and alkaline hydrolysis. An ethanol solution of **3a** and excess sodium borohydride was refluxed to afford light yellow prisms (**5a**), mp 195° (decomp.) as a sole product in a high yield. Similar treatment of **3b** and **3d** also gave **5a**, and a piperidine analog of **5a** (**5b**) was obtained by the reduction of **3f**. The molecular formulae of **5a**, $C_{30}H_{35}O_2N_3$ (M^+, *m/e* 469), and **5b**, $C_{31}H_{37}ON_3$ (M^+, *m/e* 467) shows that **3a** and **3f** lost the iodide anion

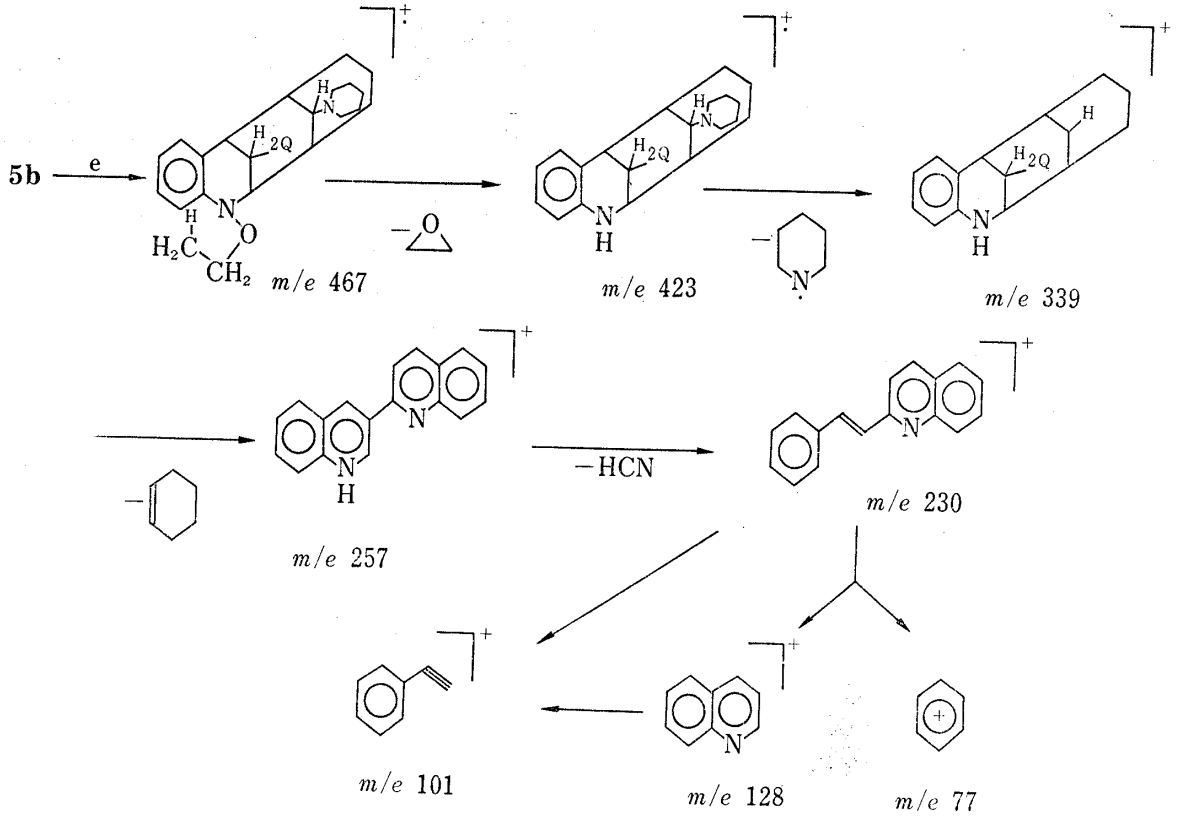


Chart 2

11) H. Weidel and G. Glänser, *Monatsh. Chem.*, **7**, 308 (1886), and also see ref. 6*b*

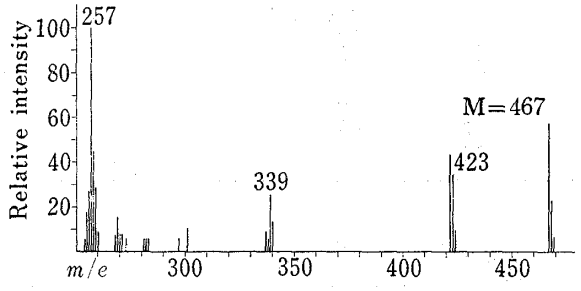


Fig. 2. Mass Spectrum of **5b**

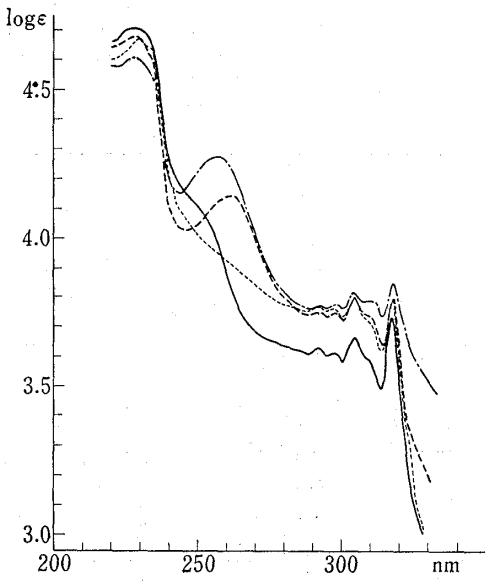


Fig. 3. Ultraviolet Spectra in Ethanol

——— : **3a** ——— : **6**
——— : **5a** ---------- : **7**

by reduction of the azomethinium function. The high-resolution mass spectrum of **5b** exhibited the fragmentation pattern in good agreement with the proposed structure (Chart 2, Fig. 2).

