Studies on Fish-killing Components of *Callicarpa candicans*

Part II. Structure of Callicarpone*

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It was deduced from the spectral data of callicarpone (I), the tetraol (IV), the chlorohydrin (VII) and the anhydro-diacetyl derivative (II) that I was a tricarbocyclic diterpene having an ene-1,4-dione and an \( \alpha \)-hydroxy-isopropyl attached to an oxide ring. The structure of the rearranged product obtained by treatment with sodium carbonate was established to be IX by converting it to 11-methoxy-ferruginol methyl ether. As this rearrangement was assumed to be initiated by proton abstraction by base, the structure I was required for callicarpone to explain the formation of IX.

In the preceding paper it was suggested from the spectral data that callicarpone, \( \text{C}_{20}\text{H}_{28}\text{O}_{4} \), has conjugated carbonyl groups, double bond and one hydroxyl group although it did not afford any carbonyl derivatives and was not acetylated with acetic anhydride in pyridine. In this paper, we wish to report the details of the structural elucidation of callicarpone (I).

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\begin{align*}
\text{II} & : \text{C}_{24}\text{H}_{30}\text{O}_{5} \quad (M.W. 398, M^{+}, m/e 398), \text{m.p.} 197\sim198^\circ \text{C} \\
\text{III} & : \text{C}_{24}\text{H}_{32}\text{O}_{5}, \text{m.p.} 187.5\sim189^\circ \text{C}
\end{align*}
\]

Callicarpone (I), treated with acetic anhydride in the presence of sodium acetate, gave in poor yield a product (II), \( \text{C}_{24}\text{H}_{30}\text{O}_{5} \) \( (M.W. 398, M^{+}, m/e 398) \), m.p. 197\sim198\(^{\circ}\)C, which appeared to be a diphenol diacetate from the infrared (IR) \( (\nu_{\text{C=O}} 1780\text{cm}^{-1}) \) and nuclear magnetic resonance (NMR) \( (2.23, 2.33\text{p.p.m., 3H singlets}) \) spectra. The two tertiary methyl proton signals \( (1.18, 1.29\text{p.p.m.}) \) of the five in the NMR spectrum of I were not observed, there appeared instead signals characteristic for vinylic methyl \( (2.05\text{p.p.m.}) \) and terminal methylene \( (5.08, 5.22\text{p.p.m., multiplets}) \). Its dihydro-derivative (III), \( \text{C}_{24}\text{H}_{32}\text{O}_{5} \), m.p. 187.5\sim189\(^{\circ}\)C did not exhibit these signals but two three-proton doublets \( (J=7\text{c.p.s.}) \) at 1.20 and 1.24 p.p.m. and one-proton septet \( (J=7\text{c.p.s.}) \) at 2.94 p.p.m. ascribed to isopropyl group attached to a benzene ring. This indicates that II is a diphenol diacetate having isoprenyl group on the benzene ring and consequently that I contains \( \alpha \)-hydroxy-isopropyl group which is dehydrated on acetylation concurrent with aromatization.

Lithium aluminum hydride reduction of I gave a tetraol (IV), \( \text{C}_{20}\text{H}_{34}\text{O}_{4} \), m.p. 150\sim152\(^{\circ}\)C, with only end absorption in the ultraviolet (UV) spectrum, showing the presence of the double bond. This and the absence of olefinic proton signals in the NMR spectrum of I.

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* A preliminary account of this work was previously outlined: K. Kawazu and T. Mitsui, Tetrahedron Letters, 3519 (1966).
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1) K. Kawazu, M. Inaba and T. Mitsui, This Journal, 31, 504 (1967).
confirm that I contains a tetrasubstituted double bond. The NMR spectrum of IV in pyridine exhibited two one-proton signals at 4.38 (triplet,  J=8.5 c.p.s.) and 4.91 p.p.m. (multiplet) assigned to hydroxyl-bearing methine protons, indicative of the presence of two secondary hydroxyl groups. Acetylation of IV gave diacetate (V), C24H38O6, m.p. 192.5~193.5°C; two hydroxyl proton signals (2.5 and 3.0 p.p.m.) and two acetoxyl-bearing methine proton signals at 5.29 (triplet,  J=8.5 c.p.s.) and 5.87 p.p.m. (multiplet) confirm that two of the four hydroxyl groups of IV are secondary and the others tertiary. The generation of two secondary hydroxyl groups on lithium aluminum hydride reduction of I, and the broad carbonyl absorption band of I show that I has two ketone groups which are suggested from the UV maximum (266.5 mλ, ε 6.68×10³) to be involved in ene-1,4-dione system. One of the two tertiary hydroxyl groups of IV is the one present originally in I and the other is considered to have been derived from an oxide ring.

