215. Takuo Okuda and Takashi Yoshida*1: Coriamyrtin. X.*2
Structures of Coriamyrtin and Derivatives produced
on the Reactions in Acid and Alkali.*3
(Faculty of Pharmaceutical Sciences, Kyoto University*1)

The structure (II) is assigned to coriamyrtin on the basis of the formation of apocori-
amyrtin (IV), dihydrocoriamyrtinpentao (X), isohydrocoriamyrtin (XI), and other derivatives,
and also of the spectral evidences.

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The chemical evidences of the carbon skeleton of coriamyrtin, \( C_{15}H_{18}O_5 \), the main
toxic principle of Coriaria japonica A. Gray, was first provided by the determination of
the structure of coriarialactone (I) which is obtained by aromatization of coriamyrtin.\(^1\)
On the basis of this structure of the aromatization product, structure (II) was proposed
to be the most plausible one for coriamyrtin.\(^2\) The presence of a hemiacetal group in
II was presumed mainly by the result of the isomerization of coriamyrtin and dihydro-
coriamyrtin in acid to produce aldehydey isomers, isocoriamyrtin, \( C_{16}H_{16}O_6 \), and isohy-
drocoriamyrtin, \( C_{15}H_{14}O_5 \). The present authors have accumulated evidences to show the
complete structure of coriamyrtin to be (II).

The nuclear magnetic resonance (NMR) spectrum\(^*4\) (in pyridine) of coriamyrtin
(Fig. 1) shows signals assignable to the isopropenyl group (8.05 and 5.03\( \tau \)), the angular
methyl group (8.52\( \tau \)), and the methylene group (8.06~8.26\( \tau \), m). The signals at 5.28\( \tau \)(m),
and at 6.61\( \tau \) (d, J=4 c/s) are attributable to the protons at \( C_8 \) and \( C_9 \). The isopropenyl
signals are substituted in dihydrocoriamyrtin by doublets at 8.91\( \tau \) (J=6 c/s) and 9.12\( \tau \)
(J=6 c/s) of the isopropyl group. These NMR signals are in accord with the skeleton of
coriamyrtin shown by II. However, there are two AB quartets in coriamyrtin at 6.92
and 6.69\( \tau \) (J=4 c/s) and at 6.44 and 5.94\( \tau \) (J=3 c/s), which are assignable to 2,2-disub-
tituted epoxide and to 1,2-disubstituted epoxide, respectively, taking the chemical evidences
shown later into account.

The location of the hydroxyl group in coriamyrtin is presumed to be at \( C_4 \) by the ether
formaton between \( C_4 \) and \( C_5 \): When coriamyrtin was treated with concentrated
hydrochloric acid for a few minutes at room temperature, a new isomer of coriamyrtin,
\( C_{16}H_{18}O_5 \), m.p. 248\(^o\), which is named apocoriamyrtin (IV) was obtained. Disappearance
of the double bond and the hydroxyl group is indicated by the infrared (IR) and the NMR
spectra and also by the negative response to the bromine water test. The NMR spectrum (in pyridine)
shows three methyl signals at 8.66, 8.61 and 8.49\( \tau \), while the signals of the isopropenyl
group are absent. Two of these three methyl signals are assignable to the methyl groups in
the partial structure (IVa) which could be produced by the ring closure between the isopropenyl
and the hydroxyl group as shown by \( \Pi a \rightarrow Na \). No reaction occurred when either

\[
\begin{align*}
\text{OH} & \rightarrow -O \\
-C<\text{CH}_3 & \rightarrow -C<\text{CH}_3 \\
\Pi a & \rightarrow Na
\end{align*}
\]

*1 Sakyo-ku, Kyoto (奥田拓男，吉田隆志).
*3 This paper constitutes Part X\( \text{V} \) of a series entitled "Studies on the Components of Coriaria japonica"
A. Gray.” A preliminary report of this work has been published : Tetrahedron Letters, 1964, 439.
*4 NMR spectra were determined on a Varian Associates recording spectrometer (A-60) at 60 Mc. 
Chemical shifts were recorded in \( \tau \) values, using tetramethylsilane as the internal reference.
1) T. Kariyone, T. Okuda : Yakugaku Zasshi, 73, 928 (1953).
dihydrocoriamyrtin or α-bromocoriamyrtin had been treated with hydroiodic acid in agreement with this assumption. Apocoriamyrtin was also obtained by an analogous treatment of coriamyrtin with concentrated hydrochloric acid, or by treating coriamyrtin with hot dilute sulfuric acid. Although isocoriamyrtin has been known to be produced by the latter treatment, it is likely that apocoriamyrtin is formed as the main product at the initial stage of the reaction, because the yield of N on this treatment increased when the reaction was terminated in a shorter time. The formation of apocoriamyrtin under these reaction conditions would be a proof of spatially nearby location of the hydroxyl group to the isopropenyl group in coriamyrtin.

When picrotoxinin (V) was treated with concentrated hydrochloric acid analogously, the ring closure took place to produce an isomer, C₁₅H₁₈O₄, m.p. 324° (decomp.), which was identified with anhydropicrotorn (VI) which had been obtained by dehydration of picrotorn (VIII), and has been considered to possess an ether linkage between C₅ and C₆. The treatment of picrotoxinin with concentrated hydriodic acid was found to give mixtures of anhydropicrotorn and another isomer of picrotoxinin, which is regarded as being neopicrotoxinin (VIII). The increase of the latter product and the decrease of the former product were observed on the prolonged treatment.

