[Chem. Pharm. Bull. 13(11)1332~1340(1965)]

UDC 582.932 : 581.19 : 547.92

171. Hiroshi Mitsuhashi and Taro Nomura: Studies on the Constituents of Asclepiadaceae Plants. XVI.*1 On the Components of *Metaplexis japonica* MAKINO. III. The Structure of Benzoylramanone.*2

(*Faculty of Pharmaceutical Sciences, Hokkaido University**3)

It was reported in the preceeding papers*1,1) that sarcostin (I), metaplexigenin (II), benzoylramanone (III), and four other aglycones were isolated from *Metaplexis japonica* MAKINO, and the structure of mataplexigenin was proposed as II. In this paper, experiments leading to the structure determination of benzoylramanone (III) are described. Benzoylramanone (III) forms needles, m.p. 222~226°, $[\alpha]_D^{14}$ +48° (c=1, pyridine), for which the molecular formula, $C_{28}H_{36}O_5$ was proposed from its elemental analysis. Benzoylramanone has absorption maxima at 233 mμ (log ε 4.10), 278 (log ε 3.13) (Fig. 1). The infrared absorption maxima at 3500, 1720, 1690, 1600, 1590, 1270 cm^{-1} indicate hydroxyls, ketone (open chain or six-membered), ester and aromatic double bond (Fig 2). These facts highly suggest that III is a monobenzoate ester. The conversion of III to a mono oxime confirms the presence of a keto group. Acetylation of III with acetic anhydride in pyridine yielded a mono acetate (IV), m.p.

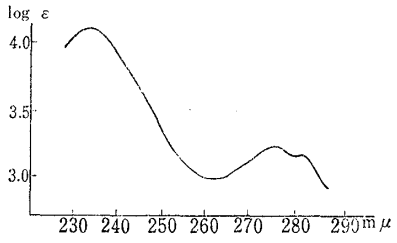

Fig. 1. Ultraviolet Absorption Spectra of Benzoylramanone (III) (in EtOH)

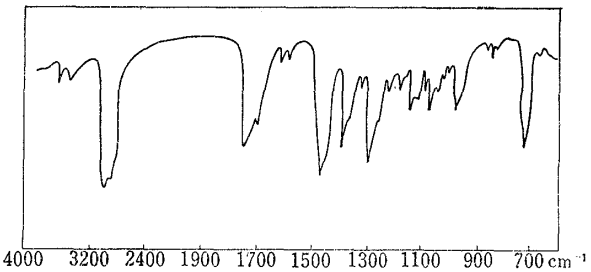

Fig. 2. Infrared Spectra of Benzoylramanone (III) (in Nujol)

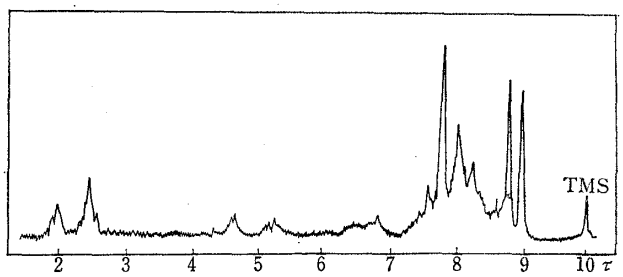

Fig. 3. Nuclear Magnetic Resonance Spectra of Benzoylramanone (III), measured in Deuterochloroform at 60 Mc.p.s.

224~226°, $C_{30}H_{38}O_6$, which still showed infrared absorption for a free hydroxyl group at 3500 cm^{-1}.

Hydrolysis of III with 5% methanolic potassium hydroxide gave an acidic substance. This acid was identified as benzoic acid by paper chromatography (1.5*N* NH_3/BuOH) and mixed melting point. The neutral fraction was a mixture of two materials, as shown by paper chromatography ($CHCl_3$/formamide).2) This mixture was separated by partition chromatography over Celite (benzene+BuOH/H_2O), to give isoramanone

*1 Part XV: This Bulletin, **13**, 274 (1965).

*2 Part of this work was reported at the Hokkaido Branch Meeting of the Pharmaceutical Society of Japan, Dec. 20, 1963. Preliminary reports of this work have been published. H. Mitsuhashi, T. Nomura: This Bulletin, **11**, 1333 (1963); *Idem*: Steroids, **3**, 271 (1964).

*3 Kita-12-jo, Nishi-5-chome, Sapporo, Hokkaido (三橋 博, 野村太郎).

1) H. Mitsuhashi, T. Nomura, Y. Shimizu, I. Takemori, E. Yamada: This Bulletin, **10**, 811 (1962).

2) H. Mitsuhashi, Y. Shimizu, E. Yamada, I. Takemori, T. Nomura: This Bulletin, **10**, 808 (1962).

(VI) and ramanone (VII). The ratio of VI to VII was about 1:4. Isoramanone (VI), m.p. 226~234°, $[\alpha]_{589}^{25}$ +40°(c=0.2, MeOH, from ORD measurement), analyzed for $C_{21}H_{32}O_4$. The infrared peaks at 3450, 1675 cm^{-1} showed the presence of hydroxyl and carbonyl groups. Ramanone (VII), m.p. 184~196°, $[\alpha]_{589}^{25}$ −55° (c=0.2, MeOH, from ORD measurement), analyzed for $C_{21}H_{32}O_4$. The infrared spectra was similar to that of VI. Acetylation of VII with acetic anhydride in pyridine yielded a diacetyl derivative (VIII), m.p. 199~202°, which showed hydroxyl absorption at 3500 cm^{-1}. VII formed a mono oxime (IX), m.p. 274~278°. These results suggest that III has one carbonyl group (open chain or six-membered ketone as suggested from its infrared spectrum), two secondary hydroxyl groups (one as a benzoate), and one tertiary hydroxyl group. These three hydroxyls do not exist as 1.2-glycol groups, since VII did not consume lead tetraacetate. The nuclear magnetic resonance spectra of III (measured in $CDCl_3$, Fig. 3) showed three singlets at 8.99 (3H, 19-CH_3), 8.73 (3H, 18-CH_3), 7.84 τ (3H, 21-CH_3).