Treatment of **3a** with potassium cyanide in boiling ethanol resulted in formation of 13-cyano derivative (**6**), colorless scales, mp 221.5° (decomp.), by addition of cyanide anion to the azomethinium double bond; the IR spectrum of **6** exhibited a band at 2210 cm^{-1} characteristic of cyano group. Heating **6** at 230—240° gave 2,3′-biquinolyl (**4**) in the same manner with **3a**.

Subsequently in order to hydrolyze the azomethinium group, **3a** was refluxed with 10% ethanolic potassium hydroxide to give colorless prisms (**7**), mp 160—161.5°, together with small amounts of biquinolyl (**4**) and the reduction product (**5a**). The ketonic structure of **7** was ascertained by its composition $C_{26}H_{26}O_2N_2$ (M^+, *m/e* 398), an absorption in the IR spectrum at 1734 cm^{-1} and the absence of resonance signals in the NMR spectrum due to morpholine ring-protons. It was further supported by similar formation of **7** from **3f**. Reduction of **7** in boiling ethanol with sodium borohydride afforded only the single alcohol (**8**).

Whereas attempts under various conditions to eliminate the component of ethanol from **3a**—**f** were unsuccessful, it was found that thermolysis of **5a** proceeded at 200—230° accompanied by evolution of gas and afforded crystalline product (**9**), mp 209—210°, which conceivably could arise by splitting off of ethylene oxide from its composition $C_{28}H_{31}ON_2$ as well as the lack of signal due to an ethoxy group in the NMR spectrum. Apparently this mode of thermolysis is involved as the first step in the fragmentation pattern of mass spectrum of **5b** (Chart 2). In addition, the same type of thermolysis was also observed with both the ketone (**7**) and the corresponding alcohol (**8**) to give respective de-ethoxylated products (**10**) and (**11**); **10** was easily converted to **11** by sodium borohydride reduction.

It is possibly assumed that no skeletal change occurred during the course of the above-mentioned reactions because **3a**, **5**, **6** and **7** showed fairly similar ultraviolet (UV) spectra with one another, especially two pairs of spectra, namely those of azomethinium compound (**3a**) and ketone (**7**) and those of saturated compounds (**5a**) and (**6**), beared close resemblance in each case as shown in Fig. 3.

The results of experiments described above indicate that **3a** contains 2,3′-biquinolyl skeleton, an ethoxy group and a cyclohexylidenemorpholinium iodide. However its behavior cannot be satisfactorily explained by structure A or B; on the contrary it evidently supports structure C.

The reason why the azomethinium iodide structure in **3a** is anomalously stable is not completely understandable at present. However with respect to the stability of the azomethinium moiety, the possibility may be considered from inspection of model that this is at least partly due to the action of the benzene nucleus located in the neighborhood as a donor of π-electrons. The feeble reactivity towards anion exchange cannot be rationalized even by X-ray analysis.

It is also noticeable that **3a** stoutly resists the liberation of the component of ethanol and the ethoxy group of somewhat more stable **5a**, **7** and **8** can be eliminated only as ethylene oxide under thermolytic condition. This is quite unlike the behavior of planar 1,2-dihydro- and 1,4-dihydroquinolines such as A and B, and should be closely related with the stereochemistry of the adjacent α position of the original quinoline ring. If the carbon atom is a bridgehead one, the formation of a double bond by β-elimination of ethanol from **3a** might be impossible unless the mother skeleton undergoes breakdown. This is exactly the case for structure C.

Addition reaction of hydride and cyanide anions to the azomethinium bond of **3a** and also reduction of the corresponding ketone (**7**) were shown to proceed stereoselectively and always afford the single product in each case despite of the possible formation of its stereoisomer. These observations lead to the consideration that **3a** has some stereochemically rigid and crowded configuration of non-coplanarity which allows reagents to approach only from one side to the bonds concerned. These reactions can be well explained by the stereochemistry of structure C; reagents attacking at the azomethinium bond of **3a** and the ketonic group of **7** are capable of approaching to them only from the opposite side of the tetrahydroquinoline ring bearing the ethoxy and 2-quinolyl groups, and **5a—c**, **6** and **8** should have the same configuration concerning the 13 position as formulated in Chart 1.

In addition to these observations, the following findings are also in agreement with structure C. Resonance signals due to methyl and methylene protons of N-ethoxy group appear as a triplet at δ 1.00 and a multiplet centered at δ *ca.* 3.8, respectively, in 100 MHz NMR spectrum of **5a**. While the former triplet becomes a singlet by irradiation at the methylene group, the irradiation at the methyl group changes the methylene signal from a multiplet to an AB-quartet. These observations may be explained in term of nonequivalence of two methylene protons resulting from the inhibition of not only inversion of configuration at nitrogen but also the free rotation about the N-O bond owing to the rigidity of the ring system and the serious steric hindrance (Fig. 4).

