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Structures of the Oxidation Products of Grayanotoxins

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Structures of oxidation products of grayanotoxins are determined by chemical and spectroscopic methods. The IR spectra of numerous derivatives of triketo-G-II and diketo-G-I derived from grayanotoxins by chromium trioxide oxidation showed that the triketone and diketone compounds should be represented such as XXVII and XXII, respectively.

In previous report it has been shown that grayanotoxin-I (G-I), $C_{22}H_{36}O_7$, and grayanotoxin-III (G-III), $C_{20}H_{34}O_6$, the toxic constituents of *Leucothoe grayana* and other *Ericaceae* plants, can be represented by structures (I) and (III),[2a,b] respectively, including the stereochemistry.[2c,d] Iwasa, *et al.* proved independently that the third constituent of *Leucothoe grayana*, grayanotoxin-II (G-II), $C_{20}H_{32}O_5$, has structure (II).[3] Tallent has also derived the same stereochemistry for the grayanotoxins,[4] excepting the relative configuration of C-3, which was left undefined, and the absolute configuration. The structural relation between G-II and G-III was experimentally confirmed by the dehydration of G-III in refluxing acetone with anhydrous copper sulfate to give G-II.[5] Structures of the various oxidation products of grayanotoxins are presented in this report, which were obtained during the structural studies.

Catalytic hydrogenation of G-II affords α-dihydro-G-II (IV).[6] This was oxidized with sodium periodate or lead tetraacetate to yield the hemiacetal (V), which was further oxidized with chromic trioxide in acetic acid to give α-dihydroanhydrodiketolactone (VI). The diketolactone (VI) was dehydrated with phosphorous oxychloride to afford a new lactone (VII), the infrared (IR) spectrum of which showed the presence of a γ-lactone (1780 cm^{-1}), five-membered ring ketone (1730 cm^{-1}), exocyclic double bond (1670 and 895 cm^{-1}), but no hydroxy group. An exo-type dehydration had thus occured to produce the exocyclic double bond, the presence of which was confirmed by the near-infra-red (N.I.R.) spectrum of VII showing bands attributable to a terminal methylene group at 2118 and 1626 mμ. Although dehydration of the C_{16}-OH group in G-I had afforded the endo-cyclic double bond upon treatment with anhydrous copper sulfate in acetone, dehydration of keto-G-II derivatives with phosphorous oxychloride afforded in all cases exo-double bond compounds such as VII (*vide infra*).

1) Location: *a*) *Ohtsuka, Bunkyo, Tokyo*; *b*) *Hiromachi, Shinagawa, Tokyo*; *c*) *Katahiracho, Sendai.*
2) *a*) H. Kakisawa, M. Kurono, S. Takahashi and Y. Hirata, *Tetrahedron Letters*, **1961**, 59; *b*) H. Kakisawa, *J. Chem. Soc. Japan.* **82**, 1096, 1216 (1961); *c*) H. Kakisawa, M. Yanai, T. Kozima, K. Nakanishi and H. Mishima, *Tetrahedron Letters*, **1962**, 215; *d*) H. Kakisawa, T. Kozima, M. Yanai and K. Nakanishi, *Tetrahedron*, **21**, 3091 (1965).
3) J. Iwasa, Z. Kumazawa and M. Nakajima, *Chem. Ind.* (London), **1961**, 511; *Agr. Biol. Chem.*, **25**, 782 (1961).
4) W.H. Tallent, *J. Org. Chem.*, **27**, 2968 (1962); **29**, 2756 (1964).
5) H. Meguri, *J. Pharm. Soc. Japan*, **79**, 1060 (1959).
6) M. Nakajima and J. Iwasa, *Botyu-Kagaku*, **13**, 11 (1949).