Lead tetraacetate oxidation of V, which furnished acetone and a product, C19H26O3 (VI), suggests that the two tertiary hydroxyl groups in V construct 1,2-glycol and consequently that α-hydroxy-isopropyl group is attached to the oxide ring in I. The oxidation product (VI), m.p. 158~160°C, is a phenol having (only one acetoxyl group νC=O 1720 cm⁻¹; 2.15 p.p.m. singlet), which may have resulted from the counterpart by aromatization concurrent with removal of acetate.

The presence of oxide in I was confirmed by conversion of I to chlorohydrin (VII) C20H29O4Cl, m.p. 213~214°C, with hydrochloric acid in dioxane. The UV absorption maximum at 265.5 mλ (ε 9.28×10³) showed the ene-1,4-dione system being kept unchanged in VII and the NMR spectrum also exhibited all the signals due to five tertiary methyl groups and showed the presence of two hydroxyl groups which, being not acetylated with acetic anhydride-pyridine, appeared to be tertiary. A one-proton doublet (J=0.8 c.p.s.) at 4.15 p.p.m. is apparently assigned to a chlorine-bearing methine proton.

It is, therefore, concluded that I is a tricarbocyclic diterpene having an ene-1,4-dione and an α-hydroxy-isopropyl group attached to an oxide ring.

On ozonolysis and subsequent alkaline hydrogen peroxide oxidation, I gave a dicarboxylic acid (VIII), C12H20O4, m.p. 164~166°C, [α]D ^20 -11° (acetone) and (+)-terebic acid, m.p. 172~174°C. The melting point, optical rotation and IR spectrum of the dicarboxylic acid (VIII) were in good agreement with those of (−)-trans-2,6,6-trimethyl-2-carboxycyclohexylacetic acid obtained from dehydroabietane.² The NMR spectrum of VIII in benzene which showed three signals due to tertiary methyls at 0.53, 0.74 and 1.21 p.p.m. and three-proton signals of A₂B-type at 2.15~2.62 p.p.m. gave a support on this structure.

On treatment with sodium carbonate in methanol, I gave diphenol A (IX), C20H28O4, m.p. 158~159°C (dec.), [α]D ^20 +18° (chloroform) in 75% yield and diphenol B (X), C17H22O3, m.p. 236~237°C (dec.), [α]D ^20 +65° (methanol) in 10~15% yields. IX exhibited intense green color with ferric chloride in methanol and wine-red color on addition of sodium carbonate, and showed intramolecularly associated hydroxyl absorption bands at 3370 and 3130 cm⁻¹ in the infrared spectrum. This suggests that it is an o-diphenol. The NMR spectrum displayed all the five signals due to tertiary methyl groups originally present in I

and three hydroxyl proton signals, showing that pendant methyl groups were kept unchanged on this reaction and two new hydroxy (phenolic) groups had generated. Anhydro-diacetate, C\textsubscript{24}H\textsubscript{30}O\textsubscript{5}, m.p. 197~198°C, with $\nu\textsubscript{C=O}$ 1697 cm\textsuperscript{-1} (aryl ketone), derived quantitatively from IX by acetylation with acetic anhydride-sodium acetate was identical with II derived from I. Diphenol A dimethyl ether (XI), C\textsubscript{25}H\textsubscript{32}O\textsubscript{4}, m.p. 108~109°C, obtained by methylation of IX with methyl iodide in the presence of potassium carbonate in acetone, appeared to hold $\beta$-hydroxy-isopropyl group (NMR, 1.60 p.p.m., 6H singlet) and one hydrogen on the phenolic ring (NMR, 7.86 p.p.m., 1H singlet) and to have aryl ketone (IR, $\nu\textsubscript{C=O}$ 1694 cm\textsuperscript{-1}). Thus it may be considered that IX is an $\alpha$-hydroxy-isopropyl catechol whose phenolic ring is conjugated with ketone group.

This $\alpha$-diphenol (IX) was also ozonized to afford (-)-trans-2,6,6-trimethyl-2-carboxy-cyclohexylacetic acid (VIII).