The bromination of coriamyrtin has been reported to produce α-bromocoriamyrtin, C₁₅H₁₇O₃Br, which lacks the double bond and the hydroxyl group. The NMR spectrum (in CDCl₃) of α-bromocoriamyrtin now examined shows signals of two methyl groups on the tertiary carbon at 8.67 and 8.40, and an AB quartet which is assignable to the protons of the bromomethyl group at 6.51 (J=11 c/s) and 6.26 (J=11 c/s) supporting

7) S.N. Slater : Ibid., 1949, 806.
the partial structure of α-bromocoriamyrtin presumed previously.\(^8\) The debromination of α-bromocoriamyrtin has been carried out with zinc and ammonium chloride to regenerate coriamyrtin. The bromination of coriamyrtin is thus shown to be analogous to the bromination of picrotoxinin to β-bromopicrotoxinin (X).\(^9\) Further investigations on the hydroxyl group in coriamyrtin provided additional data which are in accord with the location of the hydroxyl group at C₄: Attempted oxidation of dihydrocoriamyrtin with chromic acid, and acetylation of coriamyrtin and dihydrocoriamyrtin with acetic anhydride in pyridine resulted in recovery of the starting material, while the acetylation of dihydrocoriamyrtin in the presence of ferric chloride, carried out in an analogous way to the acetylation of tertiary hydroxyl group in dihydropicrotoxinin,\(^9\) produced an amorphous acetate which shows the acetyl peak at 7.98\(^r\) (3H, s) in the NMR spectrum (in CHCl₃).

The ether formation on both the isomerization and bromination, and other properties of the hydroxyl group, coupled with the stereochemical consideration indicate that the hydroxyl group in coriamyrtin is located at C₄, and that the hydroxyl group and the isopropenyl group are located within bonding distance on the same side of the cyclohexane ring as found in picrotoxinin.\(^9\)

A chemical evidence which shows the presence of two oxides in coriamyrtin has been obtained by the alkaline hydrolysis: Dihydrocoriamyrtin was treated with 10% sodium carbonate to produce a water soluble neutral compound, C₁₄H₂₄O₇, m.p. 212~214\(^\circ\), which is named dihydrocoriamyrtinpentanol (XI). This product did not give the 2,4-dinitrophenylhydrazone nor did it reduce Fehling solution. The presence of the lactone and marked strengthening of the hydroxyl absorption are observed in the IR spectrum (in KBr) at 1767 (shoulder), 1740, and 3460 cm\(^{-1}\). The product X gave a triacetate (XII), C₁₄H₂₄O₁₈, m.p. 174~175\(^\circ\), whose NMR spectrum (in pyridine) shows the presence of three acetyl groups by the signals at 8.13\(^r\), 8.08\(^r\), and 7.91\(^r\), while the IR spectrum (in KBr) of this acetate shows the absorption band of hydroxyl group (3540 cm\(^{-1}\)) in addition to the lactone (1770 cm\(^{-1}\)) and the acetyl (1743 and 1250 cm\(^{-1}\)) absorptions. Since three of five oxygen in coriamyrtin are accounted for a lactone and a hydroxyl group, and other two are for oxides, the properties of the hydrolysis product indicate that the hydrolysis occurred at the two ethers, and that each of the two ether oxygens should be separated by more than one carbon in coriamyrtin. This observation coupled with the NMR spectrum of coriamyrtin which lacks the proton attributable to an acetal indicates the absence of either acetal or hemiacetal group in coriamyrtin.

More information concerning the ether linkages in coriamyrtin has been supplied by the inspection of isohydrocoriamyrtin (XIII). The NMR spectrum of XIII (Fig. 1) exhibits an aldehydic proton at 0.40\(^r\) (s) and an olefinic proton at 3.35\(^r\) (d, J=3 c/s), while the two AB quartets which were present in dihydrocoriamyrtin (in pyridine, 6.92 and 6.71\(^r\), J=4 c/s, and 6.43 and 5.94\(^r\), J=3 c/s) are absent. The signals attributable to the angular methyl

\[\text{Fig. 1. Nuclear Magnetic Resonance Spectra of Coriamyrtin (II) (in pyridine) and Isohydrocoriamyrtin (XII) (in CDCl₃)}\]

group (8.77, s) which appear along with the methyl protons of the isopropyl group (9.11, d, J = 6 c/s, and 8.91, d, J = 6 c/s), and a proton which is assignable to C11–H (7.35, d, J = 3.5 c/s) indicate that these parts in dihydrocoriamyrtin has been retained on the formation of isohydrocoriamyrtin. The UV spectrum, \( \lambda_{max}^{max} = 322 \text{ mµ, (log } \varepsilon = 3.96) \), and the IR spectrum, \( \nu_{OH}^{max} \text{ cm}^{-1} = 1690 \) and 1615, coupled with the NMR spectrum, show the presence of an aldehyde group conjugated with a trisubstituted double bond.