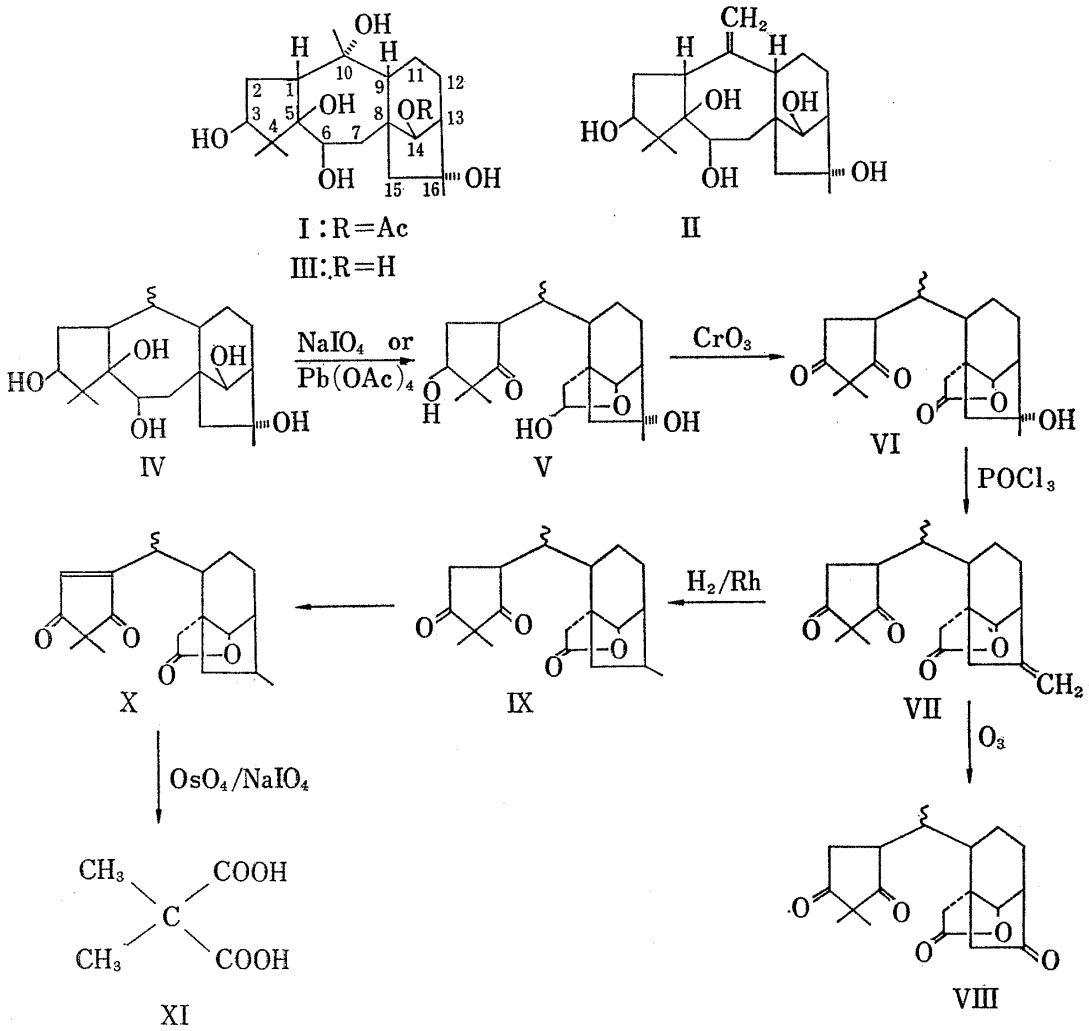

Chart 1

Ozonolysis of VII afforded the α-dihydronortriketolactone (VIII). Reduction of the terminal methylene group in VII by catalytic hydrogenation afforded 16-desoxy-α-dihydrodiketolactone (IX); the C_{16}-methyl group of IX is considered to have the β-configuration as suggested from the stereochemical course of catalytic hydrogenation. Selenium dioxide oxidation of IX in dioxane yielded a compound which is formulated as the enedione–lactone (X) on the basis of spectroscopic data which were consistent with a cyclopentene-3,5-dione chromophore.[7] Thus the IR spectrum of X showed the presence of γ-lactone (1790 cm^{-1}) and ketone (1745 and 1703 cm^{-1}), and the ultraviolet (UV) spectrum of X showed an absorption maximun at 235 mμ (ε 12800). The presence of such group was confirmed by oxidation of X with osmium tetroxide and sodium periodate to yield dimethylmalonic acid (XI).

Ozonolysis of G-II (II) gave norketo-G-II (XII),[8] which was easily dehydrated with alkali to give anhydronorketo-G-II (XIII), IR ν_{max}^{KBr}: 1643 and 1600 cm^{-1}. UV λ_{max}^{EtOH}: 251 mμ (ε 9000). The IR and UV spectra of XIII indicated that this compound had an α,β-unsaturated ketone chromophore, and this was supported by chromium trioxide oxidation of XIII in pyridine to afford the enedione (XV), IR ν_{max}^{KBr}: 1669 and 1600 cm^{-1}, UV λ_{max}^{EtOH}: 265 mμ (ε 7870). Treatment of XIII with *p*-toluenesulfonyl chloride gave the monotosylate (XIV), UV λ_{max}^{EtOH}: 226 mμ (16500) and 253 mμ (ε 8900), which was oxidized with chromium trioxide in pyridine to the enedione-monotosylate (XVI), IR ν_{max}^{KBr}: 3450, 1680, 1610, 1603, 1190 and 1175 cm^{-1}, UV

7) C.H. Depuy and E.F. Zaweski, *J. Am. Chem. Soc.*, **81**, 4920 (1959).
8) M. Nakajima and J. Iwasa, *Botyu-Kagaku*, **16**, 28 (1951).