Thus, it is inferred that IX is possibly represented by the partial formula IX\textsubscript{a} or IX\textsubscript{b}.

\begin{center}
\begin{tikzpicture}
\node at (0,0) {\text{IX a}};
\node at (3,0) {\text{IX b}};
\end{tikzpicture}
\end{center}

Diphenol A monomethyl ether (XII), C\textsubscript{23}H\textsubscript{32}O\textsubscript{4}, m.p. 212~213°C, obtained by methylation of IX with diazomethane was dehydrated by boiling in methanolic sulfuric acid to anhydro-diphenol A monomethyl ether (XIII), C\textsubscript{22}H\textsubscript{29}O\textsubscript{3}, m.p. 172~173.5°C. Its dihydro derivative (XIV), C\textsubscript{21}H\textsubscript{27}O\textsubscript{3}, m.p. 202~204°C, accorded with cryptojaponol\textsuperscript{3} in respects of melting point, optical rotation, UV and IR spectra, whose acetate (XV), C\textsubscript{23}H\textsubscript{35}O\textsubscript{5}, m.p. 168~169°C, $[\alpha]_{D}\textsuperscript{20} + 43^\circ$ (methanol) was proved to be identical with cryptojaponol acetate\textsuperscript{3} by mixed melting point and IR spectrum. In order to get further proof on the structure, XIV was transformed via desoxocryptojaponol (XVI), C\textsubscript{21}H\textsubscript{29}O\textsubscript{3}, m.p. 93~95°C to desoxocryptojaponol methyl ether (XVII), C\textsubscript{22}H\textsubscript{31}O\textsubscript{2}, m.p. 89.5~91°C, $[\alpha]_{D}\textsuperscript{20} + 100^\circ$ (ethanol) which was shown to be identical with 11-methoxy-ferruginol methyl ether\textsuperscript{4} derived from ferruginol in respects of melting point, optical rotation, IR and NMR spectra. It is, therefore, established that diphenol A is represented by the formula IX.

The response (deep blue color) of diphenol B (X) to phosphomolybdate test and the NMR spectrum in trifluoroacetic acid which exhibited a pair of one-proton doublets at 6.83 and 7.32 p.p.m. ($J=3$ c.p.s.), suggested that X was a $m$-diphenol. The loss of two downfield three-proton singlets, attributable to the methyls of $\alpha$-hydroxy-isopropyl group indicated that acetone was lost on the reaction. The

Ozonolysis of XVIII affording the dicarboxylic acid (VIII) led to representation of X as Xa or Xb. The largely deshielded proton on the phenolic ring (7.32 p.p.m. for X and 7.71 p.p.m. for XVIII) requires the formula Xa. The rearrangement of I to IX and X on treatment with sodium carbonate is assumed to be initiated by proton abstraction by base, as formulated in the following mechanism.
The placement of the oxide linkage in 12,13-positions in I is required to explain the formation of IX and X. In case of a base attacking the hydrogen on the oxide, I was rearranged to IX, whereas I gave X with loss of acetone in rare case of a base attacking the tertiary hydroxyl hydrogen. The structure of callicarpone is, therefore, elucidated to be represented by I, configuration of the epoxide being left unestablished.

Two proton signals of an AB-type quartet at 2.43 and 3.41 p.p.m. in the NMR spectrum of I are ascribed to axial and equatorial hydrogens on C14, respectively. The equatorial hydrogen is coupled to the hydrogen on C12 (3.71 p.p.m.) through long range.

(±)-Terebic acid obtained on ozonolysis of I, followed by oxidation, is considered in terms of the structure I to have resulted from α,β-epoxy-δ-hydroxyisopropyl-glutaric acid formed on the ozonolysis.

On treatments with hydroiodic acid in acetic acid and with zinc in acetic acid, I afforded monophenol (XIX), C_{20}H_{26}O_{2}, m.p. 230~232°C, [α]_{D}^{25}+49° (chloroform) and monophenol (XX), C_{20}H_{28}O_{3}, m.p. 220~222°C, [α]_{D}^{25}+44° (methanol), respectively. The facile aromatizations of the C-ring on these reactions are reasonably understood from the proximity of epoxide to ene-1,4-dione in I.
Studies on Fish-killing Components of Callicarpa candicans. Part II

EXPERIMENTAL

Treatment of Callicarpone (I) with Acetic Anhydride-sodium Acetate

A solution of I (200 mg) and anhydrous sodium acetate (100 mg) in acetic anhydride (5 ml) was boiled under reflux for one hour. Addition of water afforded crystals of a product (II) (100 mg), which were collected and recrystallized from methanol: m.p. 197–198°C; [α]D430 +48° (c 1.5, chloroform); νmax 2230 (s 2.32 × 104), 252 (2 1.26 × 104), 300 mµ (s 2.15 × 104); νmax (nujol) 1780, 1697, 1630, 1600, 1550 cm⁻¹; δCDCl3 0.96, 0.98, 1.35, 2.23, 2.33 (3H each, s), 2.05 (3H, q., J=1.4 and 0.9), 5.08, 5.22 (1H each, m), 7.98 p.p.m. (1H, s). Found: C, 72.27; H, 7.57. Calcd. for C2H4O: C, 72.33; H, 8.59%.