The signal at 7.84 τ, shows the presence of a methyl ketone group in III. Tschesche, *et al.* isolated a glycoside from the leaves of *Digitalis purpurea*,[3] and obtained digipurpurogenin-I, and digipurpurogenin-II as the genin.

The structure of these compounds were determined as X and XI respectively.[4,5] The physical properties of VI and VII are similar to those digipurpurogenin-II and isodigipurpurogenin-II, respectively, the latter was obtained by the treatment of XI with alkaline solution, and is thought to be a C-17 epimer.[6] The identity of isoramanone (VI) with digipurpurogenin-II, and ramanone (VII) with isodigipurpurogenin-II was confirmed by mixed melting point and paper chromatography with authentic samples kindly supplied by Prof. Tschesche. A C/D *trans* ring juncture was proposed by Tschesche for XI and its C-17 epimer, but we propose a C/D *cis* ring juncture on the basis of the following results. The optical rotatory dispersion (ORD) curve of VII showed a negative Cotton effect, trough $[\phi]_{301}$ −4542°, peak $[\phi]_{260}$ +4308° in MeOH, and VI showed a positive Cotton effect peak $[\phi]_{305}$ +3114°, trough $[\phi]_{265}$ −2283° in MeOH. But the curve of III, peak $[\phi]_{305}$ +2404.6°, trough $[\phi]_{270}$ −3073.6° in MeOH, is very similar to that of VI, so it appears that the two compounds have the same configuration at C-17. VII was refluxed for 5 hours with 5% potassium hydroxide-methanol and the resulting mixture examined by paper chromatography. The results indicate that VII is the main product and VI, a minor product. The same experiment starting with VI gave identical results. Moreover the ratio of VI and VII could be obtained from ORD measurements.[7] III was treated with 3% potassium hydroxide-methanol for 24 hours at 32°, the ORD curve measured to give a small negative Cotton effect.

The reaction mixture showed only spots for VI and VII on paper chromatography. By comparison with the curves of VI and VII, the ratio of VI and VII was calculated to be about 1:3 (Fig. 4). These observations suggest that VI and VII are epimer at C-17 and VII is the more stable form in alkaline solution. If we assume that VI and VII have a C/D *trans* ring juncture, the most stable form in alkaline solution is the 17α-H type,[8] and this type of structure should show a strong positive Cotton effect.[9] Although ramanone (VII) is more stable than isoramanone (VI) it gave a negative Cotton effect.

3) R. Tschesche, G. Grimmer : Ber., **88**, 1569 (1955).
4) R. Tschesche : Angew. Chem., **73**, 727 (1961).
5) R. Tschesche, H. W. Marquardt, H. Machleidt : Ann., **648**, 185 (1961).
6) Private communication from Prof. R. Tschesche.
7) C. Djerassi : "Optical Rotatory Dispersion, Application to Organic Chemistry," McGraw-Hill Book Co., New York (1960).
8) M. R. Rubin : Steroids, **2**, 561 (1963).
9) E. W. Foltz, A. E. Lipman, C. Djerassi : J. Am. Chem. Soc., **77**, 4359 (1955); C. Djerassi, R. Riniker, B. Riniker : Bull. Soc. chim. France, **1957**, 741; C. Djerassi, O. Halpern, V. Halpern, O. Shindler, Ch. Tamm; Helv. Chim. Acta, **41**, 250 (1958).

These results are inconsistent with the above reasoning. On the other hand, for C/D *cis* steroids the more stable form is the 17β-H type[10,11] and they show a negative Cotton effect,[11,12] while the 17α-H type show a positive Cotton effect.[11,12] The molecular amplitude of the 17β-H type, such as deacylcynanchogenin (XII),[13] is very similar to that of VII. Deacylcynanchogenin (XII) is easily isomerized in hot alkaline solution to give a 7:3 equilibrium mixture of XII and 17-isodeacylcynanchogenin (XIII).[14] The structures of XII and XIII have been proposed by Reichstein, *et al.*[12] and Mitsuhashi and Shimizu.[13] The ORD curve of XII showed a negative Cotton effect with the molecular amplitude of a=−78°,[13] while its diacetate showed a remarkable shift of amplitude to the negative side, a=−112°.[11]

