Studies on Tertiary Amine Oxides. LV. 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]tricycle[5,3,1,1.8.8]dodecan-13-yldenemorpholinium 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 invoked 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 agreed 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. 5

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\[
\begin{align*}
\text{Add.} & \quad \text{Elimn.} \\
N^+ & \quad \text{PhCOO} \\
\text{Cl}^- & \quad \text{Ph}=\text{phenyl}
\end{align*}
\]
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This type of reaction has widespread applicability and it has been recently disclosed that the reaction occurs also with 1(10)-dehydroquinolizidine and enamines of N-acyl-4-piperidones besides enamines of cyclohexanone and isobutyraldehyde. 5

* Dedicated to the memory of Prof. Eiji Ochiai.
2) Location: a) Maitashi, Higashi-ku, Fukuoka; b) Ropponmatsu, Chuo-ku, Fukuoka.
On the other hand, the reaction of N-ethoxyquinolinium iodide (1a) with 1-morpholino-cyclohexene (2a) was found to give not the expected 2-(2-quinoyl)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.\textsuperscript{6)}

![Chemical structures of A, B, and C.](image)

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-quinoyl)-3-azabenzo[\textit{d}]tricyclo[5,3,1,1\textit{\textsuperscript{4,8}}]dodecan-13-ylidenemorpholinium iodide (C, Fig. 1),\textsuperscript{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,\textsuperscript{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,\textsuperscript{9)} mp 216—217° (decomp.), in a good yield of 61%.\textsuperscript{10)}

Product 3a is a fairly stable compound with an empirical formula C\textsubscript{38}H\textsubscript{34}O\textsubscript{2}N\textsubscript{3}I, 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 deuterochloroform. 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.


\textsuperscript{7)} I. Ueda, H. Noda, and M. Hamana, \textit{Acta Crystallographica}, 1976 32.

\textsuperscript{8)} The product could not be extracted with 10% hydrochloric acid.

\textsuperscript{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.

\textsuperscript{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.
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-Alkoxynquinolinium Salts (1) with Enamines of Cyclohexanone (2)

<table>
<thead>
<tr>
<th>N-Alkoxynquinolinium salt 1</th>
<th>Enamine 2</th>
<th>Product 3</th>
<th>Yield (%)</th>
<th>mp (decomp.) (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>X</td>
<td>Z</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a  C₂H₅</td>
<td>I</td>
<td>2a</td>
<td>3a</td>
<td>99(61)ᵃ</td>
</tr>
<tr>
<td>1b  C₂H₅</td>
<td>Br</td>
<td>2a</td>
<td>3b</td>
<td>50</td>
</tr>
<tr>
<td>1c  C₂H₅</td>
<td>ClO₄</td>
<td>2a</td>
<td>3c</td>
<td>30</td>
</tr>
<tr>
<td>1d  C₂H₅</td>
<td>BF₄</td>
<td>2a</td>
<td>3d</td>
<td>72</td>
</tr>
<tr>
<td>1e  CH₄</td>
<td>ClO₄</td>
<td>2a</td>
<td>3e</td>
<td>44</td>
</tr>
<tr>
<td>1f  C₂H₅</td>
<td>I</td>
<td>2b</td>
<td>CH₃</td>
<td>59</td>
</tr>
</tbody>
</table>

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'-biquinolinyl (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'-biquinolinyl 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 azonemethinium 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, C₂₀H₂₅O₂N₅ (M⁺, m/e 469), and 5b, C₂₁H₂₃ON₃ (M⁺, m/e 467) shows that 3a and 3f lost the iodide anion

\(^{11}\) H. Weidel and G. Glänsor, Monatsh. Chem., 7, 308 (1886), and also see ref. 6b
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 C₂₉H₃₃O₂N₂ (Mr, 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 C₂₉H₃₃ON₂ 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 abovementioned 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), bear 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.

Although 3a contains five asymmetric carbons, that is C2, C8 and C14 originated from the 2, 4 and 3 positions of one quinoline ring, respectively, and C4 and C9 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.
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 transferred 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. 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.