Hydrogenation of the diacetate (II). Compound II (100 mg) in acetic acid (5 ml) in the presence of platinum oxide (10 mg) absorbed one mole of hydrogen. After removal of acetic acid, water was added to the residue. Crystals (III) (100 mg) were recrystallized from methanol: m.p. 187.5–189°C; [α]D430 +45° (c 2.3, chloroform); νmax 2120 (c 3.01 × 104), 258.5 mµ (c 2.32 × 104), 252 (e infl. 1.26 × 104), 282.5 (e 1.84 × 103), 287 mp (s shoulder 1.73 x 103); δCDCl3 3541, 3455, 1720, 1708 cm⁻¹; δCDCl3 0.89 (6H, s), 1.17 (3H, s), 1.18 (6H, s), 2.07, 2.13 (3H each, s), 2.5, 3.0 (1H each, two hydroxyls), 5.29 (1H, t., J=8.5), 5.87 (1H, m). Found: C, 68.51; H, 8.85. Calcd. for C2H4O: C, 68.22; H, 9.07%.

Lead Tetraacetate Oxidation of Tetaol Diacetate (V).

Compound V (100 mg) in benzene (50 ml) was mixed with lead tetraacetate (249 mg) in benzene (30 ml), and the mixture was left at room temperature over-night. A slow stream of dry nitrogen was passed through the mixture to sweep out any volatile fragments into a receiver containing 2 N hydrochloric acid (30 ml) saturated with 2.4-dinitrophenylhydrazine. The crude hydrazone formed was filtered off and air dried, 13 mg, m.p. 125–126°C, no depression on mixing with acetone 2.4-dinitrophenylhydrazone. Water was added to the mixture left in the reaction flask, and extracted with ether. Removal of ether gave crystals, which were separated on preparative thin layer chromatography on silica gel (benzene-ethyl acetate, 10 : 3) to one major product (VI) (50 mg) and the unchanged acetate (25 mg). The major product was recrystallized from benzene-hexane: m.p. 158–160°C; [α]D430 +20° (c 1.4, chloroform); νmax 282.5 (ε 1.84 × 104), 287 mµ (ε shoulder 1.73 × 104); δNaOH 305 mµ (ε 2.42 × 103); νmax 3300, 1720, 1622, 1584 cm⁻¹; δCDCl3 0.93, 0.94, 1.24, 2.14 (3H each, s), 6.01 (1H, t., J=8), 5.84 (1H, s), one hydroxyl), 6.61 (lH, d., J=3), 6.73 (1H, q., J=8 and 3), 7.08 (1H, d., J=8). Found: C, 75.92; H, 8.99. Calcd. for C2H2O: C, 75.46; H, 8.67%.

Chlorohydrin (VII). To a solution of I (100 mg) in dioxane (4 ml) was added conc. hydrochloric acid (0.3 ml). After being allowed to stand at room temperature for four hours, the mixture was poured into ice water and the resulting crystals were recrystallized from ether-n-hexane giving pale yellow prisms of VII (100 mg): m.p. 213–214°C; [α]D430 +38° (c 1.0, chloro-
form); positive to Beilstein test; \( \lambda_{\text{max}}^\text{EH} = 265.5 \text{ m}\mu \) (\( \varepsilon = 9.28 \times 10^3 \)); \( \delta_{\text{CDCl}_3} = 9.28 \times 10^3 \); \( \nu_{\text{CHCl}_3} = 3617, 3535, 1707, 1679 \text{ cm}^{-1} \);

\( \delta_{\text{CDCl}_3} = 0.93, 0.94, 1.38 \text{ (3H each, s.)}, 1.43 \text{ (6H, s.)}, 2.2, 3.3 \text{ (1H each, two hydroxyls)}, 4.15 \text{ (1H, d., } J = 0.8 \text{)}. \) Found: C, 65.27; H, 7.93; Cl, 10.19. Calcd. for C\(_{20}\)H\(_{29}\)O\(_4\)Cl: C, 65.11; H, 7.93; Cl, 9.61%.