Absence of \( \alpha \)-hydrogen, and presence of a \( \gamma \)-hydrogen, as shown by the partial structure (\( \text{XIIa} \)) are also indicated. Besides the aldehydic carbonyl band, two peaks of the carbonyl band are shown at 1768 and 1744 cm\(^{-1} \) in the IR spectrum measured in KBr disk. It might be necessary to confirm whether the latter peak is due to a ketone since \( \text{XII} \) has been reported to react with two moles of \( \alpha \)-methylphenylhydrazine to give a derivative, \( \text{C}_{13}\text{H}_{13}\text{O}_{4}\text{N}_{4} \). However, the following experiments indicate that no other carbonyl group than those of aldehyde and lactone is present in \( \text{XIII} \). By sodium borohydride reduction of \( \text{XIII} \), a dihydro-derivative, \( \text{C}_{13}\text{H}_{15}\text{O}_{4} \), m.p. 182–183\( ^\circ \), which is named tetrahydrocoriamyrtin (\( \text{XIII} \)), has been produced. The reduction of the aldehyde to the primary hydroxyl group is shown by the IR and NMR (in pyridine, 5.40\( ^\circ \), diffused singlet, \( -\text{CH}_{2}\text{OH} \)) spectra. Tetrahydrocoriamyrtin gave a diacetate (\( \text{XIV} \)), \( \text{C}_{13}\text{H}_{16}\text{O}_{7} \), m.p. 113–114\( ^\circ \), whose NMR spectrum (in CHCl\(_3\)) exhibits the proton of \( -\text{OCH}_{2} \) at 5.35\( ^\circ \), a proton assignable to C11–H at 4.58\( ^\circ \), and the acetyl protons at 7.92\( ^\circ \) (6H). The IR spectrum (in Nujol) shows a hydroxyl band at 3330 cm\(^{-1} \). An isopropylidene derivative (\( \text{XV} \)), \( \text{C}_{13}\text{H}_{16}\text{O}_{6} \), m.p. 109–110\( ^\circ \), which shows the presence of a hydroxyl group by the IR band at 3425 cm\(^{-1} \) (in CHCl\(_3\)) was also produced from \( \text{XII} \). It is indicated by these observations of the derivatives that three hydroxyl groups are present in \( \text{XIII} \), and accordingly that there are two hydroxyl groups in \( \text{XII} \). Isohydrocoriamyrtin-2,4-dinitrophenylhydrazone (\( \text{XVI} \)) also yielded an isopropylidene derivative (\( \text{XVII} \)), \( \text{C}_{24}\text{H}_{26}\text{O}_{8}\text{N}_{4} \), m.p. 272\( ^\circ \) (decomp.). The possibility that an additional carbonyl group is present in \( \text{XII} \) is thus excluded. Tetrahydrocoriamyrtin consumed one-mole equivalent of periodate, indicating that two hydroxyl groups are vicinal to each other. Accordingly, a hydroxyl group should be located adjacent to \( \text{C}_6\text{–OH} \) in \( \text{XII} \).

On the periodate oxidation of \( \text{XIII} \), the product (\( \text{XVIII} \)), \( \text{C}_{13}\text{H}_{23}\text{O}_{6} \), m.p. 202–203\( ^\circ \) (decomp.), whose IR spectrum shows absorptions of \( \alpha \), \( \beta \)-unsaturated aldehyde at 2830, 1660, and 1615 cm\(^{-1} \) was isolated. It is suggested by the UV absorption, \( \lambda_{max}^{max} \text{ mµ, (log } \varepsilon = 4.01) \), that the conjugated double bond might be exocyclic. The NMR spectrum shows an aldehydic proton at \(-0.20(\text{d, } J = 6.5 \text{ c/s}) \), and an olefinic proton at 4.12\( ^\circ \) (\( q, J_1 = 6.5 \) c/s, \( J_2 = 2 \) c/s). The oxidation product \( \text{XVIII} \) gave the 2,4-dinitrophenylhydrazone, \( \text{C}_{26}\text{H}_{26}\text{O}_{8}\text{N}_{4} \), m.p. 236\( ^\circ \) (decomp.), UV \( \lambda_{max}^{max} \text{ mµ, (log } \varepsilon = 3.82) \). The IR spectrum of \( \text{XVIII} \) shows absence of the ketone which is expected to be produced by the periodate oxidation of \( \text{XIII} \). Accordingly, the formation of a hemiketal in \( \text{XVII} \) is presumable.

The analysis of the spin–spin coupling of C11–H \( \sim \) C13–H and C12–H \( \sim \) C14–H in \( \text{XVII} \) was made with the aid of nuclear magnetic double resonance as shown in Table I. These results are consistent with the partial structure (\( \text{XVIIa} \)).

Catalytic hydrogenation of isohydrocoriamyrtin was formerly reported to yield hexahydrocoriamyrtin, \( \text{C}_{13}\text{H}_{26}\text{O}_{6} \), m.p. 199–200\( ^\circ \).\(^{11} \) This product has been found by thin-layer chromatography to be composed of two constituents, and these have been isolated by elution chromatography through an alumina column. One constituent, \( \text{C}_{13}\text{H}_{26}\text{O}_{6} \), m.p. 183–184\( ^\circ \), whose IR and NMR spectra show the presence of a double bond, has