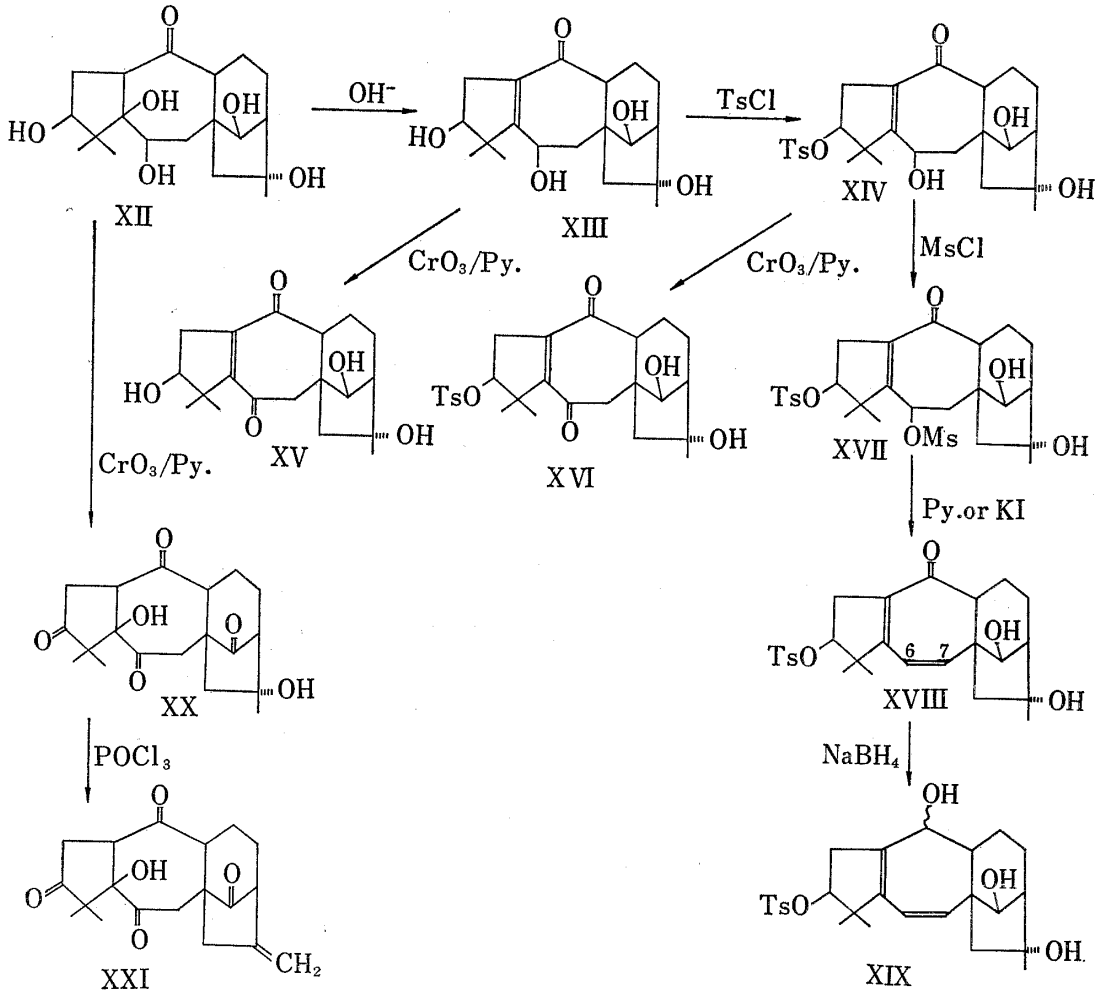

Chart 2

λ_{max}^{EtOH}: 227 (13600) and 263 mμ (ε 7050). These chemical and spectroscopic properties of XIII—XVI suggested that the tosyl group in XIV is attached to C_3 and not to C_6. The monotosyl-monomesylate (XVII) obtained upon treatment of the tosylate (XIV) with methansulfonyl chloride was converted into a dienone (XVIII) by refluxing in pyridine or by heating with potassium iodide in methyl ethyl ketone. Whereas the UV spectrum of the enone (XVII) showed absorption maxima at 226 (17800) and 246 mμ (ε 9050), the dienone (XVIII) showed the maxima at 222 (19700) and 310 mμ (ε 5180). These spectral properties indicated that the compound (XVIII) has an $\alpha,\beta,\gamma,\delta$-unsaturated ketone group. The structure (XVIII) is also supported from its NMR spectrum which exhibited an AB-type quartet at 5.78 and 6.77 ppm (J=12.6 Hz) due to the two protons attached to C_6 and C_7. Reduction of (XVIII) with sodium borohydride afforded a homodiene XIX. UV λ_{max}^{EtOH}: 225 (19600) and 264 mμ (ε 9470). These facts supported the fact that the B-ring of grayanotoxins is seven membered.

The three secondary hydroxyl groups in norketo-G-II (XII) were oxidized with chromium trioxide in pyridine to give nortetraketo-G-II (XX). IR ν_{max}^{KBr}: 3570, 3440, 1745 and 1715 cm^{-1}, which was dehydrated with phosphorous oxychloride to afford anhydronortetraketo-G-II (XXI). IR ν_{max}^{KBr}: 3470, 3060, 1755, 1740, 1715, 1660 and 895 cm^{-1}. From the IR spectrum it is obvious that this dehydration also occurred at C_{16} in the direction of a terminal methylene group.