The same relation has been found, VII a=−88°, and its diacetate (VIII), a=−117°. These facts have been explained in terms of steric effects by the 12β-acetoxy group in the 14β,17α-pregnan-20-one derivatives.[11] The above evidence lead to the probable structure (VII) for ramanone (=isodigipurpurogenin-II) and VI for isoramanone (=digipurpurogenin-II). Synthetic proof for these proposals was obtained in the following way. The method of Plattner, *et al.*[15] was followed for introduction of the 14β-hydroxyl group. Rockogenin diacetate (XVa) was produced from hecogenin acetate (XIV), then converted to ϕ-rockogenin triacetate (XVIb) by Cameron's method,[16] although the yield was poor. Reduction of ϕ-hecogenin with sodium borohydride, followed by acetylation, to give ϕ-rockogenin triacetate (XVIb) proved to be a better route. XVIb was oxidized with chromic acid, and treated with acetic acid, to give 3β,12β-diacetoxy-5α-pregn-16-en-20-one (XVII), m.p. 136~139°, $[\alpha]_D^{17}$ +21.6°. Compound (XVII) was converted to the dienone (XVIII), m.p. 152~154°, $C_{25}H_{34}O_5$, $[\alpha]_D^{17}$ +279°, by N-bromosuccinimide. The ultraviolet spectrum of XVIII showed a maximum at 304 mμ (log ε 4.16). Treatment of XVIII with mono perphthalic acid afforded an epoxide (XIX), m.p. 148~153°, $[\alpha]_D^{17}$ +88°, with ultraviolet absorption at 244 mμ (log ε 3.65). The configuration of the epoxide ring, was assumed to be β since Plattner, *et al.*[15] reported the conversion of 3β-acetoxy-5α-pregna-14,16-dien-20-one to its 14β,15β-epoxide by the same method. Moreover, since the 12β-acetoxy group is equatorial, it was assumed that this group would not effect the formation of epoxide ring. The following results are in agreement with this assumption. When XIX was hydrogenated with 5% Palladium-barium sulfate in ethanol, three crystalline substances, XX, XXI, and XXII, were obtained after chromatography on alumina.

XX had m.p. 169~172° and analyzed for $C_{25}H_{38}O_6$. The infrared spectrum of XX showed peaks at 3650, 3550, 1750, 1710, 1690, 1270, 1235 cm^{-1} indicating the presence of hydroxyl group, nonconjugated open chain ketone, and acetate. XX showed no characteristic absorption in the ultraviolet. The ORD curve of XX gave negative Cotton effect (Table I). These facts suggest that XX is 3β,12β,14β-trihydroxy-5α,14β,17α-pregnan-20-one-3,12-diacetate. Correlation with ramanone was achieved by hydrogenation of diacetylramanone (VIII) using platinic oxide, then oxidizing with chromic acid to give dihydrodiacetylramanone, m.p. 169~171°, which proved to be identical with XX by mixed melting point and comparison of infrared spectra. The structure of the other two products, XXI and XXII, obtained from the epoxide (XIX) were proven in the

10) A. Lardon: Helv. Chim. Acta, **32**, 1517 (1949); H. Hasegawa, Y. Sato, K. Tsuda: This Bulletin, **11**, 1275 (1963).
11) H. Mitsuhashi, T. Nomura, M. Fukuoka: Steroids, **4**, 483 (1964).
12) K. A. Jaeggi, E. K. Weiss, T. Reichstein: Helv. Chim. Acta, **46**, 694 (1963).
13) H. Mitsuhashi, Y. Shimizu: Steroids, **2**, 373 (1963).
14) H. Mitsuhashi, Y. Shimizu, T. Nomura, T. Yamada, E. Yamada: This Bulletin, **11**, 1198 (1963).
15) A. Plattner, L. Ruzicka, E. Angliker: Helv. Chim. Acta, **30**, 385, 395 (1947).
16) A. F. B. Cameron, R. M. Evans, T. S. Hant, P. G. Jones, A. G. Long: J. Chem. Soc., **1955**, 2807.

following manner. XXI, $C_{25}H_{38}O_5$, had m.p. 175~178°, and the ORD curve showed a negative Cotton effect (Table I). The infrared spectrum showed a peak at 1700 cm^{-1} indicating the presence of non conjugated open chain ketone, but no hydroxyl absorption could be found in its spectrum. This same compound (XXI) was also obtained from dienone (XVIII) by hydrogenation with palladium-calcium carbonate. The epoxide (XIX) used in the preparation of XXI was completely homogeneous by thin-layer chromatography and XXI must thus arise through hydrogenolysis of the epoxide group. A very simalar example has been reported by Plattner, *et al.*[15] Hence the structure of XXI is 3β,12β-diacetoxy-5α,14β,17α-pregnan-20-one. XXII, $C_{25}H_{38}O_6$, showed m.p. 180~183°, neither a hydroxyl group nor a conjugated double bond was detected in its infrared spectrum. The ORD curve of XXII showed a negative Cotton effect (Table I), and its nuclear magnetic resonance spectrum had a broad singlet at 6.75 τ (1 proton), characteristic of an epoxy proton. A very similar compound, 3β-acetoxy-14β,15β-epoxy-5α,17α-pregnan-20-one (XXV), gave the same type of singlet. On this basis, XXII was assigned structure of 3β,12β-diacetoxy-14β,15β-epoxy-5α,17α-pregnan-20-one. For comparison of the ORD data 3β,14β-dihydroxy-5α,17α-pregnan-20-one 3-acetate (XXIII), 3β-acetoxy-5α,17α,14β-pregnan-20-one (XXIV), and XXV were synthesized by

Table I.

