Faculty of Pharmaceuticl Sciences,
Kyushu University
Katakasu, Fukuoka

YUKIHIRO SHOYAMA
TOSHIO FUJITA
TATSUO YAMAUCHI
ITSUO NISHIOKA

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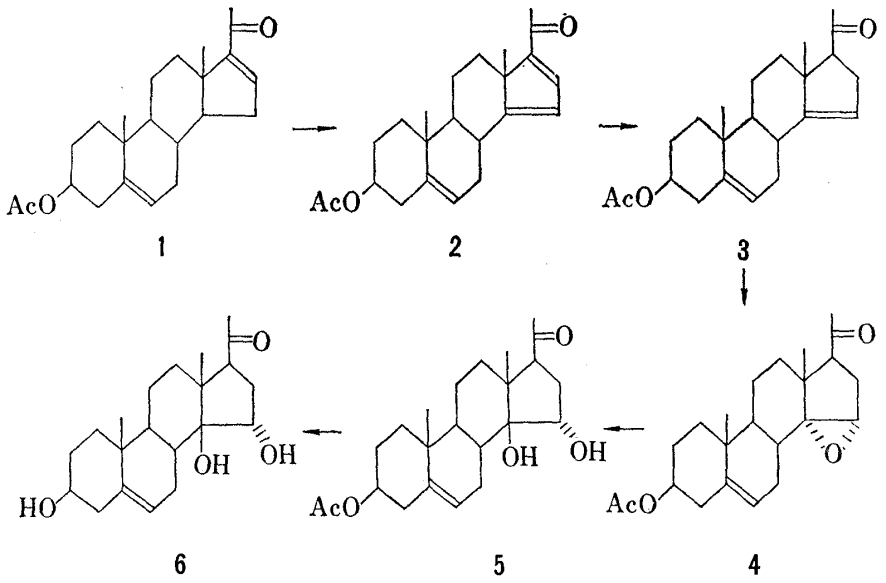
Synthesis of Purpnigenin

Purpnigenin is a digitenol of the simplest structure initially isolated from *Digitalis purpurea* L. leaves as a glycoside purpnin.[1] The structure **6** was determined by Ishii[2] by identification of an oxidation product with unambiguously prepared authentic sample. We wish here to describe the partial synthesis of purpnigenin starting with 3β-acetoxypregna-5,16-dien-20-one(**1**). Our synthetic method has its significance in that one may find general applicability in the syntheses of other digitenols such as purprogenin.[3]

3β-Acetoxypregna-5,16-dien-20-one(**1**) was converted by the known method of Solo and Singh[4] into 3β-acetoxypregna-5,14,16-trien-20-one(**2**). Saturation of the 16 double bond in the trienone(**2**) was achieved by the reduction either with triphenyltin hydride or with triethylsilane in the yields of 80%.[5] 3β-Acetoxypregna-5,14-dien-20-one(**3**) thus obtained had mp 148—150°[6] and showed the following spectral data that supported the structure; nuclear magnetic resonance (NMR)[7]: 0.87 (18-H), 1.03 (19-H), 2.03 (OAc), 2.15 (21-H), 5.13 (15-H, peak width at half-height=5 cps), 5.38 (6-H, half-width=9 cps); infrared absorption spectrum (IR) (KBr) cm^{-1}: 1738 (OAc), 1710 (20-one); ORD (c=0.102, MeOH) $[M]_D^{20}$ (mμ): +3895 (311) (peak), −7230 (268) (trough). The dienone **3** was then oxidized with an equimolar amount of monoperphthalic acid giving a single monoepoxide, mp 158°, in the yield of 65%.[8] That this is a 14,15-oxide was confirmed by NMR in which 15-H was observed as a singlet at 3.31,[9] and 6-H at 5.28 as a broad peak with half height width of 9 cps. The stereochemistry **4** was deduced from the known steric course of epoxidation[10] and supported by ORD which showed positive Cotton effect (a=+103).[11]