As a continuation of this study we examined the reaction of **1a** with some other enamines and found that the same type of reaction occurred with enamines of ketones such as cyclopentanone and diethyl ketone but only de-ethoxylation took place with 1-morpholinoisobutene. These results agree with the fact that availability of both α and α' positions of enamine should be essential for the proceeding of the reaction.

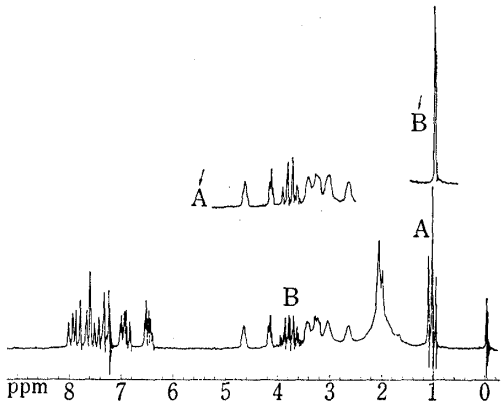


Fig. 4. NMR Spectrum of **5a** (100 MHz, $CDCl_3$)

Although **3a** contains five asymmetric carbons, that is C_2, C_8 and C_{14} originated from the 2, 4 and 3 positions of one quinoline ring, respectively, and C_1 and C_9 corresponding to α and α' positions of cyclohexanone enamine, inspection of model indicates that structure C is the only one capable of existing among various configurations and all others cannot be conceived because of serious steric hindrance. In fact X-ray analysis has established that crystals of **3a** are constituted with equivalent amounts of C and its enantiomer.

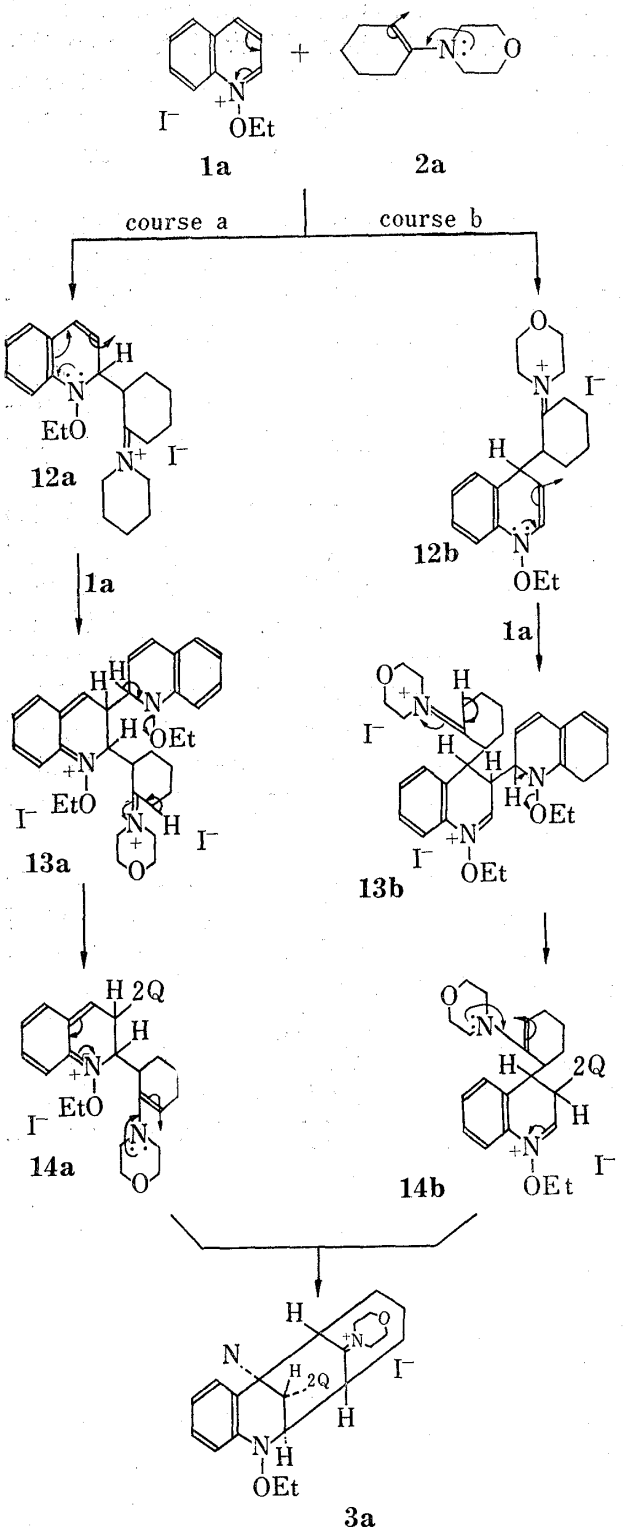


Chart 3

The formation of **3a** may be explained by the course shown in Chart 3. From analogy with the reaction of acyl-adducts of aromatic N-oxides, the first step is undoubtedly nucleophilic addition of enamine (**2a**) to quaternary salt (**1a**) to form 1,2- or 1,4-dihydroquinoline intermediate (**12a** or **12b**). Consecutively, the 3-position of **12** attacks at the 2-position of the second molecule of **1a** by means of its enamine-like polarization to give the second intermediate (**13a** or **13b**) containing both dihydroquinolinium and 1,2-dihydroquinoline structures. Subsequently, one mole of ethanol is eliminated from 1,2-dihydroquinoline moiety of **13** forming 2-quinolyl substituent, and at the same time cyclohexylidenemorpholinium moiety is transfered into a new enamine having no substituent at the end of double bond (**14a** or **14b**). The final step is the intramolecular attack of the enamine moiety at the electron-deficient 4- or 2-position of dihydroquinolinium ring in **14a** or **14b**; neither elimination of the component of ethanol nor further transformation of azomethinium structure is stereochemically possible in **3a**.