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. 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**

Reaction of N-Ethoxyquinolinium Iodide (1a) with 1-Morpholinocyclohexene (2a)—1) To a water-cooled solution of 1a (12.0 g, 4 mmole) in CHCl₃ (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 CHCl₃ filtrate was shaken with 20% HCl and the acidic layer was made alkaline to give crystalline precipitates which were extracted with CHCl₃. The extract was dried over Na₂SO₄, evaporated and the resulting residue was solidified by triturating with

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[5,3,1,1²⁸]dodecan-13-yldienemorpholinium iodide (3a), pale yellow pillars (the orthonomic system?), mp 216—217° (decomp.). IR \( \nu_{\text{max}} \) cm⁻¹: 1643 (>N=C), 1113 (C—O—C), 1039 (N—O). UV \( \lambda_{\text{max}} \) nm (log e): 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, infsec.), 228 (4.72). Anal. Calcd. for C₂₉H₄₆O₅N₃I (dried at 60° in vacuo over P₂O₅): C, 60.50; H, 5.75; N, 7.06. Found: C, 60.76; H, 5.73; N, 7.02. Anal. Calcd. for C₂₉H₄₆O₅N₃I-1/2H₂O (dried at room temp. in vacuo over P₂O₅ 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,\(^9\) mp 208—209° (decomp.), which were interconvertible with those of the orthonomic system. Although its IR spectrum in solid state slightly differed from that of orthonomorcrystals, both spectra in CHCl₃ were identical. Anal. Calcd. for C₂₉H₄₆O₅N₃I·1/2H₂O (dried at room temp. in vacuo over P₂O₅ 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 K₂CO₃ and extracted with CHCl₃ to give 11.7 g of crude 3a.

3) To a stirred solution of 2a (15 g, 8.8 mmole) in CHCl₃ (30 ml), a solution of 1a (6.02 g, 2 mmole) in CHCl₃ (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 hydroxiodide was filtered and the CHCl₃ layer was stirred with 10% HCl (80 ml) to give 5.8 g (97.3%) of 3a.

Reactions of N-Alkoxynolinolinium Salts (1a, 1b, 1c, 1d and 1e) with Enamines of Cyclohexanone (2a and 2b)—1) Reaction of N-Ethoxyquinolinolimum Bromide (1b) with 2a: Similar treatment of 1b (2.43 g) with 2a (4 g) in CHCl₃ (20 ml) afforded 1.3 g of 3b,\(^{10}\) colorless pills, mp 198—199° (decomp.) (EtOH). IR \( \nu_{\text{max}} \) cm⁻¹: 1643 (>N=C), 1114 (C—O—C), 1031 (N—O).

2) Reaction of N-Ethoxyquinolinolimum Perchlorate (1c) with 2a: Similar treatment of 1c (2.74 g) with 2a (3.68 g) in CHCl₃ (60 ml) gave 0.84 g of 3c, colorless plates, mp 215—216° (decomp.). Anal. Calcd. for C₉₂H₄₂O₅N₃Cl: C, 63.43; H, 6.05; N, 7.40. Found: C, 63.23; H, 5.99; N, 7.25.

3) Reaction of N-Ethoxyquinolinolimum Tetrafluoroborate (1d) with 2a: Similar treatment of 1d (1.25 g) with 2a (1.7 g) in CHCl₃ (20 ml) gave 0.7 g of 3d,\(^{10}\) colorless plates, mp 198—199° (decomp.) (EtOH). IR \( \nu_{\text{max}} \) cm⁻¹: 1643 (>N=C), 1114 (C—O—C), 1031 (N—O).

4) Reaction of N-Methoxyquinolinolimum Perchlorate (1e) with 2a: Similar treatment of 1e (2.62 g) with 2a (3.68 g) in CHCl₃ afforded 1.2 g of 3e, colorless plates, mp 214—215° (decomp.) (EtOH). IR \( \nu_{\text{max}} \) cm⁻¹: 1654 (>N=C), 1090 (ClO₄ and C—O—C), 1033 (N—O). Anal. Calcd. for C₂₉H₂₆O₅N₃Cl: 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 CHCl₃ (40 ml) was kept at room temperature for 1 day. The reaction mixture was shaken with 20% HCl and the acidic solution was decomposed as described at first to give 3.5 g of 3f, colorless prism, mp 216—217° (decomp.) (EtOH). IR \( \nu_{\text{max}} \) cm⁻¹: 1632 (>N=C), 1030 (N—O). Anal. Calcd. for C₂₁H₂₆O₅N₃·2H₂O: 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[5,3,1,1²⁸]dodecan-13-yldienemorpholinium Iodide (3a) and Related Compounds (3b, 3d, 3e and 3f)—1) Thermalysis 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 NaHCO₃ solution and extracted with CHCl₃. The extract residue was recrystallized from EtOH to give 104 mg of 2,3'-biquinolyly (4), pale yellow rods, mp 170—171°. Anal. Calcd. for C₂₁H₁₈N₂O₄: 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.\(^1³\)

2) Thermalysis of 3f: Similar thermalysis of 3f (500 mg) at 230° gave 180 mg of 4.

3) Anion Exchange of 3a: A solution of 3a (300 mg) and NaClO₄ (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 280 mg of colorless plates, mp 215—217°. This was proved identical with 3c prepared from 1c and 2a.