We have previously reported that treatment of grayanotoxin-I (I) with chromium trioxide in pyridine afforded, by oxidation of the two secondary hydroxyl groups, a diketo-G-I, $C_{22}H_{32}O_7$, and furthermore, alkaline hydrolysis of the diketo compound gave monoketo-G-III-carboxylic acid having structure (XXIV).[2b] Formation of the monoketo-G-III-carboxylic acid

from diketo-G-I by alkaline hydrolysis suggested that a β-diketone group or a potential β-diketone group should be present in diketo-G-I. The genesis of the keto acid (XXIV) is explained as follows. The α-glycol group of G-I is first oxidized to an α-ketol (XXII), which is further transformed to the β-diketone (XXIII) *via* an acyloin rearrangement accompanied by a change in the ring system. Thus the monoketo-G-III-carboxylic acid can be considered to be formed through the β-diketone intermediate (XXIII).[9] However, since such rearrangements as the conversion of XXII to XXIII takes place even under mild conditions, it was not possible to determine whether diketo-G-I should be represented by XXII or by XXIII. To clarify this point the following oxidation reactions were performed on G-II.

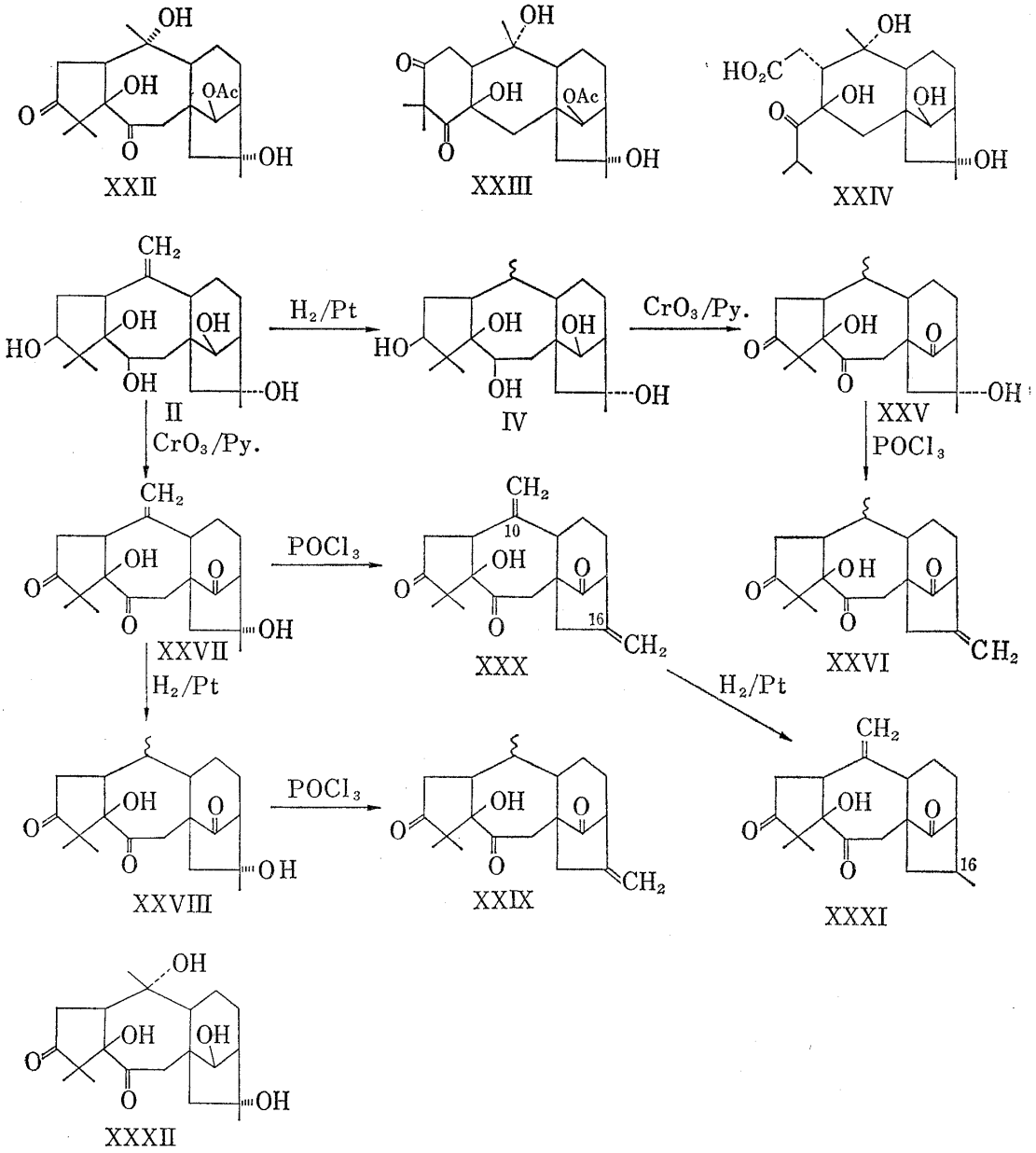

Chart 3

Oxidation of α-dihydro-G-II (IV) with chromium trioxide in pyridine yielded triketo-α-dihydro-G-II (XXV), which was dehydrated to XXVI with phosphorous oxychloride. The IR spectrum of XXVI also exhibited bands due to the terminal methylene group at 3072, 1660

9) W. Cocker, *Chem. Ind.* (London), **1955**, 1485; D.G. Hardy, *J. Chem. Soc.*, **1957**, 2955.