The reason is not yet clear why the enamine-like polarization preferentially appears instead of extrusion of ethanol leading to aromatization in the first dihydroquinoline intermediate **12**. In connection with this aspect, we tried the reverse procedure involving addition of **1a** in small portions to a chloroform solution of **2a**, but obtained **3a** as a sole product also in high yield, no monosubstituted quinoline being detected. Moreover, attempted reactions quinaldine and lepidine N-oxides with **2a** was found to result only in deethoxylation. Therefore, the formation of 2,3′-biquinolyl linkage of **13** should be considered to be a highly reactive reaction and the crucial step essential for promoting the reaction to the final step.

Whereas course a through 1,2-dihydroquinoline intermediate **12a** seems more probable in view of the mode of reaction in the presence of an acylating agent, course b *via* **12b** is apparently more favorable to the appearance of enamine-like polarization.

Although the details of the mechanism have not been established, it seems likely that the reaction proceeds by some concerted process rather than multistep one.

There is reported the reaction of N-methylisoquinolinium iodide with nitroalkane which formally resembles our reaction and is proposed to progress by the course shown in Chart 4.[12] This one apparently differs from our reaction in some detailed features; N-methylisoquinolinium salt is prone to transfer into 1,2-dihydroisoquinolines and its methyl group can be eliminated only with great difficulty. However this finding seems to provide supporting evidence for the above-mentioned mechanism.

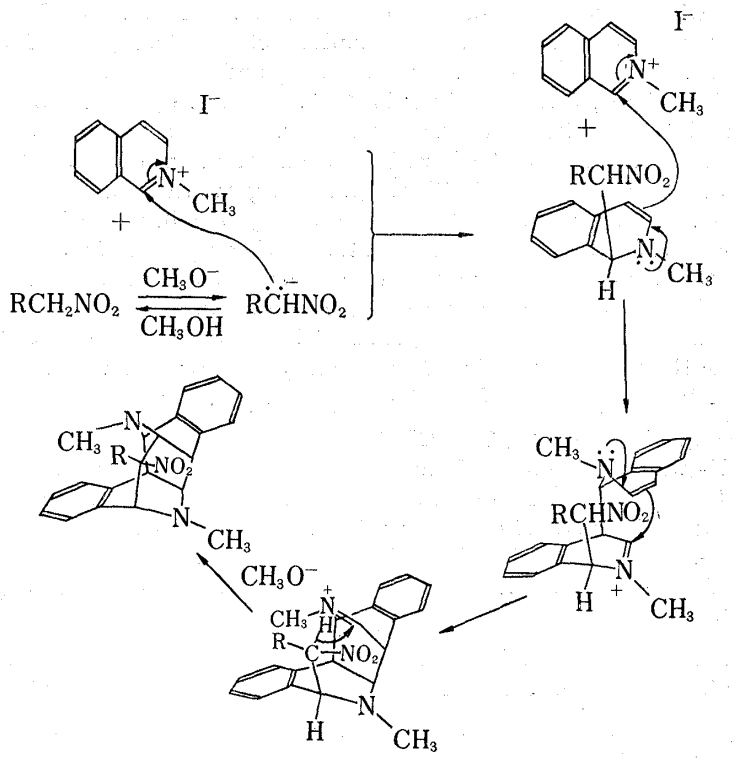


Chart 4

Previously the reaction of quinoline N-oxide with electrophilic olefins was carried out in the presence of acetic anhydride with an aim to develop a new reaction which involves electrophilic substitution of 1,2- or 1,4-dihydroquinoline intermediate by means of its enamine-like activity. This object was not achieved, but it was found that unexpected reaction occurred.[6a,13] It is very remarkable that this type of reaction was realized by treatment of N-ethoxyquinolinium salts with enamines although in an unexpected fashion. Further work is in progress in our laboratory in order to explore the essential features of this reaction. Details of this work involving reactions of **1a** with enamines of cyclopentanone and diethyl ketone will be published in the near future.

Experimental[14]

Reaction of N-Ethoxyquinolinium Iodide (1a) with 1-Morpholinocyclohexene (2a)——1) To a water-cooled solution of **1a** (12.04 g, 4 mmole) in $CHCl_3$ (40 ml) was added with stirring **2a** (15 g, 8.8 mmole), and stirring was continued to deposit colorless morpholine hydroiodide after *ca.* 30 min. The whole was kept at room temperature for 5 days, and precipitates were filtered and recrystallized from EtOH to give 1.36 g of morpholine hydroiodide, colorless pillars, mp 214—215°. The $CHCl_3$ filtrate was shaken with 20% HCl and the acidic layer was made alkaline to give crystalline precipitates which were extracted with $CHCl_3$. The extract was dried over Na_2SO_4, evaporated and the resulting residue was solidified by triturating with