Compound	Trough $[\phi]_{302}$ (°C)	Peak $[\phi]_{259}$ (°C)	a (°C)
XX	−6684	+5989	−126.7
XXI	−4062	+6671	−107.3
XXII	−2681	+4757	− 74.3
XXIII	−4286	+4211	− 84.9
XXIV	−2556	+4784	− 73.4
XXV	−2083	+3811	− 58.9

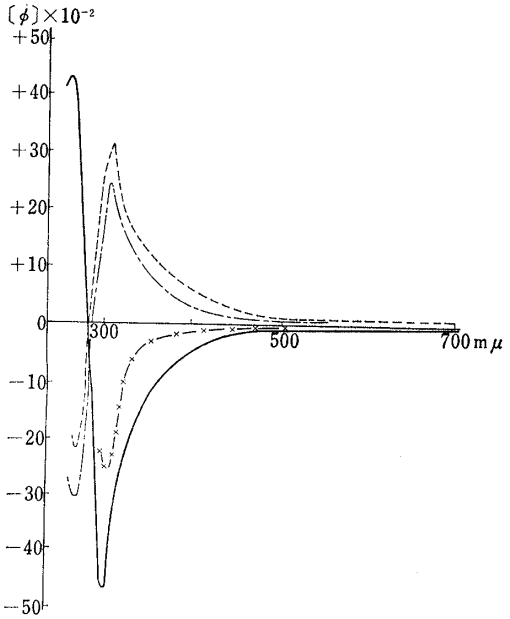

Fig. 4. The Optical Rotatory Dispersion Curves

——— VII ····· VI •—• III
×—× Equilibrium mixture of VI and VII (in MeOH)

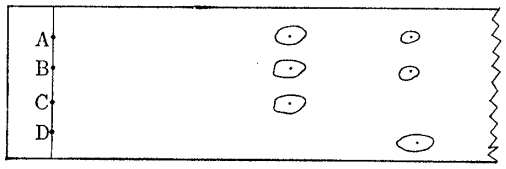

Fig. 5.

A : 5% KOH-MeOH treatment products of VI
B : 5% KOH-MeOH treatment products of VII
C : VII
D : VIII
($CHCl_3$/formamide). ($SbCl_3$). 3 hr.

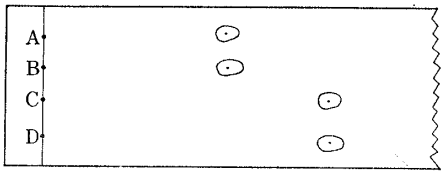

Fig. 6.

A : Ramanone (VII)
B : Isodigipurpurogenin-II
C : Isoramanone (VI)
D : Digipurpurogenin-II
($CHCl_3$/formamide) ($SbCl_3$)

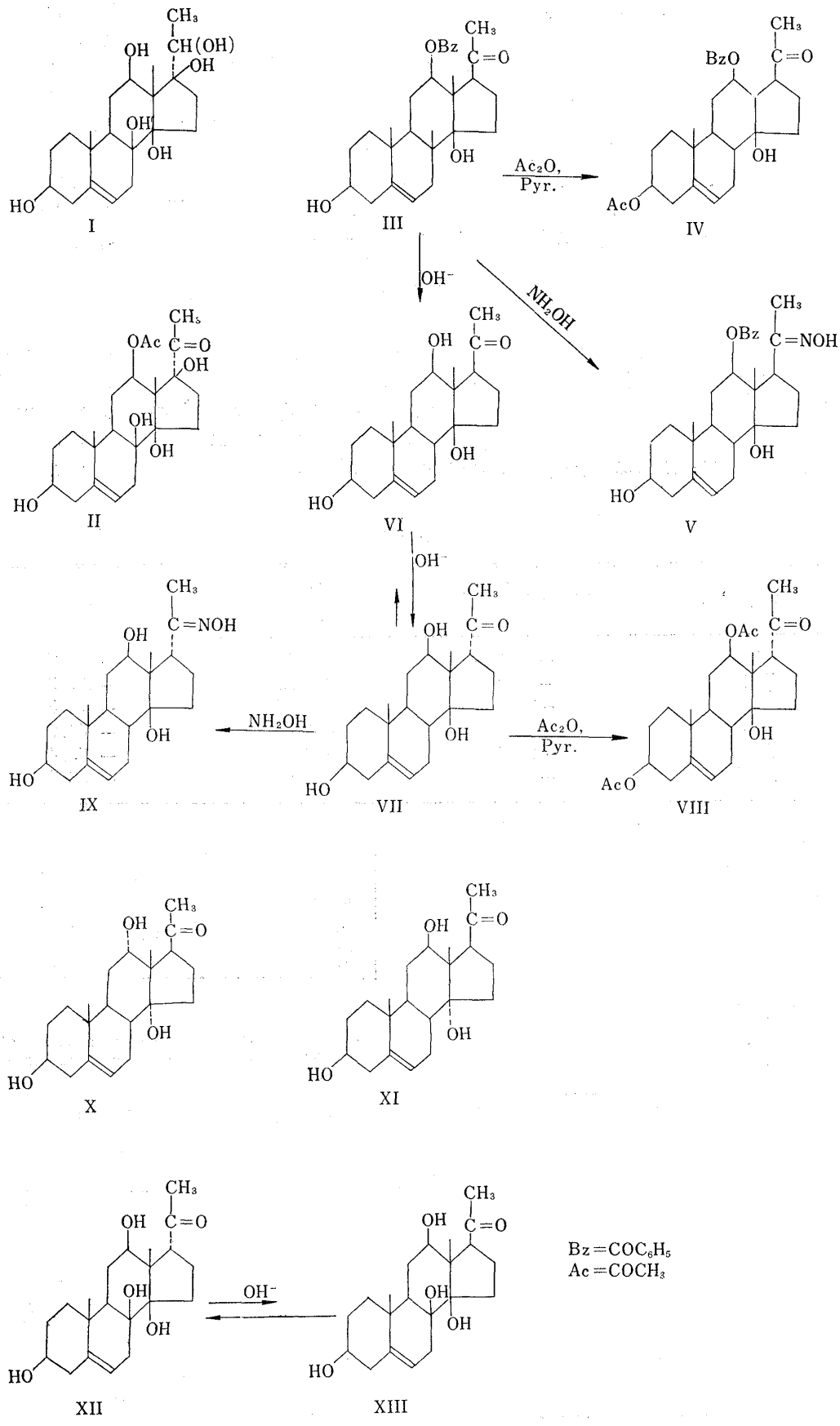

Chart 1.