and 895 cm^{-1}. Similar oxidation of G-II (II) gave triketo-G-II (XXVII), which was also dehydrated with phosphorous oxychloride to afford anhydrotriketo-G-II (XXX). Catalytic hydrogenation of XXX in ethanol with platinum oxide absorbed one mole of hydrogen to yield 16-desoxytriketo-G-II (XXXI). The IR spectrum of XXVII shows bands due to the terminal methylene group at 3100, 1635, and 916 cm^{-1}, whereas that of XXX shown absorption at 3090, 1655, 1630, 920 and 895 cm^{-1}, indicating that the bands due to the $C_{10}=CH_2$ and the $C_{16}=CH_2$ groups absorb at different regions in the IR spectra. The dihydro compound (XXXI) resulting from the catalytic hydrogenation of compound (XXX) shows bands at 3100, 1640 and 915 cm^{-1} and therefore it is clear that the $C_{16}=CH_2$ group in XXX had been preferentially reduced. There is also the possibility that XXXI may be the C_{10} epimer of XXVI ,but this was eliminated on the basis of the following observations.

Catalytic hydrogenation of XXVII with platinum oxide in ethanol gave a dihydro compound (XXVIII), the physical properties of which differed from those of XXV indicating that XXVIII and XXV should be epimers at C_{10}. If the compound (XXXI) described above was a stereoisomer of XXVI, it should be obtained by dehydration of XXVIII. However, treatment of XXVIII with phosphorous oxychloride in pyridine afforded a compound differing from both XXXI and XXVI even though the product showed terminal methylene bands at 1660 and 890 cm^{-1} in the IR spectrum. It follows that XXXI is a compound formed by hydrogenation of the $C_{16}=CH_2$ group, and that XXVI and XXIX are C_{10} epimers.

The triketone compounds (XXV—XXIX) described above all exhibited the carbonyl bands at about 1740 and 1710 cm^{-1} in the IR spectra, the former being the stronger in all cases, a fact which indicated that these compounds have two five-membered ketones and one seven-membered ketone. Furthermore, treatment of XXV and XXVII with alkali gave acid products, though they could not be induced to crystallize. Accordingly it is apparent that the triketone compounds formed by chromium trioxide oxidation of G-II (II) and α-dihydro-G-II (IV) have structures (XXV—XXIX) in which the A-ring is five membered, and that acyloin rearrangements affording compounds such as XXIII had not occured during these oxidation reaction. Base hydrolysis of diketo-G-I (XXII) obtained from G-I by chromium trioxide oxidation in pyridine afforded a corresponding diketo-G-III (XXXII). IR spectrum of this diketone exhibited two carbonyl bands at 1730 and 1707 cm^{-1}. These properties showed that diketo-G-I and diketo-G-III should be formulated as XXII and XXXII, respectively, and not rearranged structures such as XXIII.

Experimental

Melting points were measured on a micro hot-stage and are uncorrected. The IR spectra were measured with JASCODS 301 and DG 201. The UV spectra were measured with Hitachi EP-2 recording spectrophotometer in 90% ethanol. The NMR spectrum was measured with Varian A-60 (at 60Mc).

Dehydrolactone VII——α-Dihydroanhydrodiketolactone (VI)[3] (950 mg) was dissolved in 5 ml of anhydrous pyridine and treated with 0.75 ml of $POCl_3$ for 10 hr at room temperature. The solution was poured onto 100 ml of ice-water and the separated crystals (860 mg) were collected, which were recrystallized twice from MeOH, mp 158—160°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1780, 1730, 1670, 895. *Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.86; H, 7.86.

α-Dihydronortriketolactone (VIII)——Air containing O_3 (10 g/1000 liter) was passed through a solution of dehydro-lactone (VII) (1.0 g) in acetic acid (50 ml) and the solution was left overnight at room temperature. Evaporation of the solvent *in vacuo* and addition of AcOEt to the residue gave needles (500 mg), which were recrystallized from AcOEt, mp 211—213°. IR ν_{max}^{KBr} cm^{-1}: 1780, 1748, 1713. *Anal.* Calcd. for for $C_{19}H_{24}O_5$; C, 68.05; H, 7.28. Found: C, 68.42; H, 7.16.

16-Desoxy-α-dihydrodiketolactone (IX)——Dehydrolactone (VII) (1.00 g) was catalytically hydrogenated in 35 ml of dioxane with 5% rhodium on Al_2O_3. The solution absorbed 1 mole of hydrogen within 10 min. The catalysts were removed by filtration and concentration of the filtrate gave needles in quantitative yield, which were recrystallized from hexane, mp 166—168°. IR ν_{max}^{KBr} cm^{-1}: 1785, 1730. *Anal.* Calcd. for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49. Found: C, 72.31; H, 8.39.

Endionelactone (X)——To a solution of 1.0 g of 16-desoxy-α-dihydrodiketolactone (IX) in 25 ml of dioxane, was added dropwise a solution of 420 mg of SeO_2 in 4 ml of H_2O during 2 hr under reflux. The solu-

tion was refluxed for a further 10 hr under stirring. After cooling, the precipitated Se was separated by filtration and the filtrate was concentrated *in vacuo* to give yellow crystals (860 mg). Repeated recrystallizations from MeOH gave endionelactone (X), mp 165°. IR ν_{max}^{KBr} cm^{-1}: 3080, 1790, 1745, 1703, 1610. UV λ_{max}^{EtOH} mμ (ε): 235 (12800). *Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.82; H, 7.81.