12) *a*) W.R. Schleigh, *Tetrahedron Letters*, **1969**, 1405; *b*) *Idem*, *J. Heterocycl. Chem.*, **9**, 675 (1972).
13) M. Hamana, K. Funakoshi, and Y. Kuchino, *Chem. Pharm. Bull.* (Tokyo), **22**, 1806 (1974).
14) Melting points are uncorrected. NMR spectra were run on JNM-3H-60 and JNR-4H-100 spectrometers, using TMS as an internal standard. Mass spectra were recorded at 75 eV on a JMS-OISG spectrometer.

ether and recrystallized from EtOH to give 7.22 g of 3-ethoxy-14-(2-quinolyl)-3-azabenzo[*d*]tricyclo[5,3,1,$1^{2,8}$]-dodecan-13-ylidenemorpholinium iodide (**3a**), pale yellow pillars (the orthorhombic system[7]), mp 216—217° (decomp.). IR ν_{max}^{KBr} cm^{-1}: 1643 (>$\overset{+}{N}$=C), 1113 (C–O–C), 1039 (N–O). UV λ_{max}^{EtOH} nm (log ε): 317.3 (3.74), 309 (3.60, sh.), 304 (3.68), 297 (3.62), 291.5 (3.64), 285 (3.63, sh.), 247 (4.14, inflec.), 228 (4.72). *Anal.* Calcd. for $C_{30}H_{34}O_2N_3I$ (dried at 60° *in vacuo* over P_2O_5): C, 60.50; H, 5.75; N, 7.06. Found: C, 60.76; H, 5.73; N, 7.02. *Anal.* Calcd. for $C_{30}H_{34}O_2N_3I \cdot 1/2H_2O$ (dried at room temp. *in vacuo* over P_2O_5 and then kept overnight at the ordinary temp. and pressure over silica gel): C, 59.60; H, 5.84; N, 6.95. Found: C, 59.79; H, 6.08; N, 6.78. In some cases, **3a** formed crystals of the triclinic system,[7] mp 208—209° (decomp.), which were interconvertible with those of the orthorhombic system. Although its IR spectrum in solid state slightly differed from that of orthorhombic crystals, both spectra in $CHCl_3$ were identical. *Anal.* Calcd. for $C_{30}H_{34}O_2N_3I \cdot H_2O$ (dried at room temp. *in vacuo* over P_2O_5 and then kept overnight at the ordinary temp. and pressure over silica gel): C, 58.72; H, 5.91; N, 6.85. Found: C, 58.84; H, 5.97; N, 6.72.

2) The reaction mixture resulted from another run using the same amounts of reactants under the same condition was stirred with 10% HCl (100 ml) with ice-cooling and then at room temperature for 1 hr, and treated with K_2CO_3 and extracted with $CHCl_3$ to give 11.7 g of crude **3a**.

3) To a stirred solution of **2a** (15 g, 8.8 mmole) in $CHCl_3$ (30 ml), a solution of **1a** (6.02 g, 2 mmole) in $CHCl_3$ (40 ml) was added dropwise at room temperature during a period of 2 hr. After the reactants were kept at room temperature for 4 days, a small amount of morpholine hydroiodide was filtered and the $CHCl_3$ layer was stirred with 10% HCl (80 ml) to give 5.8 g (97.3%) of **3a**.

Reactions of N-Alkoxyquinolinium Salts (1a, 1b, 1c, 1d and 1e) with Enamines of Cyclohexanone (2a and 2b)——1) Reaction of N-Ethoxyquinolinium Bromide (**1b**) with **2a**: Similar treatment of **1b** (2.43 g) with **2a** (4 g) in $CHCl_3$ (20 ml) afforded 1.3 g of **3b**,[15] colorless pillars, mp 198—199° (decomp.) (EtOH). IR ν_{max}^{Nujol} cm^{-1}: 1643 (>$\overset{+}{N}$=C), 1114 (C–O–C), 1031 (N–O).

2) Reaction of N-Ethoxyquinolinium Perchlorate (**1c**) with **2a**: Similar treatment of **1c** (2.74 g) with **2a** (3.68 g) in $CHCl_3$ (60 ml) gave 0.84 g of **3c**, colorless plates, mp 215—216° (decomp.). *Anal.* Calcd. for $C_{30}H_{34}O_6N_3Cl$: C, 63.43; H, 6.03; N, 7.40. Found: C, 63.23; H, 5.99; N, 7.25.

3) Reaction of N-Ethoxyquinolinium Tetrafluoroborate (**1d**) with **2a**: Similar treatment of **1d** (1.25 g) with **2a** (1.7 g) in $CHCl_3$ (20 ml) gave 0.7 g of **3d**,[15] colorless plates, mp 198—199° (decomp.) (EtOH). IR ν_{max}^{Nujol} cm^{-1}: 1643 (>$\overset{+}{N}$=C), 1114 (C–O–C), 1031 (N–O).

4) Reaction of N-Methoxyquinolinium Perchlorate (**1e**) with **2a**: Similar treatment of **1e** (2.62 g) with **2a** (3.68 g) in $CHCl_3$ afforded 1.2 g of **3e**, colorless plates, mp 214—215° (decomp.) (EtOH). IR ν_{max}^{Nujol} cm^{-1}: 1645 (>$\overset{+}{N}$=C), 1090 (ClO_4 and C–O–C), 1033 (N–O). *Anal.* Calcd. for $C_{29}H_{32}O_6N_3Cl$: C, 62.87; H, 5.82; N, 7.59. Found: C, 63.18; H, 5.81; N, 7.54.