Mr. Fukuoka in this laboratory, these results were consistent with the data from XX, and XXII (Table I).

In veiw of the above facts, the most reasonable conclusion is that the structure of ramanone, isoramanone correspond to VII and VI, respectively. Benzoylramanone is a monobenzoate of isoramanone, and the 12β-benzoyl structure (III) is the most probable from biogenetic analogy. Recently, Tschesche, *et al.*[17] reported in a communication that they have revised their structure for digipurpurogenin-II, and reached the same conclusions as presented in this paper.

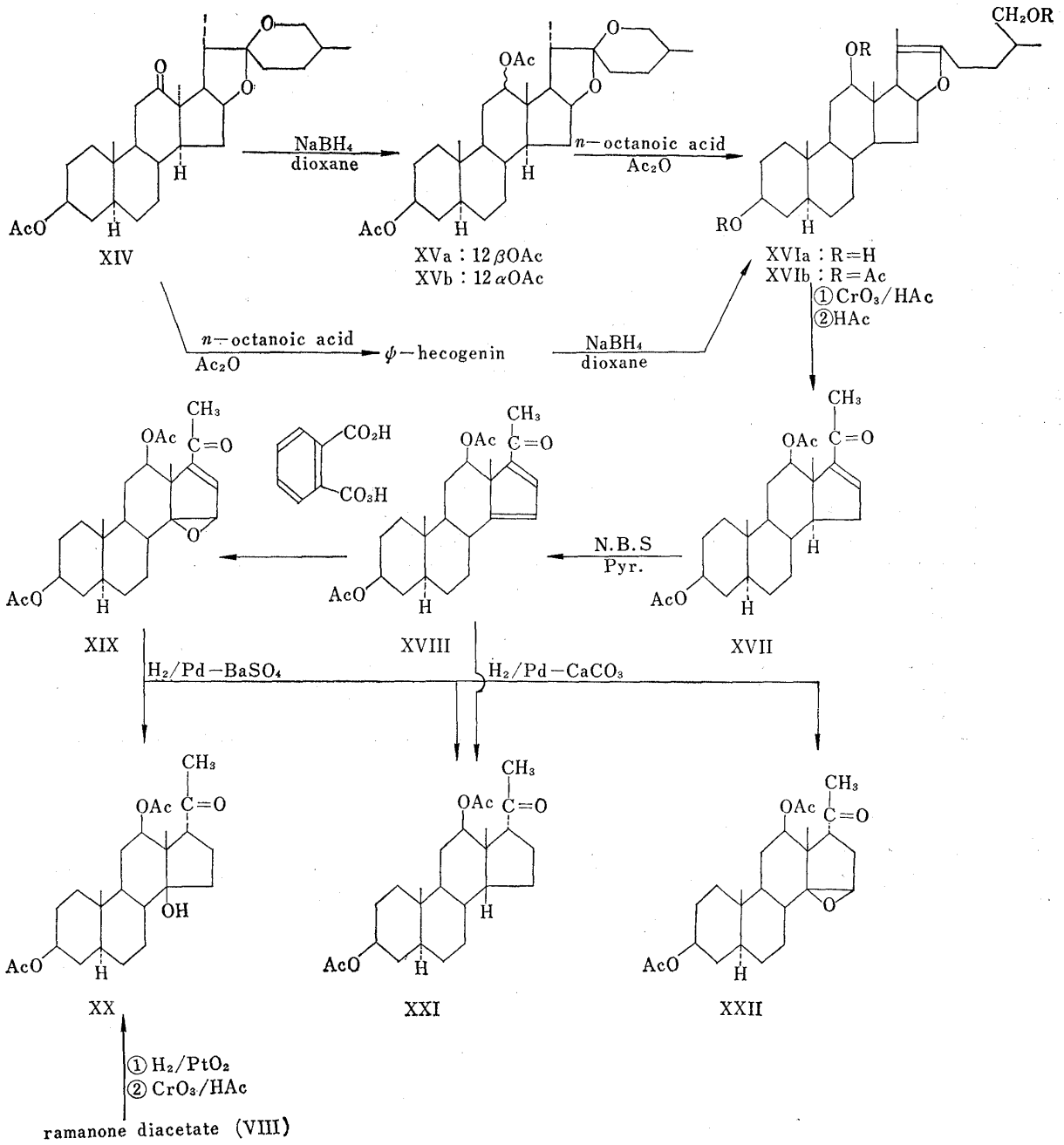

Chart 2.

17) R. Tschesche, G. Brugmann, G. Snatzke : Tetrahedron Letters, **1964**, 473.

Experimental

Melting points are not corrected. The rotatory dispersion data were obtained with an automatic Rudolph recording photoelectric spectropolarimeter and O. R. D.-U. V.-5-Niphon Bunko. The NMR spectra were measured with a Japan Electron Optics Lab., 3H-60.