\(^{10} \) T. Kariyone, K. Kashiwagi: Yakugaku Zasshi, 54, 9 (1934).
\(^{11} \) T. Kariyone, N. Kawano: \textit{Ibid.} 71, 924 (1951).
been found to be identical with tetrahydrocoriamyrtin in all respects. Another constituent (XIX), C_{16}H_{16}O_{4}, m.p. 165~166\degree, has been shown by the IR and NMR spectra to be saturated. The structural correlation of XIX to XIII has been proved by catalytic hydrogenation of the latter. Up to about half a mole equivalent of hydrogen was slowly absorbed, and then no more uptake of hydrogen was observed. The product was identified with "hexahydrocoriamyrtin," and then was fractionated by chromatography on alumina into two constituents which were identified as XIII and XIX, respectively. This result indicates that XIX is the saturated derivative of XIII. Although the IR spectrum of XIX in Nujol shows the carbonyl absorption at 1740 cm\(^{-1}\), it is attributable to the \(\gamma\)-lactone on the basis of the above result. When equal amounts of XIII and XIX were dissolved together in ethanol, and then the solvent was distilled, the residue was
found to be identical with "hexahydrocoriamyrtin." These results, combined with the fact that the melting point of "hexahydrocoriamyrtin" is higher than either one of the constituents indicates that "hexahydrocoriamyrtin" could be a molecular compound composed by 1:1 ratio of III and XIX. "Hexahydrocoriamyrtin" was also obtained when coriamyrtin, dihydrocoriamyrtin, or α-bromocoriamyrtin were treated with Raney nickel in boiling ethanol, although it happened sometimes in these experiments that the product was composed mostly of tetrahydrocoriamyrtin. The formation of "hexahydrocoriamyrtin" by both procedures shown above and the hydrogenation of XII, in addition to the spectral evidences would be indicative of retention of the carbon skeleton of coriamyrtin in XII.

It is now considered that the only part in the molecule of XII where the partial structure XIXA can be present is C₁₁-C₁₄, with the aldehyde group located at C₁₄. Since one hydroxyl group in XII has been shown to be located adjacent to C₅-OH, the former will be at C₁₁. The structure of isohydrocoriamyrtin thus expressed by XII is consistent with all data shown above. It is observed in the NMR spectrum of XII (in CDCl₃) that one of the methylene protons shows a large downfield shift to 6.89 ppm (doublet, J₁ = 15 c/s, J₂ = 4 c/s), while another proton of the methylene group is shown at 8.38 ppm as a single doublet (J = 15 c/s). The downfield shift of one proton will be attributable to the presence of the carbonyl group at C₁₄. The secondary splitting of this lower signal will be due to the spin–spin coupling with C₅-H.

The location of the methylene group at C₂ and the couplings within each set of the AB quartets in dihydrocoriamyrtin have been confirmed by the spin–spin decoupling technic. This technic was also applied to apocoriamyrtin to prove the coupling of the

Table I. Nuclear Magnetic Double Resonance Data

<table>
<thead>
<tr>
<th>Compound solvent</th>
<th>Irradiated proton (τ)</th>
<th>Observed proton (τ)</th>
<th>Multiplicity change</th>
</tr>
</thead>
<tbody>
<tr>
<td>(XVII) CDCl₃</td>
<td>12-H 4.14</td>
<td>11-H -0.20</td>
<td>d → s</td>
</tr>
<tr>
<td></td>
<td>11-H -0.20</td>
<td>12-H 4.14</td>
<td>q → ds</td>
</tr>
<tr>
<td></td>
<td>14-H 5.33</td>
<td>12-H 4.14</td>
<td>q → d</td>
</tr>
<tr>
<td>(XX) pyridine</td>
<td>2-H 8.33</td>
<td>3-H 5.32</td>
<td>m → d</td>
</tr>
<tr>
<td></td>
<td>14-H 6.93</td>
<td>14-H 6.72</td>
<td>d → s</td>
</tr>
<tr>
<td></td>
<td>11-H 6.43</td>
<td>12-H 5.94</td>
<td>d → s</td>
</tr>
<tr>
<td>(or 12-H)</td>
<td>(or 11-H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N) pyridine</td>
<td>3-H 5.23</td>
<td>4-H 6.98</td>
<td>a)</td>
</tr>
<tr>
<td></td>
<td>4-H 6.98</td>
<td>5-H 6.51</td>
<td>dd → ds</td>
</tr>
<tr>
<td></td>
<td>14-H 6.95</td>
<td>14-H 6.73</td>
<td>d → s</td>
</tr>
<tr>
<td></td>
<td>11-H 6.41</td>
<td>12-H 6.03</td>
<td>d → s</td>
</tr>
<tr>
<td>(or 12-H)</td>
<td>(or 11-H)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

s: singlet d: doublet q: quartet ds: diffused singlet dd: diffused doublet

a) One of the peaks centered in the quartet was markedly sharpened.

AB quartets (Table I). Since the structure of isohydrocoriamyrtin XII indicates that two oxides in coriamyrtin are bound with four carbons at C₁₁-C₁₄, and that one oxide would be the terminal epoxide at C₁₃-C₁₄, which is shown as the AB quartet at the higher field in the NMR spectrum of coriamyrtin, another AB quartet at lower field will be assigned to the epoxide at C₁₁-C₁₃. This location of the latter epoxide is also supported by the NMR spectra (in pyridine) of dihydrocoriamyrtinpentaol which shows an AB quartet at 5.17τ (J = 6 c/s) and 4.76τ (J = 6 c/s), and of the triacetate XII which shows downfield shift of the AB quartet to 4.69τ (J = 6 c/s) and 4.12τ (J = 6 c/s). The structure
of dihydrocoriamyrtin thus elucidated to be (XX) is compatible with both the acid catalyzed isomerization to XI, and the alkaline hydrolysis to the pentaol X. Accordingly, the structure of coriamyrtin is expressed by the formula III. Apocoriamyrtin and α-bromocoriamyrtin would then have the structure (IV) and (XXI), respectively, although alternative isomeric structures of XXI which will be discussed in a subsequent paper can not be disregarded at present. The structure of isocoriamyrtin is shown by XXII based on the indications of the NMR spectrum (in CDCl₃) which shows three singlets of methyl protons at 8.58, 8.55 and 8.42τ, and the absence of the isopropenyl group to indicate the ether formation at C₅=C₆, and also signals at 0.32τ (s), 3.19τ (d, J=3 c/s), and 5.32τ (d, J=3 c/s), which show that the partial structure XIIa will be present in isocoriamyrtin.