4) Reduction of 3a with NaBH₄: A solution of 3a (500 mg) and NaBH₄ (770 mg) in EtOH (20 ml) was refluxed for 2 hr, concentrated in vacuo and the residue was treated with H₂O and extracted with CHCl₃. The extract residue was recrystallized from EtOH to give 420 mg of the reduced product 5a, colorless prisms, mp 104—105° (decomp.). IR \( \nu_{\text{max}} \) cm⁻¹: 1116 (C—O—C), 1025 (N—O). UV \( \lambda_{\text{max}} \) nm (log e): 317.5 (3.81), 310 (3.74, infsec.), 304.5 (3.81), 297.5 (3.76), 282 (3.70), 216.5 (4.15), 233 (4.63, infsec.), 228 (4.69). NMR (CDCl₃): δ: 6.40—8.04 (10H, aromatic protons) 4.66 (1H, H₂-c=H) 4.16 (1H, m, C₁=H—H) 3.79 (2H, complex AB-q, \( Jₐm=12.5 \) Hz, —OCH₃CH₃) 2.80—3.56 (6H, m, C₂=H—C₆=H and 2,6-protons of morpholyl group) 2.68 (2H, m, C₁=H and C₆=H) 1.32—2.56 (10H, m, C₁0=H, C₁1=H, C₁₅=H and 5,5-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 NaBH₄.
5. Reduction of 3b and 3d with NaBH₄: Similar reduction of 3b and 3d gave 5a in 65 and 72% yields, respectively.

6. Reduction of 3e with NaBH₄: A solution of 3e (500 mg) and NaBH₄ (700 mg) in EtOH (10 ml) was refluxed for 1.5 hr to give 190 mg of 5e, colorless prisms, mp 191–192° (EtOH). IR ν₂max cm⁻¹: 1118 (C=O-C), 1022 (N-O). NMR (CDCl₃) δ: 6.60–8.05 (10H, m, aromatic protons), 4.70 (1H, m, C₆H₄), 4.15 (1H, m, C₆H₅), 3.55 (3H, s, OCH₃), 2.83–3.60 (6H, m, C₆H₅, C₆H₂ and 2,6-protons of morpholyl group), 2.65 (2H, m, C₆H₅ and C₆H₂), 1.50–2.51 (10H, m, C₆H₄-CH₃, C₆H₅-CH₃ and 3,5-protons of morpholyl group). Mass Spectrum m/e: 455 (M⁺).

7. Reaction of 3a with KCN: A solution of 3a (500 mg) and KCN (80 mg) in EtOH (20 ml) was refluxed for 5 hr and concentrated in vacuo. The residue was extracted with CHCl₃ and the extract residue was recrystallized from EtOH to give 244 mg of 6, colorless needles, mp 220–221.5° (decomp.). IR ν₂max cm⁻¹: 2210 (C=O), 1120 (C=N-C), 1028 (N-O). UV λmax nm (log ε): 317.6 (3.88), 309.8 (3.84), 304.8 (3.83), 297.5 (3.78), 291.8 (3.78), 286.0 (4.28), 281.4 (4.58, inf.), 266.1 (4.62). Mass Spectrum m/e: 104 (M⁺), 103 (M⁺-H₂O), 48 (C₃H₆O₂), 47 (M-C₆H₅), 46 (M-C₆H₅-C), 45 (M-C₆H₅-C₂H₅), 44 (M-C₆H₆O₂), 25 (C₃H₆), 23 (C₃H₄), 13 (C₆H₅), 12 (C₆H₄), 11 (C₆H₃), 7 (C₆H₄), 5 (C₆H₃), 4 (C₆H₂), 3 (C₆H), 2 (C₆), 1 (C). Mass Spectrum m/e: 104 (M⁺), 103 (M⁺-H₂O), 48 (C₃H₆O₂), 47 (M-C₆H₅), 46 (M-C₆H₅-C), 45 (M-C₆H₅-C₂H₅), 44 (M-C₆H₆O₂), 25 (C₃H₆), 23 (C₃H₄), 13 (C₆H₅), 12 (C₆H₄), 11 (C₆H₃), 7 (C₆H₄), 5 (C₆H₃), 4 (C₆H₂), 3 (C₆H), 2 (C₆), 1 (C), 0. 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 H₂O and extracted with CHCl₃. The CHCl₃ 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 ν₂max cm⁻¹: 1734 (C=O-C), 1038 (N-O). UV λmax nm (log ε): 317.5 (3.80), 308 (3.73, sh.), 304.2 (3.81), 297.5 (3.77), 292.7 (3.78), 260.0 (3.93, inf.), 234.3 (4.65), 231.3 (4.67, inf.), 229 (4.68). NMR (CDCl₃) δ: 6.68–8.12 (10H, m, aromatic protons). 4.72 (2H, m, C₆H₅, C₆H₂ and C₆H₁), 3.52–4.0 (2H, m, C₆H₅ and OCH₃), 3.18 (1H, m, C₆H₄), 2.72 (1H, m, C₆H₂), 2.38 (4H, m, C₆H₄, C₆H₂ and C₆H₁), 1.2–3.2 (2H, m, C₆H₂), 1.10 (3H, t, J = 9 Hz, OCH₃). Mass Spectrum m/e: 398.1922 (M⁺, C₂H₄O₄, N₃), 398.1994, 369.1671 (M-C₆H₅-C₂H₄O₄, N₃), 369.1603, 354.1667 (M-C₆H₅O₄, N₃), 354.1732, 353.1638 (C₃H₄O₄, N₃), 301.1337 (M-C₆H₅O₂, N₃), 257.1078, 257.1078, 257.1109 (2,3-biquinolyl-H, C₆H₆O₂, N₃), 150.0591 (C₃H₄), 101.0406 (C₆H₅, C₆H₄, C₆H₃, C₆H₂, C₆H, C₆). The second eluate from 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.