Benzoylramanone Acetate (IV)——40 mg. of benzoylramanone (III) was dissolved in 1 ml. of Ac_2O. The mixture was allowed to stand for 24 hr. at 25°, then poured on ice and a white powder which appeared was collected and washed several times with H_2O. Repeated recrystallization from MeOH+H_2O gave 15 mg. of IV, m.p. 224~226°, *Anal.* Calcd. for $C_{30}H_{38}O_6$: C, 72.85; H, 7.74. Found: C, 72.81; H, 7.85. IR ν_{max}^{Nujol} cm^{-1}: 3500, 1730, 1705, 1600, 1590, 1270, 1240.

Benzoylramanone Oxime (V)——To 39 mg. of III dissolved in 2 ml. of MeOH was added a solution of 100 mg. of $NH_2OH \cdot HCl$, 300 mg. of $NaAc \cdot 3H_2O$, in 0.2 ml. of H_2O. After allowing the solution to reflux on a boiling water-bath for 3 hr., H_2O was added. A crystalline substance separated out. Recrystallization of this product from MeOH-H_2O afforded 20 mg. of V, m.p. 286~291°. *Anal.* Calcd. for $C_{28}H_{37}O_5N$: C, 71.92; H, 7.98; N, 3.00. Found: C, 71.72; H, 7.89; N, 3.11. IR ν_{max}^{Nujol} cm^{-1}: 3550, 3450, 1700, 1655, 1600, 1590, 1270, 710.

Hydrolysis of Benzoylramanone (III)——105 mg. of III was heated in 4 ml. of 5% methanolic KOH for 5 hr. under N_2 atmosphere. After adding 2 ml. of H_2O, MeOH was removed under red. press. The aqueous solution was extracted with small amounts of ether successively, the solvent was evaporated and 85 mg. of crystalline substances were obtained. Paper partition chromatography ($CHCl_3$/formamaide)[2] showed two spots: $R_{D.C.}$*4=1.95, 1.35. The aqueous layer was acidified with H_3PO_4 and extracted with ether. After the removal of the solvent, it gave 15 mg. acidic substance. The identification of the acid fraction was carried out as follows: paper chromatography (solvent system: BuOH/1.5*N*-NH_3, paper Toyo Roshi, No. 50) showed one spot (Rf 0.30), benzoic acid (Rf 0.30). Recrystallization from H_2O, gave a crystalline substance, m.p. 121°, confirmed as benzoic acid by mixed melting point.

Partition Chromatography of Hydrolysate of III——85 mg. of the neutral fraction, obtained from the alkaline hydrolysate of III, was submitted to partition chromatography[1] over 30 g. of Celite, giving the results shown in Table II.

Table II. Partition Chromatography of the Hydrolysate from III

Fraction No.	Solvent	Eluted product (mg.)	PPC ($CHCl_3$/formamide)
1~ 3	C_6H_6/H_2O	—	—
4~ 6	〃	15	VI
7~ 9	〃	4	VI+one spot (small)
10~11	〃	5	VI (small)+VII+one spot (small)
12~28	〃	65	VI (small)+VII
29~34	1% BuOH+C_6H_6/H_2O	trace	—

1 fraction 30 ml. Celite 30 g.

Isoramanone (VI)——Fr. No. 4~6 in Table II was recrystallized from acetone to give needles, m.p. 226~233° (6 mg.). It showed pink color $SbCl_3$, and blue→reddish violet with the Liebermann-Burchard reaction. *Anal.* Calcd. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 71.94; H, 9.23. IR ν_{max}^{Nujol} cm^{-1}: 3450, 1750 (shoulder), 1675.

Ramanone (VII)——Fr. No. 12~28 in Table II was recrystallized from isopropyl ether-acetone to give prisms, m.p. 195~198° (total 42 mg.). It showed reddish violet with $SbCl_3$, and pink→green→orange with the Liebermann-Burchard reaction. Kedde and Legal test (−). *Anal.* Calcd. for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26. Found: C, 72.31; H, 9.22. IR ν_{max}^{Nujol} cm^{-1}: 3500, 1680.

Ramanone Diacetate (VIII)——36 mg. of VII was dissolved in 1 ml. of pyridine and 0.5 ml. of Ac_2O was added. This mixture was treated as described for IV. Repeated recrystallization from MeOH+H_2O gave 32 mg. of diacetate (VIII), m.p. 199~202°. *Anal.* Calcd. for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39. Found: C, 69.39; H, 8.43. IR ν_{max}^{Nujol} cm^{-1}: 3600, 3450, 1725, 1705, 1240.

Ramanone Oxime (IX)——To 30 mg. of VII dissolved in 2 ml. of MeOH, a solution of 100 mg. of $NH_2OH \cdot HCl$, 300 mg. of $NaAc \cdot 3H_2O$, in 0.2 ml. of H_2O, was added. The mixture was treated as described for V. Recrystallization from MeOH+H_2O, afforded ramanone oxime (IX), m.p. 274~278°. *Anal.* Calcd. for $C_{21}H_{33}O_4N$: N, 3.85. Found: N, 3.79. IR ν_{max}^{Nujol} cm^{-1}: 3550, 1680 (very weak).

*4 $R_{D.C.} = R_{Deacylcynanchogenin}$

Estimation of $Pb(OAc)_4$ Consumption of Ramanone (VII)——To a solution of 0.05 mol. of Ⅶ dissolved in dioxane (5 ml.), 10 ml. of *N*/25 $Pb(OAc)_4$ in AcOH was added and mixture was allowed to st and at room temperature (15~20°) and 2 ml. aliquants titrated by iodometry. A blank was prepared and titrated similarly. The following results were obtained. 0.5 hr. (0 mol.), 5 hr. (0.16 mol.), 15 hr. (0.12 mol.).

