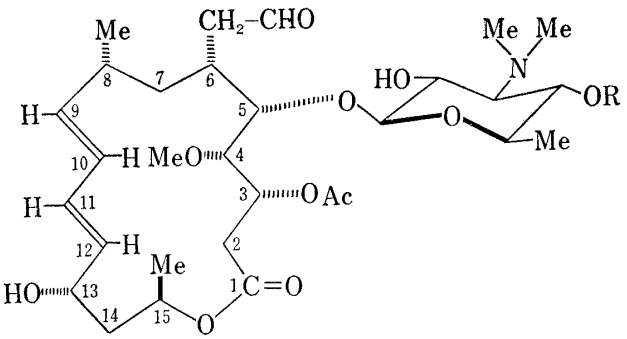


II : R=H

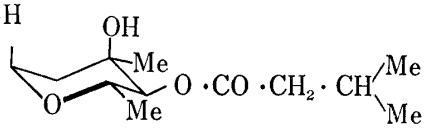
IV : R= 

Chart 2

of proton at C-9, as stated above, and the lowering of pK_a' to 5.70 from 6.70 of I. Catalytic reduction of the mono acetate (V) gave a tetrahydro compound (VI), $C_{44}H_{75}O_{16}N$, $[\phi]_D^{25}$ −818° (c=5, methanol), which was derived to 3,5-dinitrobenzoate (VII), $C_{51}H_{77}O_{21}N_3$, $[\phi]_D^{25}$ −934° (c=5, methanol). It was found from the application of the "benzoate rule"[6] that VI and VII belong to the R system by the comparison of their molecular rotation ($\Delta[\phi]_D^{25}$ −116°).

Therefore, from the present results and the previously reported results on the two glycosidic linkages, configuration of the diene system, and the X-ray crystal structure analysis, the absolute configuration of leucomycin A_3 has been revealed as represented by formula (I).

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6) J.H. Brewster, *Tetrahedron*, **1961**, 106.

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Synthesis of Rubrosterone

As part of our research program directed to the investigation of compounds having insect moulting hormone activities, the synthesis of androstane compounds the nuclear structures of which are closely related to that of ecdysone have been progressed. Quite recently, Takemoto, *et al.*[1] isolated a new insect moulting hormone-like substance, "rubrosterone" from *Achyranthes rubrofusca* Wight and proposed its chemical structure as 2β,3β,14α-trihydroxy-5β-androst-7-ene-6,17-dione (I) on the basis of spectroscopic evidences. The synthesis of rubrosterone by the similar methods used in the synthesis of ecdysone[2] will be described in this communication.

3β,17β-Dihydroxy-5α-androstan-6-one (II)[3] easily obtainable from dehydroepiandrosterone in 5 steps was served as a starting material. The introduction of 2β-hydroxyl grouping

1) T. Takemoto, Y. Hikino, H. Hikino, S. Ogawa, and N. Nishimoto, *Tetrahedron Letters*, **1968**, 3053.
2) H. Mori, K. Shibata, K. Tsuneda, and M. Sawai, *Chem. Pharm. Bull.* (Tokyo), **16**, 563 (1968).
3) H.B. MacPhillany, and C.R. Scholz, *J. Am. Chem. Soc.*, **74**, 5512 (1952).

in II was made by the modified method described in the previous paper.[4] The ketalization of II with the usual manner gave the ketal (III) (mp 132—135°, $[\alpha]_D$ +1°[5]), which was oxidized with pyridine–chromium trioxide complex to the dione (IV) (mp 161—163°, $[\alpha]_D$ +81°). The autoxidation of the ketal (IV) in the presence of potassium *tert*-butoxide in *tert*-butanol