**Ozonolysis of callicarpone (I).** A stream of ozone was passed through a solution of I (350 mg) in carbon tetrachloride (20 ml) under cooling at 5°C for five hours. Hydrogen peroxide (30%) (3 ml) was added to the mixture, and it was left overnight. After removal of carbon tetrachloride, the residue was extracted with ether, and the ether layer was extracted with 2 N sodium carbonate solution. The alkaline solution was acidified with 2 N hydrochloric acid and extracted with ether. Removal of ether gave an oil (312 mg). To this oil dissolved in 2 N sodium hydroxide solution (12 ml) was added 30% hydrogen peroxide (12 ml), and the mixture was allowed to stand overnight and acidified with conc. hydrochloric acid to furnish crystals. The crystals (VIII) (82 mg) were collected and recrystallized from ether-hexane; m.p. 164°–166°C, [\( \alpha \]_D] = -11° (c 2.3, acetone). These constants and the infrared spectrum are in good agreement with those\(^2\) (m.p. 162°C, [\( \alpha \]_D] = 6° (c 1.04, acetone)) of (-)-trans-2,6,6-trimethyl-2-carboxy-cyclohexylacetic acid derived from abietic acid. NMR: \( \delta \) (benzene) 0.53, 0.74, 1.21 (3H each, s.), 2.15–2.62 (3H, A\(_2\)B-type), \( \delta \) (CDCl\(_3\)) 0.87, 1.00, 1.30 (3H each, s.), 2.40 (2H, s. overlapped with 1H, m.), 10.38 (2H, two hydroxyls). Found: C, 62.86; H, 8.89. Calcd. for C\(_{12}\)H\(_{20}\)O\(_4\): C, 63.13; H, 8.83%.

The filtrate from the crystals (VIII) was extracted with ether, and ether was evaporated to give an oil, which was triturated with a small amount of ether to afford needles (17 mg), m.p. 164–166°C, \( \delta \) (pyridine) 1.51, 1.65 (3H each, s.), 2.52–3.65 (3H, A\(_2\)-type). This acid was identified as (±)-terebic acid by no depression of the melting point on admixture with synthetic (±)-terebic acid, m.p. 173–174°C and comparing their infrared spectra.

**Diphenol A (IX) and Diphenol B (X).** Sodium carbonate (12 g) solution (200 ml) was added to a solution of I (20 g) in methanol (200 ml), and the mixture was boiled under reflux for ten minutes. After an addition of water, the mixture was shaken with ether, and separated to alkaline and ether layers. The alkaline layer was acidified with 2 N sulfuric acid, and the crystals collected were dissolved in ether. After being washed with saturated sodium bicarbonate solution, the ether layer was concentrated to yield crystals (16.5 g), which were recrystallized from dilute methanol to give prisms of diphenol A (IX), m.p. 158–159°C (dec.). [\( \alpha \]_D] = +18° (c 1.0, chloroform); deep green with ferric chloride in methanol, turning to wine-red on addition of sodium carbonate; dark green (response of catechol type) to phosphomolybdate test. \( \lambda_{\text{max}}^\text{EF} = 240 \) (\( \varepsilon = 1.35 \times 10^4 \)), 290.5 (\( \varepsilon = 9.36 \times 10^3 \)), 305 (\( \varepsilon \) shoulder 7.30 \times 10^3), 365 \text{ mp} (\( \varepsilon \) infl. 1.32 \times 10^3); \( \lambda_{\text{max}}^\text{IN NaOH} = 257.5 \) (\( \varepsilon = 8.55 \times 10^3 \)), 281 (\( \varepsilon \) shoulder 7.30 \times 10^3), 340 (\( \varepsilon \) shoulder 3.67 \times 10^3), 435 \text{ mp} (\( \varepsilon \) 5.88 \times 10^3). \( \delta_{\text{max}}^\text{nujol} = 3520, 3370, 3130, 1665, 1610, 1565 \text{ cm}^{-1} \); \( \delta_{\text{CDCl}_3} = 0.95, 1.00, 1.30 \text{ (3H each, s.)}, 2.40 (2H, s. overlapped with 1H, m.), 10.38 (2H, two hydroxyls). Found: C, 72.45; H, 8.38. Calcd. for C\(_{12}\)H\(_{20}\)O\(_4\): C, 72.26; H, 8.49%.