The structure of dihydrocoriamyrtinpentaol could be shown by (Xa) if no other reaction than the hydrolysis of the two epoxides in XX occurred during the formation of X. The possibility that the retroaldol cleavage took place at C₅=C₆ to produce the
cyclopentanone (Xb) in an analogous way to the retroaldol cleavage of dihydropicrotoxinin⁸⁵) is excluded since the IR spectrum of the potassium salt, which was obtained by further hydrolysis of X shows no carbonyl absorption besides new peaks at 1370 cm⁻¹ and 1400 cm⁻¹. However, structure (Xc) which could be produced by the opening of the lactone during the hydrolysis followed by relactonization with C₁₂-OH is also assignable to the pentaol, while structures (Xd) and (Xe), which could be formed if the relactonization occurred with C₁₂-OH or C₁₄-OH, are incompatible with the lactone carbonyl absorption of the triacetate XI.

The stereochemistry of coriamyrtin and problems of its derivatives will be discussed in the subsequent papers.

Experimental⁸⁵

Apocoriamyrtin (IV) a) To finely ground crystals of coriamyrtin (III) (100 mg.), conc. HI (1 ml., sp.

⁸⁵ Melting points are uncorrected. Specific rotations were recorded with a Rex Photoelectric Polarimeter. Neutral alumina (Woelm), and silica gel G acc. to Stahl (E. Merck) were used for elution chromatography and thin-layer chromatography, respectively.

gr. 1.7) was added. Complete dissolution was effected immediately. Water (5 mL) was added 3 min. later, and after standing 4 hr., crystals were filtered. The filtrate was extracted with ether, and the organic phase was washed with Na₂SO₄ and water successively. After drying over Na₂SO₄, the solvent was distilled to give an additional crop of crystals. Total yield: 70 mg. Recrystallization from EtOH afforded colorless needles, m.p. 248°. Anal. Calcd. for C₂₃H₂₉O₅: C, 64.73; H, 6.52. Found: C, 64.58; H, 6.53. NMR₆max(δ): 8.66(s), 8.61(s), 8.49(s) ((CH₃)₂C-O-), 6.17-7.17); 8.36(d), 8.22(difused doublet) (-CH₂-); AB q, 6.95, 6.73(J=4 c/s) (terminal epoxide); Abq, 6.41, 6.03 (J=3 c/s) (C₁₁-C₁₀ epoxide).

When the solution of (Ⅶ) (200 mg) in conc. HIC (2 mL) was left to stand for 2 hr., and then treated in analogous way as above, 66 mg of crude crystals were obtained. After recrystallization from EtOH, the product was identified with (Ⅶ) obtained above.

b) A suspension of finely ground crystals of coriamyrtin (0.5 g) in conc. HCl (5 mL) was vigorously stirred for 1 hr., and then 2.5 mL of conc. HCl was added. Stirring was continued for an additional 2 hr. A small amount of insoluble material was filtered, and water (20 mL) was added to the filtrate. The diluted filtrate was extracted with ether, and the dried extract was evaporated to give a viscous residue which was dissolved in a small amount of boiling EtOH. The solution was concentrated to yield colorless crystals which were collected (90 mg.), and recrystallized from EtOH to give colorless needles, m.p. 249-250°. Identification with the product obtained in a) was done by mixed fusion and IR spectra.

c) To finely ground coriamyrtin (1 g.), 1% H₂SO₄ (350 mL) was added, and the suspension was heated on a boiling water-bath. The crystals were dissolved within 1 hr., and the solution was neutralized with NaOH, concentrated to 50 mL in vacuo, and extracted with ether. The extract was dried over MgSO₄, and was distilled to give an oily residue which deposited colorless crystals on standing. The crystals were collected (0.1 g.), and recrystallized from EtOH to give pure crystals of (Ⅶ). The oily filtrate was chromatographed on an alumina column (1 x 25 cm.) using CHCl₃ as eluant to give iso-coriamyrtin (XIII).

Anhydropiroctin (Ⅵ) and Neopiroctoxin (Ⅷ)——a) To finely ground piroctoxin (Ⅶ) (200 mg), conc. HIC (1.2 mL) was added. With vigorous stirring, complete dissolution was effected in a few minutes. Water (5 mL) was added 10 min. later, and the diluted solution was left to stand for 1 hr. to complete deposition of crystals which were collected by filtration (130 mg.). Recrystallization from EtOH afforded colorless crystals of (Ⅷ), m.p. 324° (decomp.), which were identified by mixed fusion and IR spectra with anhydropiroctin obtained from piroctin.a Anal. Calcd. for C₂₃H₂₉O₅: C, 61.60; H, 5.50. Found: C, 61.66; H, 5.59.