Oxidation of Enedionelactone (X) with OsO_4-$NaIO_4$——To a solution of 1.91 g of enedionelactone (X) in 15 ml of H_2O and 45 ml of pyridine, 100 mg of OsO_4 was added, and the solution was strirred for 30 minutes at room temperture. Finely powdered $NaIO_4$ was added within an hour and stirred for a further 5 hours. The pale-yellow mixture was extracted with ether (50 ml×10). The extract was dried over anhydrous Na_2SO_4 and concentrated to dryness *in vacuo* to give a solid (120 mg), which was dissolved in ether and extracted with 10% aqueous $NaHCO_3$ solution. The aqueous layer was acidified with HCl and extracted again with ether repeatedly. The ether extracts were treated as usual to yield 80 mg of dimethylmalonic acid (XI), mp 186—188° (decomp.), which no showed depression in mixed melting point with an authentic sample.

Nor-keto-G-II (XII)——Air containing O_3 (18 g/1000) was passes through an ice cooled solution of 10 g of G-II in 300 ml of AcOH–AcOEt (1:1). After 300 ml of the air was passed, the solution was treated with 100 ml of water and left overnight. The solvent was removed *in vacuo*, and the residue was treated with AcOEt to separate the crystals, which were recrystallized from methanol/ethyl acetate, mp 225—226°. IR ν_{max}^{KBr} cm^{-1}: 3400, 1690. UV λ_{max}^{EtOH} mμ (ε): 286 (30). *Anal.* Calcd. for $C_{19}H_{30}O_6$: C, 64.38; H, 8.53. Found: C, 64.38; H, 8.34.

Anhydro-norketo-G-II (XIII)——a) To a solution of 1.0 g of norketo-G-I (XII) in 20 ml of methanol, was added 0.5 ml of aqueous KOH solution. After standing overnight at room temperature, evaporation of methanol *in vacuo* gave crystals, which were recyrstallized from methanol, mp 248°. IR ν_{max}^{KBr} cm^{-1}: 3480, 3400, 3330, 3000, 1645, 1600. UV λ_{max}^{EtOH} mμ (ε): 257 (9000). *Anal.* Calcd. for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39. Found: C, 67.25; H, 8.09.

b) A solution of 2.5 g of KOH in 20 ml of water was added to a solution of triacetylnorketo-G-II (5.5 g) in 50 ml of ethanol. After let standing overnight, the reaction mixture was concentrated *in vacuo*. Crystals separated upon addition of saline. The IR and mp of the crystals showed them to be identical with the anhydronorketo-G-II (XIII) obtained in method (a).

Tosylanhydronorketo-G-II (XIV)——Anhydronorketo-G-II (XIII) (1.00 g) in 20 ml of anhydrous pyridine was treated overnight with *p*-toluenesulfonyl chloride at room temperature. The reaction mixture was poured into H_2O and the aqueous solution was made neutral with $NaHCO_3$. The aqueous solution was gently warmed on a steam-bath. After cooled, the separated crystals were filtered and washed with water (yield 1.40 g). Recrystallization from acetone–*n*-hexane gave white crystals, mp 131°. IR ν_{max}^{KBr} cm^{-1}: 3500, 3440, 3270, 1665, 1640, 1617, 1603. UV λ_{max}^{EtOH} mμ (ε): 223 (16500), 253 (8900). *Anal.* Calcd. for $C_{26}H_{34}O_7S$: C, 63.67; H, 6.94. Found: C, 63.40; H, 7.00.

Endione (XV)——To a mixture of 2.5 g of anhydrous CrO_3 and 25 ml of pyridine, a solution of anhydronorketo-G-II (XIII) (4.00 g) in 50 ml of pyridine was added and then left overnight at room temperature. The mixture was poured into water and extracted with ethyl acetate. The extract was treated as usual to afford pale yellow crystals, which were recrystallized from ethyl acetate, mp 216°. IR ν_{max}^{KBr} cm^{-1}: 3250, 1669, 1600. UV λ_{max}^{EtOH} mμ (ε): 265 (7870). *Anal.* Calcd. for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84. Found: C, 67.54; H, 7.97.

Acetylation of enedione (XV) with acetic anhydride and pyridine gave the diacetate, mp 210°. *Anal.* Calcd. for $C_{23}H_{30}O_7$: C, 66.06; H, 7.23. Found: C, 66.01; H, 7.22.

Tosylendione (XVI)——A solution of 200 mg of XIV in 2 ml of pyridine was added to a mixture of 500 mg of anhydrous chromic trioxide and 5 ml of pyridine, and the reaction mixture was left overnight at room temperature. The mixture was poured into 200 ml of ice-water, and extracted with ether (100 ml×4). The ether extract was washed with 1N HCl, water and saline, and dried over anhydrous sodium sulfate. Evaporation of the solvent to dryness *in vacuo* gave an amorphous residue (190 mg), which was chromatographed on silicic acid. Benzene–AcOEt (8:2) elution gave a white solid (160 mg), which was shown to be pure from thin-layer chromatography, but could not be crystallized. IR ν_{max}^{KBr} cm^{-1}: 3450, 1680, 1610, 1603, 1190, 1175. UV λ_{max}^{EtOH} mμ (ε): 227 (13600), 263 (7050).