The ether layer was extracted with 1 N sodium hydroxide solution and the alkaline solution was acidified with 2 N sulfuric acid to give crystals (2.9 g), m.p. 205°C (dec.). Purification was effected by sublimation at 145–160°C (1 mmHg) and gave needles of diphenol B (X): m.p. 236–237°C (dec.), [\( \alpha \]_D] = +65° (c 1.6, methanol); purple with ferric chloride in chloroform; deep blue color (response of resorcinol type) to phosphomolybdate test. \( \lambda_{\text{max}}^\text{EF} = 274 \) (\( \varepsilon = 9.02 \times 10^3 \)), 342.5 \text{ m}\mu  (\( \varepsilon = 3.30 \times 10^3 \)), 290.5 \text{ m}\mu  (\( \varepsilon \) shoulder 7.30 \times 10^3), 340 (\( \varepsilon \) shoulder 3.67 \times 10^3), 435 \text{ mp} (\( \varepsilon \) 5.25 \times 10^3). \( \delta_{\text{max}}^\text{nujol} = 3520, 1668, 1600, 1520 \text{ cm}^{-1} \); \( \delta_{\text{CF}_3\text{COOH}} = 1.00, 1.05, 1.48 \text{ (3H each, s.)}, 6.83, 7.32 (1H each, d., } J = 3 \text{). Found: C, 74.10, H, 8.09. Calcd. for C\(_{17}\)H\(_{22}\)O\(_3\): C, 74.42; H, 8.08%.

**Diacetyl anhydro-diphenol A (II).** A solution of diphenol A (500 mg) was treated with anhydrous sodium acetate (200 mg) in acetic anhydride (10 ml) to give diacetyl anhydro-diphenol A quantitatively; m.p. 197–198°C, (recrystallized from dilute methanol), which was shown to be identical with II derived from I, by mixed melting point and their infrared spectra.

**Diphenol A dimethyl ether (XI).** Diphenol A (IX) (100 mg) and methyl iodide (2 ml) were kept for four hours in boiling acetone (10 ml) in the presence of anhydrous potassium carbonate (200 mg). The inorganic precipitates were filtered off and washed with ether. The combined organic layer was concentrated to give crystals which were recrystallized...
from dilute methanol, 100 mg: m.p. 108–109°C, [α]D20 +35° (c 1.6, chloroform). νmax (nujol) 215 (ε 2.25 x 104), 273 mε (ε 1.21 x 104); νmax (CDCl3) 3740, 1694, 1589, 1540 cm–1; δ(CDCls) 0.94, 0.98, 1.30 (3H each, s), 1.60 (6H, s), 3.11 (1H, one hydroxyl), 3.80, 3.99 (3H each, s), 7.86 (1H, s). Found: C, 73.29; H, 8.94. Calcd. for C22H32O4, 73.30; H, 8.95%.

Monomethyl ether (XII) also gave this dimethyl ether (XI) by methylation with methyl iodide in acetone in the presence of anhydrous potassium carbonate.

Ozonolysis of diphenol A (IX). A stream of ozone was passed through a solution of IX (100 mg) in carbon tetrachloride (30 ml) till an aliquot of the solution showed no absorption at 280 μm. The mixture was treated with 30% hydrogen peroxide (6 ml) and processed as described for ozonolysis of 1. The acidic fraction gave crystals (68 mg), which were recrystallized from acetone-hexane and/or ether-hexane: m.p. 164–166°C, [α]D20 –10° (c 2.0, acetone), identical with VIII obtained from I.

Diphenol A monomethyl ether (XII). Diphenol A (IX) (100 mg) was methylated with diazomethane in ether. The resulting crystals were recrystallized from methanol to afford needles (100 mg): m.p. 212–213°C, [α]D20 +15° (c 1.1, chloroform). νmax (nujol) 230 (ε 1.3 x 104), 275 (ε 9.3 x 103), 296.5 (ε 3.9 x 103), 379 mε (ε 3.3 x 103); νmax (CDCl3) 0.91, 0.94, 1.23, 1.61, 1.66, 3.90 (3H each, s), 4.11, 6.93 (1H each, s, two hydroxyls), 7.58 (1H, s). Found: C, 72.64; H, 8.60. Calcd. for C21H35O4: C, 72.80; H, 8.73%.