5) Reaction of **1a** with 1-Piperidinocyclohexene (**2b**): A solution of **1a** (6.02 g, 2 mmole) and **2b** (7.1 g, 4.4 mmole) in $CHCl_3$ (40 ml) was kept at room temperature for 1 day. The reaction mixture was shaken with 20% HCl and the acidic solution was processed as described at first to give 3.53 g of **3f**, colorless prisms, mp 216—217° (decomp.) (EtOH). IR ν_{max}^{KBr} cm^{-1}: 1632 (>$\overset{+}{N}$=C), 1030 (N–O). *Anal.* Calcd. for $C_{31}H_{36}ON_3I \cdot 2/3H_2O$: C, 61.48; H, 6.22; N, 6.94. Found: C, 61.12; H, 6.41; N, 6.69.

Reactions of 3-Ethoxy-14-(2-quinolyl)-3-azabenzo[*d*]tricyclo[5,3,1,$1^{2,8}$]dodecan-13-ylidenemorpholinium Iodide (3a) and Related Compounds (3b, 3d, 3e and 3f)——1) Thermolysis of **3a**: Heating **3a** (500 mg) in an oil bath maintained at 230° immediately caused fusion and decomposition accompanied by evolution of gas. After gas evolution had ceased, the reaction mixture was cooled, made alkaline with $NaHCO_3$ solution and extracted with $CHCl_3$. The extract residue was recrystallized from EtOH to give 104 mg of 2,3′-biquinolyl (**4**), pale yellow rods, mp 170—171°. *Anal.* Calcd. for $C_{18}H_{12}N_2$: C, 84.35; H, 4.72; N, 10.93. Found: C, 84.25; H, 4.43; N, 10.92. It was proved identical with an authentic sample prepared by the known method.[11]

2) Thermolysis of **3f**: Similar thermolysis of **3f** (500 mg) at 230° gave 180 mg of **4**.

3) Anion Exchange of **3a**: A solution of **3a** (300 mg) and $NaClO_4$ (280 mg) in EtOH (10 ml) was refluxed for 3 hr. The hot reaction mixture was separated from a small amount of deposit and cooled to give 280 mg of colorless plates, mp 215—217°. This was proved indentical with **3c** prepared from **1c** and **2a**.

4) Reduction of **3a** with $NaBH_4$: A solution of **3a** (500 mg) and $NaBH_4$ (770 mg) in EtOH (20 ml) was refluxed for 2 hr, concentrated *in vacuo* and the residue was treated with H_2O and extracted with $CHCl_3$. The extract residue was recrystallized from EtOH to give 420 mg of the reduced product **5a**, colorless prisms, mp 194—195° (decomp.). IR ν_{max}^{KBr} cm^{-1}: 1116 (C–O–C), 1025 (N–O). UV λ_{max}^{EtOH} nm (log ε): 317.8 (3.81), 310 (3.74, inflec.), 304.5 (3.81), 297.5 (3.76), 292 (3.76), 216.5 (4.15), 233 (4.63, inflec.), 228 (4.69). NMR ($CDCl_3$) δ: 6.40—8.04 (10H, m, aromatic protons) 4.66 (1H, m, C_{14}–H), 4.16 (1H, m, C_{13}–H), 3.79 (2H, complex AB-q, J_{AB}=12.5 Hz, –O$CH_2$$CH_3$), 2.80—3.56 (6H, m, C_2–H, C_8–H and 2,6-protons of morpholyl group), 2.68 (2H, m, C_1–H and C_9–H), 1.32—2.56 (10H, m, C_{10}–H, C_{11}–H, C_{12}–H and 3,5-protons of morpholyl group), 1.06 (3H, t,

15) Although elemental analyses of **3b** and **3d** did not give satisfactory data, the structures of **3b** and **3d** were evident from spectral examinations and their conversion to **5a** with $NaBH_4$.

J=9.0 Hz, $-OCH_2C\underline{H}_3$). Mass Spectrum *m/e*: 469 (M^+), 425 ($M-C_2H_4O$), 424 (425-H), 339 (425-C_4H_8ON), 269 ($C_{19}H_{13}N_2$), 257 (2,3′-biquinolyl·H), 256 (257-H). *Anal.* Calcd. for $C_{30}H_{35}O_2N_3$: C, 76.72; H, 7.51; N, 8.95. Found: C, 76.53; H, 7.24; N, 8.98.

5) Reduction of **3b** and **3d** with $NaBH_4$: Similar reduction of **3b** and **3d** gave **5a** in 65 and 72% yields, respectively.

6) Reduction of **3e** with $NaBH_4$: A solution of **3e** (500 mg) and $NaBH_4$ (700 mg) in EtOH (10 ml) was refluxed for 1.5 hr to give 200 mg of **5c**, colorless prisms, mp 191—192° (EtOH). IR ν_{max}^{Nujol} cm^{-1}: 1118 (C-O-C), 1022 (N-O). NMR ($CDCl_3$) δ: 6.60—8.05 (10H, m, aromatic protons), 4.70 (1H, m, C_{14}-H), 4.15 (1H, m, C_{13}-H), 3.55 (3H, s, $OC\underline{H}_3$), 2.83—3.60 (6H, m, C_2-H, C_8-H and 2,6-protons of morpholyl group), 2.65 (2H, m, C_1-H and C_9-H), 1.50—2.51 (10H, m, C_{10}-H, C_{11}-H, C_{12}-H and 3,5-protons of morpholyl group). Mass Spectrum *m/e*: 455 (M^+). *Anal.* Calcd. for $C_{29}H_{33}O_2N_3$: C, 76.45; H, 7.30; N, 9.23. Found: C, 76.41; H, 7.25; N, 9.62.