The mother liquor was extracted with ether, and the organic layer was washed with Na₂SO₄ solution and then with water. The dried extract was evaporated to give a crystalline residue which was recrystallized from acetone-petroleum benzine to give colorless crystals of (Ⅷ), m.p. 210-213° (26 mg.). Anal. Calcd. for C₂₃H₂₉O₅: C, 61.60; H, 5.50. Found: C, 61.48; H, 5.73. NMR₆max(δ): 8.56(s), 8.23(s), 8.23(s) ((CH₃)₂C=), 6.17-7.17); 7.65(d, J=14 c/s), 6.86(q, J₃=14 c/s), J₃=14 c/s) (-CH₂- at C₁₁); 6.37(s, C₆-H); 5.86(d, J=3 c/s, C₃-H); 5.16(d, J=4 c/s, C₅-H); 4.22(d, J=4 c/s, C₇-H).

The treatment of piroctoxin (1.0 g) with conc. HIC (5 mL) for 2 hr. yielded 220 mg of precipitate which on recrystallization from EtOH gave 160 mg of (Ⅷ). By extraction of the mother liquor with ether, 300 mg of crude crystals were obtained, and were recrystallized from EtOH-ether to give pure crystals of (Ⅷ).

b) Finely ground piroctoxin (0.5 g) was stirred vigorously with conc. HIC (15 mL). The solution was deposited crystalline precipitate whose amount increased slowly. The precipitate was filtered and washed with ether, 300 mg of crude crystals were obtained, and were recrystallized from EtOH-ether to give pure crystals of (Ⅷ).

Bromination of Coriamyrtin and Debromination of α-Bromocoriamyrtin——Bromine was added to the solution of coriamyrtin (1.0 g) in hot water (500 mL) until the brown color persisted. After cooling, the precipitate was filtered, and recrystallized from EtOH to give colorless crystals of (XV), m.p. 229° (0.75 g.). Anal. Calcd. for C₂₃H₂₉O₅Br: C, 50.43; H, 4.76. Found: C, 50.25; H, 4.91. NMR₆max(δ): 8.67(s), 8.40 (s) (CH₃); AB q, 7.17, 6.95(J=4 c/s, epoxide); AB q, 6.71, 6.32(J=3 c/s, epoxide); AB q, 6.31, 6.26(J=11 c/s, -CH₂Br).

α-Bromocoriamyrtin (XV) (1.0 g) was suspended in boiling EtOH (20 mL), and 20% NH₄Cl solution in water (1.5 mL) was added. Zinc powder (0.5 g) was added in small portions to the boiling mixture. The equal amount of NH₄Cl solution was added 30 min. later, and zinc powder (0.5 g) was added again in small portions. After boiling for one additional hour, the solid was filtered. Recrystallization from EtOH provided needles, m.p. 226° (0.5 g.), which were identified with coriamyrtin.

Dihydrocoriamyrtinental (X)——A suspension of finely powdered coriamyrtin (1.0 g.) in 10% Na₂CO₃ (170 mL) was stirred in N₂ atmosphere at 80° for 45 min. The resulting solution was cooled, and stirred with Amberlite IR-120 (H-form, 200 mL). The resin was filtered and the filtrate was evaporated in vacuo to give yellow oily residue which was crystallized from EtOH-EtOAc. Recrystallization from the same solvent mix-
ture provided colorless prisms of (X), m.p. 212~214°C (262 mg.). *Anal.* Calcd. for C₈H₈O₂: C, 56.95; H, 7.65. Found: C, 56.99; H, 7.67. [α]D° +19.0° (c=0.9, H₂O). IR Δmax cm⁻¹: 3460, 1767(shoulder), 1740.

**Dihydrocoryamytinepentalo-triaceata (XI)**—Finely powdered dihydrocoryamytinepentalo (95 mg.) in the mixture of AcO (2 ml) and pyridine (2 ml) was allowed to stand at room temperature overnight. The resulting solution was poured into ice water, the white crystalline mass was collected, and washed with ice water. Colorless needles of XI, m.p. 174~175°C (80 mg.) were obtained on recrystallization from aqueous EtOH. *Anal.* Calcd. for C₁₉H₂₉O₁₀: C, 56.99; H, 6.83. Found: C, 57.30; H, 7.07. [α]D° +72.4° (c=0.44, CHCl₃). IR Δmax cm⁻¹: 3540(OH); 1770(γ-lactone); 1743, 1250(acetyl). νmax cm⁻¹: broad band, peaks at 1772, 1753, 1742. NMR Δmax (δ): 8.92 (d, J=6 c/s, 6H, (CH₃)₃ CH(~)); 8.32 (CH₃- C~); 8.13, 8.08, 7.91(AcO x 3); 5.62 (s, -CH₂O-); ABq. 4.69, 4.12 (J=6 c/s, -CH-CH-CH-); 4.05 (m, -CH-OAc).

**Hydrolysis of Dihydrocoryamytinepentalo**—A solution of (X) (5 mg.) in methanol 0.5N KOH (0.08 ml.) was refluxed in a boiling water-bath for 30 min. After cooling, the solvent was removed by lyophilization to provide white solid potassium salt. IR Δmax cm⁻¹: 1570, 1400 (-COO-).

**Isohydrocorymyxin (XI)**—A suspension of finely ground dihydrocorymyxin (XX) (2 g.) in 1.5% HSO₄ (700 ml.) was boiled in a boiling water-bath for 15 hr. The resulting solution was neutralized with NaOH and concentrated *in vacuo* to 300 ml., and extracted with ether. The dried extract was evaporated to provide an oily residue which was crystallized from EtOH-H₂O. Recrystallization from the same solvent afforded prisms, m.p. 148~149°C (990 mg.). *Anal.* Calcd. for C₁₉H₂₉O₁₀: C, 64.29; H, 7.14. Found: C, 64.36; H, 7.18. [α]D° +64.9° (c=0.49, CHCl₃). UV Δmax mp (log ε): 232(3.96). IR Δmax cm⁻¹: 3420(OH); 1768, 1744 (γ-lactone); 1690, 1615(α, β-unsaturated aldehyde).