Isomerization of the Side Chain of Ramanone (VII) and Isoramanone (VI)——1 mg. of Ⅶ and 5% KOH in MeOH (0.2 ml.) were sealed under nitrogen, and heated for 5 hr. on the steam bath. When cool, the reaction mixture was examined by paper chromatography ($CHCl_3$/formamide) and the formation of Ⅵ was determined. The same results were obtained, when Ⅵ was treated in the same manner. The results of PPC were shown in Fig. 5.

Identification of Isoramanone (VI) and Ramanone (VII) with Digipurpurogenin-II and Isodigipurpurogenin-II——Digipurpurogenin-Ⅱ, and isodigipurpurogenin-Ⅱ, obtained from Prof. R. Tschesche, were shown to be identical with isoramanone (Ⅵ) and ramanone (Ⅶ) respectively by mixed melting point and paper chromatography. The results obtained are as follows. Isoramanone (Ⅵ), m.p. 210° (sin.), 220~234°. Digipurpurogenin-Ⅱ, m.p. 200° (sin.), 210~228°. mixed m.p. 202° (sin.) 212~233°. Ramanone (Ⅶ), m.p. 177° (sin.) 184~196°. Isodigipurpurogenin-Ⅱ, m.p. 180° (sin.) 186~197° mixed m.p. 178° (sin.) 183~196°. The results of paper chromatography are shown in Fig. 6.

Rockogenin Diacetate (XVa) and Isorockogenin Diacetate (XVb)——A solution of 10 g. of hecogenin acetate (XIV) in 200 ml. of dioxane was treated with 2 g. of $NaBH_4$ in 40 ml. of 10% dioxane. The mixture was kept at room temperature for 38 hr., acidified with AcOH, and diluted with H_2O. The solid product was filtered off and washed with H_2O. The crude product was hydrolysed with 5% KOH in MeOH for 2 hr. on the steam bath, then treated in usual manner to give 7.8 g. of residue. This product was chromatographed over Al_2O_3, but rockogenin and isorockogenin could not be separated. This mixture was acetylated with Ac_2O, treated as usual manner, recrystallized from MeOH, to give XVa (58%). m.p. 204~207°. XVb (yield 15%) was obtained from the mother liquors after recrystallization from MeOH.

ϕ-Rockogenin Triacetate (XVIb)——A solution of XVa (1 mol.) in *n*-octanoic acid (6 mol.) and Ac_2O (3.9 mol.) was refluxed for 2 hr. The low-boiling fraction were distilled off until the temperature reached 240° and refluxing was continued for 2 hr. The reaction mixture was cooled and extracted with ether, treated as usual manner, to give an oily product, which was hydrolysed by refluxing for 0.5 hr. with 5% KOH in MeOH. Addition of large amount of hot H_2O precipitated a white solid, which was filtered off, and crystallized from MeOH-H_2O, ϕ-rockogenin (XVIa), m.p. 170~180°, was obtained. IR ν_{max}^{Nujol} cm^{-1}: 3300, 1690. XVIa was refluxed with Ac_2O in pyridine for 5 hr. and treated in the usual manner. Crystallization form MeOH, gave ϕ-rockogenin triacetate (XVIb), m.p. 100~105° (yield from XVa, 35%).

3β,12β-Diacetoxy-5α-pregn-16-en-20-one (XVII)——2.8 g. of XVIb in 20 ml. of AcOH was treated with 18.7 ml. of 1.39*N* CrO_3 in 90% AcOH below 26° and after 1.5 hr. the excess oxidant was destroyed with MeOH. The reaction mixture was extracted with ether, treated as the usual manner, to give an oily product. This residue was refluxed in 30 ml. of glacial AcOH for 2 hr. The solvent was then removed *in vacuo* and the residue dissolved CH_2Cl_2, treated as the usual manner, to give 2.5 g. of residue. After chromatography on Al_2O_3, 900 mg. of XVII was obtained after recrystallization from MeOH-H_2O, m.p. 137~140°, $[\alpha]_D^{14}$ 21.6° (c=1, MeOH), IR ν_{max}^{Nujol} cm^{-1}: 1730, 1690, 1595. UV λ_{max}^{EtOH} mμ (log ε): 236 (3.97). These data were identical with literature values.[5,18]

XVII from ϕ-Hecogenin——A solution of 3.5 g. of ϕ-hecogenin, obtained from XIV by the methed of Cameron, *et al.*,[16] in 72 ml. of dioxane was treated with 720 mg. of $NaBH_4$ in 15 ml. of 50% dioxane. The mixture was kept for 48 hr. at 24°, treated as the usual manner, and the product recrystallized from MeOH-H_2O, to give 1.7 g. of ϕ-rockogenin (XVIa), m.p. 177~180°. 500 mg. of XVII, m.p. 136~140°, was obtained, after treated as described above. This product was identical with XVII, obtained from rockogenin diacetate (XVa).