Anhydro-diphenol A monomethyl ether (XIII). Compound XII (100 mg) in methanol (50 ml) containing conc. sulfuric acid (5 ml) was boiled for one hour under reflux. Water was added, and crystals were recrystallized from benzene-hexane; 100 mg, m.p. 172–173.5°C, [α]D20 +33° (c 2.5, chloroform). νmax (nujol) 254 (ε 2.3 x 104), 275 (ε 8.1 x 103), 323 mε (ε 4.1 x 103); νmax (CDCl3) 257.5 (ε shoulder 1.5 x 104), 376.5 mε (ε 4.1 x 103); δ(CDCls) 3300, 1680, 1640, 1560, 1543 cm–1; δ(CDCls) 0.95, 0.98, 1.41, 2.12, 3.79 (3H each, s), 5.24 (2H, m), 6.43 (1H, one hydroxyl) and 7.55 (1H, s). Found: C, 76.92; H, 8.60. Calcd. for C21H28O3: C, 76.92; H, 8.59%.

Dihydro-anhydro-diphenol A monomethyl ether (XIV). Compound XIII (100 mg) in acetic acid (15 ml) absorbed one mole of hydrogen in the presence of platinum oxide (20 mg). The catalyst and solvent were removed, and the crystals were recrystallized from methanol; 67 mg, m.p. 202–204°C, [α]D20 +25° (c 1.0, chloroform). νmax (nujol) 229 (ε 1.6 x 104), 274 (ε 9.5 x 103), 317.5 mε (ε 3.5 x 104); νmax (CDCl3) 254 (ε 1.6 x 104), 294.5 (ε 5.8 x 104), 385.5 mε (ε 3.5 x 104); δ(CDCls) 3470, 1687, 1604 cm–1; δ(CDCls) 0.95, 0.98 (3H each, s), 1.24, 1.26 (3H each, d, J=7), 1.40, 3.82 (3H each, s), 6.18 (1H, one hydroxyl) and 7.63 (1H, s). Found: C, 76.26; H, 9.19. Calcd. for C21H35O3: C, 76.32; H, 9.15%.

Desoxycryptojaponol (XVI). Compound XIII (300 mg) was hydrogenated (2.7 moles) over platinum oxide (45 mg) in acetic acid (10 ml) under atmospheric pressure. The solvent and catalyst were removed and the crystals (300 mg) were chromatographed in benzene over silicic acid (Mal- linckrodt) (10 g). The benzene eluate was fractionated, 30 ml for each fraction being collected. The first fraction gave the major product (126 mg), recrystallized from methanol; m.p. 93–95°C, [α]D20 +63° (c 1.3, chloroform). νmax (nujol) 230 (ε 1.38 x 104), 274 (ε 1.48 x 104), 319 mε (ε 2.95 x 103); δ(CDCls) 0.95 (6H, s), 1.22 (6H, d, J=7), 1.33 (3H, s), 3.75 (3H, s, one hydroxyl), 6.47 (1H, s). Found: C, 79.78; H, 10.27. Calcd. for C21H32O3: C, 79.70; H, 10.19%.

The seventh fraction afforded another product (56 mg), recrystallized from n-hexane, m.p. 163–164.5°C, [α]D20 +34.1° (c 0.92, methanol). The acetate (XV) was obtained by treatment of XIV with acetic anhydride in pyridine, m.p. 168–169°C (recrystallized from ethanol), [α]D20 +43° (c 1.0, methanol). Found: C, 74.32; H, 8.68. Calcd. for C21H35O3: C, 74.16; H, 8.66%. Identity with an authentic sample of cryptojaponol acetate (m.p. 204–205°C, [α]D20 +25.3° (c 1.0, chloroform), νmax (CDCl3) 3470, 1687, 1604 cm–1; δ(CDCls) 0.95, 0.98 (3H each, s), 1.24, 1.26 (3H each, d, J=7), 1.40, 3.82 (3H each, s), 6.18 (1H, one hydroxyl) and 7.63 (1H, s). Found: C, 76.26; H, 9.19. Calcd. for C23H32O4: C, 74.16; H, 8.66%.

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Desoxycryptojaponol methyl ether (XVII). Desoxycryptojaponol (XVI) (20 mg) was methylated with methyl iodide in acetone in the presence of potassium
carbonate to give needles of the methyl ether (XVII) (10 mg), m.p. 89.5-91°C (from methanol), [α]_D^25 +100° (c 0.5, ethanol), δ(CDCl₃) 0.94 (6H, s.), 1.18, 1.21 (3H each, d., J=7), 1.31, 3.76, 3.84 (3H each, s.), 6.64 (1H, s.). Found: C, 79.83; H, 10.64. Calcd. for C_{22}H_{34}O_{2}: C, 79.95; H, 10.37%. Identity with 11-methoxy ferruginol methyl ether (m.p. 89-90.5°C, [α]_D^25 +104° (c 0.13, ethanol)) was shown by IR and NMR spectra.