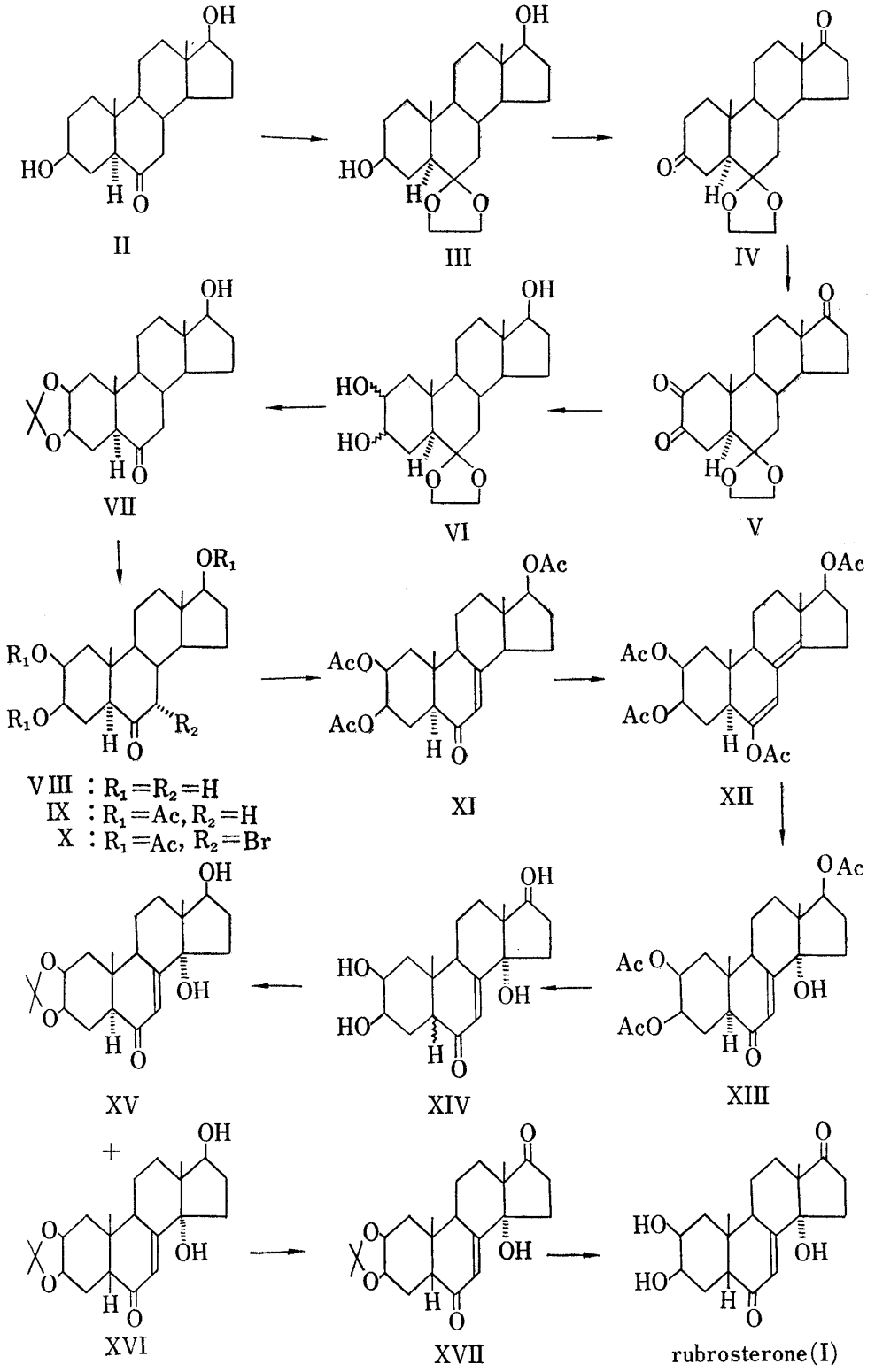

Chart 1

4) H. Mori, K. Shibata, K. Tsuneda, and M. Sawai, *Chem. Pharm. Bull.* (Tokyo), **15**, 460 (1967); H. Mori, K. Tsuneda, K. Shibata, and M. Sawai, *ibid.*, **15**, 466 (1967).