**Tetrahydrocorymyxin (XIII)**—A solution of NaBH₄ (25 mg.) in MeOH (5 ml.) was added in portions to a solution of (XI) (154 mg.) in MeOH (15 ml.). After standing 24 hr. at room temperature, the mixture was acidified with AcOH, and evaporated *in vacuo*. The residue was taken up with water and extracted with CHCl₃. The CHCl₃ layer was washed with water, dried over Na₂SO₄, and evaporated to yield a crystalline residue. Recrystallization from MeOH afforded colorless needles, m.p. 182~183°C (105 mg.). *Anal.* Calcd. for C₁₉H₂₉O₁₀: C, 63.81; H, 7.85. Found: C, 63.74; H, 8.09. [α]D° +108.7° (c=0.6, dioxane). IR Δmax cm⁻¹: 3400, 3270(OH); 1765(γ-lactone), 1650 (double bond). NMR Δmax (δ): 5.40 (diffused singlet, -CH₂O); 3.72 (m, C₁₂-H).

**Diacetyl tetrahydrocorymyxin (XIV)**—Tetrahydrocorymyxin (50 mg.) was acetylated with Ac₂O (0.3 ml.) and pyridine (0.3 ml.). The acetate was recrystallized from ligroin to afford prisms, m.p. 113~114°C (25 mg.). *Anal.* Calcd. for C₂₅H₃₀O₁₄: C, 62.25; H, 7.15. Found: C, 62.30; H, 7.16. [α]D° +208.7° (c=0.62, dioxane). IR Δmax cm⁻¹: 3330(OH); 1740, 1245, 1220(AcO). NMR Δmax (δ): 7.92 (s, AcO x 2); 5.35 (diffused singlet, -CH₂(OAc)); 4.58 (diffused doublet, C₁₁-H).

**Isopropyliden tetrahydrocorymyxin (XV)**—A solution of tetrahydrocorymyxin (50 mg.) in acetone containing a drop of conc. H₂SO₄ was stirred with anhydrous CuSO₄ (40 mg.) for 5 days at room temperature, and then refluxed for 20 hr. Filtered solution was neutralized with Na₂CO₃, and evaporated *in vacuo* to yield an oily residue which was chromatographed on a column of alumina (1.5 x 10 cm.). The acetone was eluted by CHCl₃ and was recrystallized from petr. benzine to give colorless needles, m.p. 109~110°C. *Anal.* Calcd. for C₁₉H₂₉O₁₀: C, 67.06; H, 8.13. Found: C, 67.08; H, 8.35. IR Δmax cm⁻¹: 3425, 1770, 1620, 1380, 1340. NMR Δmax (δ): 8.63 (s), 8.53 (s), 8.43 (s) (CH₃- C~); (CH₂(OAc-OAc)); 5.84 (s), 8.51 (s), 8.47 (s) (CH₃)₂CHC⃗O-; CH₃- C~.

**Isodihydrocorymyxin-2,4-dinitophenylhydrazone-acetonide (XVII)**—A solution of isodihydrocorymyxin-2,4-dinitophenylhydrazone (50 mg.) in acetone (20 ml.) containing a drop of conc. H₂SO₄ was stirred with anhydrous CuSO₄ for 2 days. The solution was neutralized with Na₂CO₃, and filtered. The solvent was removed from the filtrate, and the crystalline residue was recrystallized from acetone-EtOH to give yellow needles, m.p. 272°C (decomp.) (42 mg.). *Anal.* Calcd. for C₂₅H₂₉O₁₄N₄: C, 57.59 H, 5.64. Found: C, 57.42; H, 5.59. IR Δmax cm⁻¹: 3270(NH); 1766(γ-lactone); 1340(CH₃). NMR Δmax (δ): 8.54 (s), 8.51 (s), 8.47 (iso-Pr~); 8.48 (s), CH₃- C~); 5.3 (d, J=2 c/s, -CH₂O-); 4.12 (q, J₁=6.5 c/s, J₂=2 c/s), -0.20 (d, J=6.5 c/s, -C=CH-CHO).