6) Reduction of **3f** with $NaBH_4$: A solution of **3f** (1 g) and $NaBH_4$ (1.55 g) in EtOH (40 ml) was refluxed for 2 hr to give 780 mg of **5b**, colorless prisms, mp 181—182° (decomp.). IR ν_{max}^{KBr} cm^{-1}: 1038 (N-O). NMR ($CDCl_3$) δ: 6.40—8.12 (10H, m, aromatic protons), 4.67 (1H, m, C_{14}-H), 4.18 (1H, m, C_{13}-H), 3.85 (2H, complex AB-q, $-OC\underline{H}_2CH_3$), 3.57—0.5 (20H, m, C_1-H, C_2-H, C_{8-12}-H and protons of piperidyl group), 1.08 (3H, t, J=7.5 Hz, $-OCH_2C\underline{H}_3$). Mass Spectrum *m/e*: 467.3024 (M^+, $C_{31}H_{37}ON_3$, Calcd. 467.2937), 423.2624 ($M-C_2H_4O$, $C_{29}H_{33}N_3$, Calcd. 423.2675), 339.1912 (423.2624-$C_5H_{10}N$, $C_{24}H_{23}N_2$, Calcd. 339.1861), 301.2218 (339.1912-C_6H_{10}, $C_{20}H_{21}N_2$, Calcd. 301.1705), 269.1025 ($C_9H_{13}N_2$, Calcd. 269.1079), 257.1005 (2,3′-biquinolyl·H, $C_{18}H_{13}N_2$, Calcd. 257.1078), 230.0999 ($C_{17}H_{12}N$, Calcd. 230.0700), 130.0443 (C_9H_8N, Calcd. 130.0657), 101.0457 (C_8H_5, Calcd. 101.0391). *Anal.* Calcd. for $C_{31}H_{37}ON_3$: C, 79.62; H, 7.98; N, 8.99. Found: C, 79.43; H, 7.74; N, 9.14.

7) Reaction of **3a** with KCN: A solution of **3a** (300 mg) and KCN (80 mg) in EtOH (20 ml) was refluxed for 5 hr and concentrated *in vacuo*. The residue was extracted with $CHCl_3$ and the extract residue was recrystallized from EtOH to give 244 mg (99.7%) of **6**, colorless leaflets, mp 220—221.5° (decomp.). IR ν_{max}^{KBr} cm^{-1}: 2210 (C≡N), 1118 (C-O-C), 1028 (N-O). UV λ_{max}^{EtOH} nm (log ε): 317.6 (3.86), 309.2 (3.80), 304 (3.83), 297.5 (3.78), 291.5 (3.78), 256.6 (4.28), 231.8 (4.59, inflec.), 228.2 (4.62). Mass Spectrum *m/e*: 494 (M^+), 467 (M-HCN), 450 ($M-C_2H_4O$), 449 (450-H), 422 ($M-C_2H_5O$-HCN), 257 (2,3′-biquinolyl·H), 256 (257-H). *Anal.* Calcd. for $C_{31}H_{34}O_2N_4$: C, 75.27; H, 6.93; N, 11.32. Found: C, 75.42; H, 7.04; N, 11.38.

Treatment of **6** (100 mg) at 230—240° gave 53 mg of **4**.

8) Hydrolysis of **3a**: A solution of **3a** (1.5 g) and KOH (1 g) in EtOH (20 ml) was refluxed for 1.5 hr; the yellow solution became deep brown after *ca.* 30 min. The reaction mixture was concentrated *in vacuo*, and the residue was mixed with H_2O and extracted with $CHCl_3$. The $CHCl_3$ solution was passed through a silica gel column and the first effluent was recrystallized from isopropyl ether to give 670 mg of **7**, colorless prisms, mp 160—161.5°. IR ν_{max}^{KBr} cm^{-1}: 1734 (C=O), 1038 (N-O). UV λ_{max}^{EtOH} nm (log ε): 317.5 (3.80), 308 (3.73, sh.), 304.2 (3.81), 297.5 (3.77), 292 (3.78), 260 (3.93, inflec.), 234.3 (4.65), 231.3 (4.67, inflec.), 229 (4.68). NMR ($CDCl_3$) δ: 6.68—8.12 (10H, m, aromatic protons), 4.72 (2H, m, C_8-H and C_{14}-H), 3.52—4.0 (3H, m, C_2-H and $-OC\underline{H}_2CH_3$), 3.28 (1H, m, C_9-H), 2.72 (1H, m, C_1-H), 2.38 (4H, m, C_{10}-H and C_{12}-H), 1.2—2.2. (2H, m, C_{11}-H), 1.04 (3H, t, J=9 Hz, $-OCH_2C\underline{H}_3$). Mass Spectrum *m/e*: 398.1922 (M^+, $C_{26}H_{26}O_2N_2$, Calcd. 398.1994), 369.1671 ($M-C_2H_5$, $C_{24}H_{21}O_2N_2$, Calcd. 369.1603), 354.1667 ($M-C_2H_4O$, $C_{24}H_{22}ON_2$, Calcd. 354.1732), 353.1638 ($C_{24}H_{21}ON_2$, Calcd. 353.1654), 301.1337 ($M-C_6H_9O$, $C_{20}H_{17}ON_2$, Calcd. 301.1341), 257.1109 (2,3′-biquinolyl·H, $C_{18}H_{13}N_2$, Calcd. 257.1078), 130.0673 (C_9H_8N, Calcd. 130.0657), 101.0406 (C_8H_5, Calcd. 101.0391). *Anal.* Calcd. for $C_{26}H_{26}O_2N_2$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.20; H, 6.64; N, 7.15. The second eluate of the chromatography gave 160 mg of light brown prisms, which were shown to be a mixture of **4** and **5a** from examinations of the IR and NMR spectra.