Tosyl-mesylanhydronorketo-G-II (XVII)——Tosylnorketoanhydro-G-II (XIV) (1.28 g) was dissolved in 15 ml of pyridine and treated with 1.0 g of methansulfonyl chloride for 20 hours at 0—5°. The solution was poured into water and extracted with benzene–AcOEt (1:1). The extract was washed with water and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave crystals, which were recrystallized from acetone–hexane mp 129—130° (decomp.). IR ν_{max}^{KBr} cm^{-1}: 3450, 1655, 1610, 1600. UV λ_{max}^{EtOH} mμ (ε): 226 (17800), 246 (9050). *Anal.* Calcd. for $C_{27}H_{36}O_9S_2$: C, 57.04; H, 6.33; S, 11.26. Found: C, 57.25; H, 6.57; S, 11.01.

***α,β,γ,δ*-Unsaturatedketone (XVIII)**——a) Monomesylmonotosylate-XVII (490 mg) was refluxed in 5 ml of anhydrous pyridine for 5 hours. The solution was poured into ice-water, and extracted with AcOEt. The extract was washed with dilute HCl and saline, dried over anhydrous Na_2SO_4, and then concentrated to dryness *in vacuo* to yield a brown residue (200 mg), which was chromatographed on Al_2O_3 (*ca.* 10 g). From the ether elute, there was obtained the *α,β,γ,δ*-unsaturated ketone (XVIII). Recrystallization from

acetone–hexane gave crystals, mp 152—153°. IR ν_{max}^{KBr} cm^{-1}: 3330, 1665, 1635, 1603, 1197, 1178. UV λ_{max}^{EtOH} mμ (ε): 221.5 (19700), 310 (5180). *Anal.* Calcd. for $C_{26}H_{32}O_6S$: C, 66.10; H, 6.77; S, 6.77. Found: C, 66.30, H, 6.91; S, 6.32. NMR ($CDCl_3$) δ ppm: 1.00 (s, 3H), 1.02 (s, 3H), 1.32 (s, 3H), 4.51 (t, 1H, J=6.8 Hz), 5.78 (d, 1H, J=12.6 Hz), 6.77 (d, 1H, J=12.6 Hz), 7.32 (d, 2H, J=8 Hz), 7.76 (d, 2H, J=8 Hz).

b) Monomesylmonotosylate-XVII (780 mg) was added to 50 ml of methyl ethyl ketone in which 700 mg of finely powdered KI was suspended. After the mixture was refluxed for 4 hours, the separated precipitates were removed by filtration and the filtrate was concentrated to dryness *in vacuo*. The residue was dissolved in ethyl acetate and washed with 3% aqueous $Na_2S_2O_3$ and water, then dried over anhydrous Na_2SO_4. Evaporation of the solvent gave crystals (400 mg), which were identified as being $\alpha,\beta,\gamma,\delta$-unsaturated ketone (XVIII) by mixed melting point test with the sample obtained in (a).

Homodiene (XIX)——To a solution of 520 mg of XVIII in 10 ml of ethanol was added a solution of 290 mg of $NaBH_4$ in 30 ml of ethanol, and left overnight at room temperature. After neutralized with 10% AcOH, the solution was concentrated. By addition of water, crystals separated, which were filtered and washed with water. Recrystallization from ether–*n*-hexane afforded white crystals, mp 115°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 1603, 1189, 1175. UV λ_{max}^{EtOH} mμ (ε): 224.5 (19600), 264 (9470). *Anal.* Calcd. for $C_{26}H_{34}O_6S$: C, 65.82; H, 7.17; S, 6.75. Found: C, 65.72; H, 7.41; S, 6.50.

Nortetraketo-G-II (XX)——a) To a mixture of 500 mg of chromic anhydride in pyridine (5 ml), a solution of 400 mg of norketo-G-II (XII) in pyridine (5 ml) was added. The mixture was left overnight at 30°, and then poured into ice–water. The aqueous solution was extracted with AcOEt. The extract was washed with 1N H_2SO_4, and evaporated *in vacuo* to give an oil, which was crystallized from acetone–*n*-hexane (yield 100 mg), mp 204—206°. IR ν $_{max}^{KBr}$ cm^{-1}: 3540, 3430, 1745, 1715. *Anal.* Calcd. for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.42; H, 7.18.

b) Triketo-G-II (XXVII) (1.0 g) was dissolved in 30 ml of AcOH–AcOEt (1:1), to which oxygen containing ozone was passed through for an hour at −15——20°. Water (10 ml) was added to the reaction mixture and the solution was left overnight at room temperature. Evaporation of the solvent *in vacuo* gave crystals (700 mg), which were identified as the nor-tetraketo-G-II (XX) by direct comparison of its IR spectrum with that of the compound obtained by method a).