**Oxidation of Tetrahydrocorymyxin (XIII) with Sodium Metaperiodate**—A solution of 0.25 M NaIO₄ (2 ml.) was added to a solution of (XII) (77 mg.) in aqueous EtOH (40%, 3 ml.). After standing at room temperature for 24 hr., crystals were collected. Recrystallization from benzene afforded colorless needles of (XVII), m.p. 202~203°C (decomp.) (50 mg.). The filtrate was neutralized with NaHCO₃, concentrated *in vacuo* to 3 ml., and extracted with CHCl₃. The CHCl₃ solution was washed with H₂O, dried over MgSO₄, and evaporated to yield an additional crop of (XVII), m.p. 202~203°C (decomp.) (12 mg.). *Anal.* Calcd. for C₂₅H₂₉O₁₀N₄: C, 64.27; H, 7.19. Found: C, 64.56; H, 7.20. UV Δmax mp (log ε): 250(4.01). IR Δmax cm⁻¹: 3300(OH); 2830, 1660, 1615(α, β-unsaturated aldehyde); 1768(γ-lactone). NMR Δmax (δ): 9.07 (d, J=6 c/s), 8.90 (d, J=6 c/s) (iso-Pr~); 8.48 (s), CH₃- C~); 5.3 (d, J=2 c/s, -CH₂O-); 4.12(q, J₁=6.5 c/s, J₂=2 c/s), -0.20 (d, J=6.5 c/s, -C=CH-CHO).
The 2,4-dinitrophenylhydrazone was obtained by adding a solution of the reagent in aqueous EtoH containing sulfuric acid to the ethanolic solution of (XVII). Recrystallization from EtoH yielded orange needles, m.p. 236° (decomp.). Anal. Calcd. for C₂₃H₂₄O₁₂N₄: C, 54.78; H, 5.25; N, 12.17. Found: C, 54.85; H, 5.32; N, 12.07. UV_{max} (log ε): 382(4.32). IR_{max} cm⁻¹: 3450, 3250(OH, NH); 1741(1784 cm⁻¹ when measured in CHCl₃, γ-lactone).

**Hexahydrocoriamyrrin**—a) Isohexahydrocoriamyrrin (HI) (200 mg.) was hydrogenated over previously reduced PtO₂ (20 mg.) in EtoH to absorb 1.87 mole of H₂ during 4 hr. The catalyst was filtered, washed with EtoH, and the filtrate combined with the washing was evaporated in vacuo. The residue was recrystallized from aqueous EtoH to provide colorless prisms, m.p. 200~201° (100 mg.). Anal. Calcd. for C₂₃H₂₄O₁₂: C, 65.58; H, 8.18. Found: C, 63.41; H, 8.40. \( \text{IR}_{\text{max}} \text{ cm}^{-1} = 3410, 1770, 1220, 1190, 1170, 1225, 1060, 1030, 920. \) This product showed two spots on the thin-layer chromatography when developed with EtOAc-petr. benzine (9:1) using \( \text{I}_2 \) as the coloring indicator.

b) A solution of coriamyrrin (500 mg.) in EtoH (100 ml.) was refluxed with Raney nickel W-211° (5 g.) for 7 hr. The catalyst was filtered, washed with EtoH, and the filtrate combined with the washing was evaporated to yield an oily residue which was crystallized from petr. benzine. Recrystallization from EtoH-petr. benzine afforded colorless needles, m.p. 200~201°, which were identified with the product of a) by mixed fusion and IR comparison (100 mg.).

c) A solution of dihydrocoriamyrrin (XX) (900 mg.) in EtoH (250 ml.) was refluxed with Raney nickel W-2 (9 g.) for 7 hr. After filtration of the catalyst and distillation of the solvent, the product was crystallized from petr. benzine and then recrystallized from EtoH-petr. benzine to provide colorless needles, m.p. 199~200°, which were identified with the product of a) and b) (220 mg.).

d) \( \alpha \)-Bromocoriamyrrin (300 mg.) was treated with Raney nickel W-2 (5 g.) for 8 hr. in an analogous way as described above, and the product was recrystallized from acetone-petr. benzine to provide crystals which were identified with the product of a)~c).

**Isolation of (XIII) and (XIX) from “Hexahydrocoriamyrrin”**—“Hexahydrocoriamyrrin” (130 mg.) was dissolved in warm acetone, and the solution was poured on an alumina column (1.5 × 25 cm.). Initial eluate was EtOAc-petr. benzine (9:1), and the ratio of EtOAc was gradually increased. Fractions eluted with EtOAc-petr. benzine (95:5) provided crystals which were recrystallized from acetone-petr. benzine to afford colorless prisms of (XIII), m.p. 162~166° (42 mg.). Anal. Calcd. for C₁₀H₈O₃: C, 63.36; H, 8.51. Found: C, 63.18; H, 8.48. \( \text{IR}_{\text{max}} \text{ cm}^{-1} = 3400, 3300(\text{OH}); 1740(\text{lactone}). \) NMR_{\text{max}} (°): 7.20(d, J=4 c/s, C₆-H), 5.93(m, C₄-H x 2), 5.33(m, C₅-H).

The fraction eluted with EtOAc-petr. benzine (98:2) yielded crystals which were recrystallized from CHCl₃–hexane to afford colorless crystals, m.p. 175~176° (35 mg.). This product was identified with tetrahydrocoriamyrrin (XII) by mixed fusion and IR comparison.

“Hexahydrocoriamyrrin” from (XIII) and (XIX)—Tetrahydrocoriamyrrin (4 mg.) and the saturated product (XIX) (4 mg.) were dissolved in warm EtoH (0.5 ml.), and the solvent was removed to give a residue which was recrystallized from petr. benzine to afford crystals, m.p. 199~200°. This product was identified with “hexahydrocoriamyrrin” by mixed melting point and IR spectra.

**Hydrogenation of Tetrahydrocoriamyrrin (XIII)**—Tetrahydrocoriamyrrin (55 mg.) was hydrogenated over previously reduced PtO₂ (10 mg.) in AcOH (15 ml.) to absorb ca. half a mole equivalent of hydrogen within 4.5 hr. The filtered solution was evaporated in vacuo, and the residue was recrystallized from acetone-petr. benzine to yield crystals, m.p. 198~199° (36 mg.). This product was identified with “hexahydrocoriamyrrin” by IR comparison and mixed fusion. Chromatographic separation carried out as above provided (XIII) and (XX).

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