**Diacetyl diphenol B (XVIII).** Diphenol B (X) (200 mg) in pyridine (2 ml) was treated with acetic anhydride (4 ml) for twenty hours at room temperature. The reaction mixture was poured into water and the resulting oil was extracted with ether. Removal of ether gave an oil, which was crystallized from dilute ethanol and recrystallized from dilute methanol, m.p. 100-101°C, [α]_D^25 +51° (c 1.0, chloroform); υ_{max} (nujol) 1772, 1695, 1610, 1580, 1455 cm⁻¹; δ(CDCl₃) 0.94, 0.97, 1.35, 2.24, 2.30 (3H each, s.), 6.99, 7.71 (1H each, d., J=3). Found: C, 70.51; H, 7.37. Calcd. for C_{21}H_{26}O_{5}: C, 70.37; H, 7.31%.

**Diphenol B monomethyl ether.** Diphenol B (X) (50 mg) was methylated with diazomethane in ether. The crystals, a mixture of X and the product was dissolved in ether and the ether solution was washed with 2 N sodium hydroxide to remove X. Removal of ether gave crystals of the monomethyl ether, recrystallized from dilute methanol, m.p. 240-245°C (dec.), δ(CDCl₃) 0.97, 0.91, 1.41, 3.81 (3H each, s.), 6.48, 7.22 (1H each, d., J=3). Found: C, 74.60; H, 8.47. Calcd. for C_{18}H_{24}O_{3}: C, 74.97; H, 8.39%.

**Ozonolysis of diacetyl diphenol B (XVIII).** Compound XVIII (170 mg) was ozonized and worked up as described for ozonolysis of I. The acidic fraction gave crystals (66 mg), which were recrystallized from ether-hexane to give prisms of a dicarboxylic acid, m.p. 164-166°C, [α]_D^25 -9° (c 1.8, acetone), identical with VIII.

**Treatment of callicarpone (I) with hydroiodic acid.** Hydroiodic acid (b.p. 126°C) (0.12 ml) was added to the solution of I (0.100 g) in acetic acid (1.2 ml) and the reaction mixture was allowed to stand for one hour. Titration with sodium thiosulfate solution proved that one molar equivalent of iodine liberated on this reaction. Water was added to the mixture, which was extracted with ether. Removal of ether and acetic acid gave crystals of a monophenol (XIX) (70 mg); recrystallization from dilute methanol: m.p. 230-232°C; [α]_D^25 +49° (c 1.0, chloroform); λ_{max} (ethanol) 257.5 (ε infl. 1.1×10⁴), 240 (ε 2.4×10⁴), 337.5 με (ε 1.9×10⁴); λ_{max} (pyridine) 3300, 3150, 1667, 1632, 1600, 1565 cm⁻¹; δ(CDCl₃) 0.96, 0.98, 1.43 (3H each, s.), 1.72 (1H, one hydroxyl), 2.12 (3H, q., J=1.5 and 0.8), 5.10, 5.37 (1H each, m.), 5.78 (1H, one hydroxyl), 7.04, 7.79 (1H each, d., J=2). Found: C, 79.85; H, 8.75. Calcd. for C_{19}H_{26}O_{5}: C, 80.49; H, 8.78%.

**Zinc-acetic acid reduction of callicarpone (I).** Zinc powder (200 mg) was added to a solution of I (100 mg) in acetic acid (20 ml) and the mixture was stirred for fifteen minutes. Water was added to the mixture, the mixture was extracted with ether, and the ether was removed to leave crystals of a monophenol (XX) (100 mg); after recrystallization from chloroform-n-hexane; 91 mg, m.p. 220-222°C; [α]_D^25 +44° (c 0.6, methanol); λ_{max} (pyridine) 3400, 3300, 1672, 1605 cm⁻¹; λ_{max} (acetone) 7.29, 7.64 (1H each, d., J=2). Found: C, 75.65; H, 8.89. Calcd. for C_{18}H_{28}O_{3}: C, 75.91; H, 8.92%. When the reaction was carried out under reflux, I afforded XIX besides XX.

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