afforded an enol mixture of V. It was evident from infrared spectrum that 17-oxo function was unaltered in this reaction. This fact was shown by the model experiment on 5α-androstane-3,17-dione; the autoxidation with the same method followed by reduction with sodium borohydride yielded 5α-androstane-2β,3β,17β-triol. The enol mixture (V) was reduced with sodium borohydride to triol mixture (VI) and, without purification, VI was treated with acetone containing phosphomolybdic acid and chromatographed on Florisil to isolate the acetonide (VII) (mp 236—238°, $[\alpha]_D$ +10°). The hydrolysis of VII with phosphoric acid in ethanol gave the triol (VIII) (mp 237—240°, $[\alpha]_D$ −6° (MeOH)), which on acetylation with boiled acetic anhydride led to the triacetate (IX) (mp 210—212°, $[\alpha]_D$ −10°). The treatment of IX with one mole equivalent of bromine in acetic acid at 50° for 2 hr[6] afforded 7α-bromo compound (X) (mp 224—225° (decomp.), $[\alpha]_D$ +48°). X was dehydrobrominated with lithium carbonate in dimethylformamide to 7-en-6-one (XI) (mp 228—230°, $[\alpha]_D$ −5°, UV λ_{max} mμ (e) 242 (14000)).

The method of 14α-hydroxylation reaction reported from this laboratory[7] was applied to XI. The enol acetylation of XI with acetic anhydride in ethyl acetate containing a trace of perchloric acid as catalyst afforded an oily enol acetate (XII), from which 14α-hydroxy-7-en-6-one (XIII) (mp 237—240°, $[\alpha]_D$ +49°, UV λ_{max} mμ (e) 239 (11000)) was obtained by oxidation with monoperphthalic acid.

The hydrolysis and isomerization of XIII with 0.6% potassium carbonate in 90% methanol followed by acetonide formation with acetone containing phosphomolybdic acid afforded acetonides as an equilibrium mixture, from which 5α-acetonide (XV) (mp 280—285°, $[\alpha]_D$ +7° (MeOH), UV λ_{max} mμ (e) 243 (9900)) and 5β-acetonide (XVI) (mp 250—256°, $[\alpha]_D$ +24° (MeOH), UV λ_{max} mμ (e) 240 (10900)) were isolated in pure states by preparative thin-layer chromatography on silica gel, Merck GF_{254}. Their chemical structures were assigned by analogy with the similar experiments made on cholestane series. XVI was oxidized with pyridine-chromium trioxide complex to give rubrosterone 2,3-acetonide (XVII) (mp 233—237°, $[\alpha]_D$ +102° (MeOH), UV λ_{max} mμ (e) 239 (11000)) in satisfactory yield. The hydrolysis of XVII with 0.1 N hydrochloric acid in 90% aqueous dioxane afforded rubrosterone (I) (mp 240—244° (decomp.), $[\alpha]_D$ +125° (MeOH), UV λ_{max} mμ (e) 239 (10300), NMR δ: 0.85 (18-CH_3), 1.03 (19-CH_3), 6.24 (doublet, J=2.5 cps, 7-H)), which is in agreement with those reported.[1] The infrared spectrum of XVII was identical with that for natural rubrosterone kindly supplied by Prof. Takemoto.

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5) All melting points are uncorrected. Optical rotations were measured in chloroform at 23° and ultraviolet spectra in ethanol unless otherwise stated.
6) A. Furlenmeier, A. Fürst, A. Langemann, G. Waldvogel, U. Kerb, P. Hocks, and R. Wiechert, *Helv. Chim. Acta*, **49**, 1591 (1966).
7) H. Mori, K. Shibata, K. Tsuneda, and M. Sawai, *Chem. Pharm. Bull.* (Tokyo), to be submitted.