3β,12β-Diacetoxy-5α-pregna-14,15-dien-20-one (XVIII)——A solution of 1.92 g. of XVII and 0.94 g. of N-bromosuccinimide in 17 ml. of absolute CCl_4 was refluxed for 20 min. on the infrared lamp. Succinimide which appeared was filtered off, and the solution evaporated to dryness under red. press. in N_2 atmosphere. A solution of this residue in 27 ml. of pyridine was refluxed for 25 min., 5.4 ml. of Ac_2O was then added and refluxing continued for 10 min. After treatment in the usual manner, with active carbon, the product was chromatographed over Al_2O_3. Elutation with benzene : EtOAc (95:5) gave 500 mg. of dienone (XVIII) which was crystallized from hexane m.p. 155~157°, $[\alpha]_D^{14}$ +279° (c=0.9, $CHCl_3$). *Anal.* Calcd. for $C_{25}H_{34}O_5$: C, 72.43; H, 8.27. Found: C, 72.41; H, 8.44. IR ν_{max}^{Nujol} cm^{-1}: 1745, 1680 (shoulder), 1660, 1540. UV λ_{max}^{EtOH} mμ (log ε): 305 (4.29).

3β,12β-Diacetoxy-14β,15β-epoxy-5α-pregn-16-en-20-one (XIX)——To a solution of 500 mg. of dienone (XVIII) in 7 ml. of absolute $CHCl_3$ was added 8.5 ml. of an ether solution of 3% monoperphthalic acid (20% excess). The mixture was allowed to stand for 112 hr. at 20~23°, then diluted with ether and treated in the usual manner. The reaction product was crystallized from hexane, giving 60 mg. of XIX as needles, m.p. 147~152°. The mother liquors were chromatographed over Al_2O_3, to give 65 mg. of

18) R. K. Callow, V. H. T. James: J. Chem. Soc., **1956**, 4744.

XIX, and 100 mg. of dienone (XVIII). When the reaction time was extended to one week, the yield of XIX was raised to 50%. *Anal.* Calcd. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.86; H, 8.17. $[\alpha]_D^{14}$ +88° (c=0.9, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 1745, 1680, 1590, 1240. UV λ_{max}^{EtOH} mμ (log ε): 243 (3.63).

Catalytic Hydrogenation of the Epoxide (XIX)——100 mg. of XIX was shaken with 5% Pd-$BaSO_4$ (140 mg.) in EtOH under H_2 atmosphere for 1 hr., the catalyst was then filtered off and the solvent removed under red. press. The residue, which showed three spots on the thin-layer chromatography (Al_2O_3, benzene-acetone=90:10), was chromatographed over Al_2O_3. The product, eluted with hexane-benzene (1:1), was crystallized from hexane, to give 8 mg. of 3β,12β-diacetoxy-5α,14β,17α-pregnan-20-one (XXI). m.p. 175~178°. *Anal.* Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.69; H, 9.03. Elution with benzene gave 27 mg. of 3β,12β-diacetoxy-14β,15β-epoxy-5α,17α-pregnan-20-one (XXII), m.p. 180~182°, after crystallization from hexane. *Anal.* Calcd. for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39. Found: C, 69.53; H, 8.50. IR ν_{max}^{Nujol} cm^{-1}: 1745, 1715, 1240. The benzene-ether (1:1) fraction gave 23 mg. of 3β,12β,14β-trihydroxy-5α,17α-pregnan-20-one 3,12-diacetate XX as plates, m.p. 169~171° after crystallization from hexane-ether. *Anal.* Calcd. for $C_{25}H_{38}O_6$: C, 69.09; H, 8.81. Found: C, 69.34; H, 8.70.

XXI from the Dienone (XVIII)——50 mg. of the dienone (XVIII) was shaken with 1.2% Pd-$CaCO_3$ (150 mg.) in 10 ml. of EtOH under H_2 atmosphere. The hydrogen up-take ceased within 15 min. (2 mol). The catalyst was then filtered off and the solvent evaporated to dryness under red. press. the residue was recrystallized from hexane to give 29 mg. of plates (XXI), m.p. 175~177°, showed no melting point depression with XXI, obtained from XIX.

XX-from Ramanone Diacetate (VIII)——60 mg. of VIII was shaken with PtO_2 in AcOH for 15 hr. under H_2 atmosphere. The catalyst was then filtered off. The filtrate was added to a solution of CrO_3 (11 mg.) in 80% AcOH (1.1 ml.). The mixture was kept for 24 hr. at room temperature and the excess oxidant then destroyed with MeOH. After addition of H_2O, AcOH was evaporated under the red. press., extracted with $CHCl_3$, washed with 5% $NaHCO_3$, H_2O, and dried (Na_2SO_4). The solvent was removed to give 60 mg. of an oily substance which was recrystallized from hexane+ether, to give 12 mg. of plates. This product was identical with XX which was prepared from hecogenin acetate (XIV), by mixed melting point, IR spectrum and thin-layer chromatography (Al_2O_3, acetone-benzene=15:85), XX from VIII m.p. 167°, XX from XIV m.p. 167°, mixed m.p. 168°.

The authors express their deep gratitudes to Prof. R. Tschesche for his kind donation of digipurpurogenin-II and isodigipurpurogenin-II and Dr. Y. Shimizu for helpful discussions. We thank Dr. K. Takeda, Shionogi Research Laboratory for a generous gift of hecogenin and for ORD measurements, and Mr. S. Shimokawa, Hokkaido University, for NMR measurements. The authors are indebted to Mr. M. Fukuoka in this Laboratory for his generous gift of materials used in this study, and Mrs. T. Toma and Miss A. Maeda for the elemental analysis.

Summary

The structure of benzoylramanone (III), a new ester type aglycone from *Metaplexis japonica* MAKINO, has been proved by chemical conversions and spectroscopic examination of the conversion products. The structural conclusion have been confirmed by correlation with a degradation product from hecogenin.

(Received June 7, 1965)