7. Reduction of 7 with NaBH₄:—A solution of 7 (300 mg) and NaBH₄ (100 mg) in EtOH (10 ml) was refluxed for 1.5 hr, concentrated in vacuo, and the residue was mixed with H₂O and extracted with CHCl₃. The extract residue was recrystallized from EtOH to give 200 mg of 8, colorless crystals, mp 158–159°. IR ν₂max cm⁻¹: 3558 (OH), 1066 (N=O). NMR (CDCl₃) δ: 6.52–8.05 (10H, m, aromatic protons), 4.82 (1H, m, C₆H₄), 4.23 (1H, m, C₆H₅), 3.83 (2H, the left part of complex AB-q, J = 7.5 Hz, OCH₂CH₃), 3.7–1.5 (10H, m, C₆H₅, C₆H₄, C₆H₂ and C₆H₃), 1.24 (3H, t, J = 7.5 Hz, OCH₂CH₃). Mass Spectrum m/e: 400 (M⁺).

8. Thermolysis 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 CHCl₃. 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 200–210°. IR ν₂max cm⁻¹: 3450 (NH), 1100 (C=O-C). NMR (CDCl₃) δ: 6.02–8.06 (11H, m, aromatic protons and NH), 4.46 (1H, m, C₆H₄), 3.96 (1H, m, C₆H₅), 2.91–3.7 (6H, m, C₆H₅, C₆H₄, C₆H₂ and 2,6-protons of morpholyl group), 2.57–2.90 (2H, m, C₆H₅ and C₆H₄), 1.0–2.58 (10H, m, C₆H₅, C₆H₄ and 3,5-protons of morpholyl group). Mass Spectrum m/e: 425 (M⁺).

9. Thermolysis of 5a, 7 and 8—2) Thermolysis of 7: Heating 7 (100 mg) in an oil bath maintained at 220° brought about fusion and gas evolution. The cooled reaction mixture was extracted with CHCl₃. The extract residue was purified by chromatography on silica gel and recrystallized from n-hexane-EtOH to give 10 mg of 8, colorless crystals, mp 158–159°. IR ν₂max cm⁻¹: 3558 (OH), 1066 (N=O). NMR (CDCl₃) δ: 6.52–8.05 (10H, m, aromatic protons), 4.82 (1H, m, C₆H₄), 4.23 (1H, m, C₆H₅), 3.83 (2H, the left part of complex AB-q, J = 7.5 Hz, OCH₂CH₃), 3.7–1.5 (10H, m, C₆H₅, C₆H₄, C₆H₂ and C₆H₃), 1.24 (3H, t, J = 7.5 Hz, OCH₂CH₃). Mass Spectrum m/e: 400 (M⁺).
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} cm^{-1}: 3400 (NH), 1720 (C=O). NMR (CDCl₃) δ: 6.1—8.4 (11H, m, aromatic protons and NH), 4.56 (2H, m, C₈-H and C₁₄-H), 3.75 (1H, m, C₅-H), 1.0—3.5 (8H, m, C₁-H and C₇—C₁₃-H). Mass Spectrum m/e: 354 (M⁺). Anal. Calcd. for C₂₆H₄₂ON₂: 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} cm^{-1}: 3550, 3350 (NH and OH). NMR (CDCl₃) δ: 6.1—8.02 (11H, m, aromatic protons and NH or OH), 4.65 (1H, m, C₁₄-H), 1.2—4.05 (12H, m). Mass Spectrum m/e: 356 (M⁺). Anal. Calcd. for C₂₆H₄₂ON₂: 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 NaBH₄ reduction of 10.

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