Anhydronortetraketo-G-II (XXI)——Nortetraketo-G-II (XX) (150 mg) was dissoved in 5 ml of pyridine and treated overnight with 300 mg of phosphorous oxychloride at room temperature. The solution was poured into ice–water and extracted with AcOEt. Treatment of the extract as usual gave needles (85 mg), which were recrystallized from acetone–*n*-hexane, mp 150—153° (decomp.). IR ν_{max}^{KBr} cm^{-1}: 3470, 3060, 1756, 1743, 1715, 1660, 896. *Anal.* Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 68.75; H, 6.52.

Triketo-α-dihydro-G-II (XXV)——α-Dihydro-G-II (IV) (1 g) was dissolved in 10 ml of pyridine, and treated overnight with a mixture of chromium trioxide (2.2 g) in pyridine (22 ml) at room temperature. The precipitates were filtered and washed with pyridine and AcOEt. The filtrate was diluted with AcOEt, and the solution was washed with water, dil. H_2SO_4 and aqueous $NaHCO_3$ solution. After drying over anhydrous Na_2SO_4, the solvent was evaporated *in vacuo* to give crude needles. Recrystallization from acetone–*n*-hexane afforded white crystals, mp 232°. IR ν_{max}^{KBr} cm^{-1}: 3540, 1735, 1692. *Anal.* Calcd. for $C_{20}H_{28}O_5$: C, 68.94, H, 8.10. Found: C, 69.18; H, 8.15.

Anhydrotriketo-α-dihydro-G-II (XXVI)——To a solution of triketo-α-dihydro-G-II (XXV) (500 mg) in 10 ml of pyridine, was added 1 ml of phosphorous oxychloride. The reaction mixture was left overnight at room temperature and poured into ice-water. The aqueous solution was extracted with ether and the extract was washed with dil. H_2SO_4, aqueous $NaHCO_3$ solution and water. Evaporation of the solvent *in vacuo* afforded needles, which were recrystallized from acetone–*n*-hexane, mp 202—203°. IR ν_{max}^{KBr} cm^{-1}: 3520, 3070, 1740, 1705, 1662, 895. *Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.94; H, 7.62.

Triketo-G-II (XXVII)——G-II (6 g) was dissolved in 60 ml of pyridine and treated overnight with a mixture of chromium trioxide (16 g) in pyridine (100 ml) at room temperature. The reaction mixture was treated the same as in the preparation of (XXV) to afford triketo-G-II (3 g), which was recrystallized from methanol-water, mp 208—209°. IR ν_{max}^{KBr} cm^{-1}: 3700—3200, 1735, 1712, 1635, 916. *Anal.* Calcd. for $C_{20}H_{26}O_5 \cdot H_2O$: C, 65.91; H, 7.74. Found: C, 66.14; H, 8.12.

Triketo-β-dihydro-G-II (XXVIII)——A mixture of 800 mg of triketo-G-II (XXVII) and 100 mg of PtO_2 in 20 ml of ethanol was stirred in an atomosphere of hydrogen. The solution absorbed 52 ml of hydrogen within an hour. The catalysts were removed by filtration and evaporation of the solvent *in vacuo* yielded crystals which were recrystallized from AcOEt, mp 242—243°. The melting point and IR spectrum of the crystal differed from those of the triketo-α-dihydro-G-II (XXV). IR ν_{max}^{KBr} cm^{-1}: 3500, 3430, 1750, 1735, 1700. *Anal.* Calcd. for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 68.76; H, 8.27.

Anhydrotriketo-β-dihydro-G-II (XXIX)——To a solution of 130 mg of triketo-β-dihydro-G-II (XXVIII) in 4 ml of pyridine was added 400 mg of phosphorous oxychloride at 0°. The solution was left overnight at room temperature, and then poured into 100 ml of saline. The aqueous solution was extracted with AcOEt (70 ml×3), and the extracts were treated as usual to give white needles (60 mg), which were recrystallized from acetone–*n*-hexane, mp 176—177°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590, 1752, 1710, 1668, 891. *Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.83; H, 8.01.

Anhydrotriketo-G-II (XXX)——Triketo-G-II (XXVII) (3 g) was dissolved in 30 ml of pyridine and 4 ml of phosphorous oxychloride was added at 0°. After the mixture was left overnight at room temperature, the dark brown solution was poured into ice–water. The separated crystals were collected and recrystallized from AcOEt, mp 198°. IR ν_{max}^{KBr} cm^{-1}: 3520, 3090, 1740, 1705, 1655, 1630, 920, 895. *Anal.* Calcd. for $C_{20}H_{24}O_4$: C, 73.14; H, 7.37. Found: C, 72.96; H, 7.23.

16-Desoxytriketo-G-II (XXXI)——A solution of 1.8 g of anhydrotriketo-G-II (XXX) in 40 ml of ethanol was treated with 200 mg of PtO_2 and a few drop of conc. HCl, and the mixture was stirred in an atomosphere of hydrogen. After 2 hours, 132 ml of hydrogen was absorbed and the reaction was stopped. The catalyst was removed by filtration and the solvent was removed *in vacuo* to yield residual crystals, which were recrystallized from aqueous ethanol, mp 204—206°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 1748, 1713, 908. *Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.70; H, 7.86.