9) Hydrolysis of **3f**: A solution of **3f** (500 mg) and KOH (340 mg) in EtOH (7 ml) was refluxed for 1.5 hr and processed as in the above case to give 171 mg of **7** and 21 mg of **4**.

Reduction of 7 with $NaBH_4$——A solution of **7** (300 mg) and $NaBH_4$ (100 mg) in EtOH (10 ml) was refluxed for 1.5 hr, concentrated *in vacuo*, and the residue was mixed with H_2O and extracted with $CHCl_3$. The extract residue was recrystallized from EtOH to give 200 mg of **8**, colorless crystals, mp 158—159°. IR ν_{max}^{Nujol} cm^{-1}: 3558 (OH), 1066 (N-O). NMR ($CDCl_3$) δ: 6.52—8.05 (10H, m, aromatic protons), 4.82 (1H, m, C_{14}-H), 4.23 (1H, m, C_{13}-H), 3.83 (2H, the left part of complex AB-q, J=7.5 Hz, $-OC\underline{H}_2CH_3$), *ca.* 3.7—1.5 (10H, m, C_1-H, C_2-H and C_{8-12}-H), 1.24 (3H, t, J=7.5 Hz, $-OCH_2C\underline{H}_3$). Mass Spectrum *m/e*: 400 (M^+). *Anal.* Calcd. for $C_{26}H_{28}O_2N_2$: C, 77.97; H, 7.05; N, 7.00. Found: C, 77.84; H, 6.95; N, 6.76.

Thermolyses of 5a, 7 and 8——1) Thermolysis of **5a**: Heating **5a** (100 mg) in an oil bath maintained at 220° brought about fusion and gas evolution. The cooled reaction mixture was extracted with $CHCl_3$. The extract residue was purified by chromatography on silica gel and recrystallized from *n*-hexane–EtOH to give 20 mg of **9**, colorless powder, mp 209—210°. IR ν_{max}^{Nujol} cm^{-1}: 3450 (NH), 1100 (C-O-C). NMR ($CDCl_3$) δ: 6.02—8.06 (11H, m, aromatic protons and NH), 4.46 (1H, m, C_{14}-H), 3.96 (1H, m, C_{13}-H), 2.91—3.7 (6H, m, C_2-H, C_8-H and 2,6-protons of morpholyl group), 2.57—2.90 (2H, m, C_1-H and C_9-H), 1.0—2.58 (10H, m, C_{10-12}-H and 3,5-protons of morpholyl group). Mass Spectrum *m/e*: 425 (M^+). *Anal.* Calcd. for $C_{28}H_{31}ON_3$: C, 79.02; H, 7.34; N, 9.88. Found: C, 79.31; H, 7.00; N, 9.91.

2) Thermolysis of **7**: Similar thermolysis of **7** (100 mg) gave 20 mg of **10**, colorless needles, mp 225—226° (*n*-hexane–EtOH). IR ν_{max}^{Nujol} cm^{-1}: 3400 (NH), 1720 (C=O). NMR ($CDCl_3$) δ: 6.1—8.4 (11H, m, aromatic protons and NH), 4.56 (2H, m, C_8–H and C_{14}–H), 3.75 (1H, m, C_2–H), 1.0—3.5 (8H, m, C_1–H and C_{9-12}–H). Mass Spectrum *m/e*: 354 (M^+). *Anal.* Calcd. for $C_{24}H_{22}ON_2$: C, 81.30; H, 6.26; N, 7.90. Found: C, 81.09; H, 6.00; N, 7.54.

3) Thermolysis of **8**: Similar thermolysis of **8** (200 mg) gave 20 mg of **11**, colorless crystals, mp 191—192° (decomp.) (*n*-hexane–EtOH). IR ν_{max}^{Nujol} cm^{-1}: 3550, 3350 (NH and OH). NMR ($CDCl_3$) δ: 6.1—8.02 (11H, m, aromatic protons and NH or OH), 4.65 (1H, m, C_{14}–H), 1.2—4.05 (12H, m). Mass Spectrum *m/e*: 356 (M^+). *Anal.* Calcd. for $C_{24}H_{24}ON_2$: C, 80.86; H, 6.79; N, 7.86. Found: C, 80.72; H, 6.99; N, 7.73. Product **11** was also obtained by $NaBH_4$ reduction of **10**.

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