1) *a*) D. Satoh, H. Ishii, Y. Oyama, and T. Okumura, *Yakugaku Zasshi*, **75**, 1573 (1955); *b*) *Idem.*, *Chem. Pharm. Bull.* (Tokyo), **10**, 37 (1962); *c*) H. Freitag, S. Spengel, H.H.A. Linde, and K. Meyer, *Helv. Chim. Acta*, **50**, 1336 (1967).
2) H. Ishii, *Chem. Pharm. Bull.* (Tokyo), **9**, 411 (1961); *Idem.*, *ibid.*, **10**, 351, 354 (1962).
3) D. Satoh and J. Morita, *Chem. Pharm. Bull.* (Tokyo), **16**, 178 (1968); M. Fukuoka and H. Mitsuhashi, *ibid.*, **15**, 2007 (1967).
4) A.J. Solo and B. Singh, *J. Org. Chem.*, **30**, 1658 (1965).
5) The novel feature of this reduction method was presented at the 88th Annual Meeting of Pharmaceutical Society of Japan, Tokyo, April, 1968. Experimental details will be reported in a full paper.
6) Melting points were taken with a Yanagimoto Micro Melting Point Apparatus and uncorrected. Satisfactory elemental analytical data were obtained for all new compounds.
7) NMR spectra were measured using deuteriochloroform as solvent unless indicated otherwise and are quoted as δ(ppm) down field from tetramethylsilane as internal standard.
8) Treatment of **3** with N-bromoacetoamide in an acetate buffer, followed by alumina chromatography, afforded 3β-acetoxy-14β, 15β-epoxypregn-5-en-20-one which will serve as a precursor in the synthesis of 12-deoxyisoramanone.[1a]
9) K. Tori, T. Komeno, and T. Nakagawa, *J. Org. Chem.*, **29**, 1136 (1964); A.D. Cross, *J. Am. Chem. Soc.*, **84**, 3206 (1962).
10) H. Ishii, *Chem. Pharm. Bull.* (Tokyo), **10**, 354 (1962) ; H. Hasegawa, Y. Sato, and K. Tsuda, *ibid.*, **11**, 1275 (1963) ; D. Satoh and J. Morita, *ibid.*, **16**, 178 (1968).
11) K.M. Wellman and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 60 (1965).



Hydrolytic cleavage of the epoxide ring in **4** was carried out with 1/3 N sulfuric acid in aqueous dioxane at 30° for two days. Two major products, mp 241—243° and mp 184—186°, were isolated by fractional crystallization and alumina chromatography. The former compound was identified as purpnigenin(**6**) by mixed melting point and by comparison of the infrared spectrum with that of natural purpnigenin.[12] Also consistent with the assigned structure(**6**) were ORD ($a=+52$)[13] and the following NMR (deuteriopyridine): 1.04 (18-H), 1.20 (19-H), 2.24 (21-H), 3.7 (3α-H, broad), 5.47 (6-H, b.), 6.15 (OH), 5.3—6.5 (overlapped peak due to two hydroxyls nad 15β-H, addition of D_2O gave a doublet of 15β-H at 4.64 with $J=5$ cps). The latter product of lower melting point was assigned to 3-monoacetate(**5**) of purpnigenin on the bases of the following spectral data; IR ($CHCl_3$) cm^{-1}: 3405 (OH), 1728 (OAc), 1698 (20-one); NMR: 0.97, 0.99 (18-H and 19-H), 2.02 (OAc), 2.24 (21-H), 3.75 (OH), 4.35 (15β-H, d., $J=6$ cps), 5.40 (6-H). 3,15-Diacetate of purpnigenin prepared by the usual way had mp 128—130°[14] and gave the correct IR and NMR[1c] that are consistent with the structure.

Faculty of Pharmaceutical Sciences,
University of Toyama
Gofuku, Toyama

Eiichi Yoshii
Masaki Yamasaki

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12) We are grateful to Dr. Satoh for his generous gift of purpnigenin.
13) For ORD of 17-epimeric 3β,12β,14β,15β,15α-tetrahydroxy-5α-pregnan-20-ones, see ref. 3).
14) The reported melting points are 150—153°[2] and 127—130°/139—141°(double mp).[1c] The former datum should read mp 137—139° according to a private communication from Dr. Satoh.