3.64 (1H, br. t, J=6.0 Hz, C24-H). Mass Spectrum m/e: 500 (M^+).

It is a noticeable finding in the ^{1}H-NMR spectra that the C24-proton signal of 24*R*-derivative (XI-A) and that of IV are observed as the similar broad doublet (J=7.0 Hz), while that of 24*S*-derivative (XI-B) is observed as a broad triplet (J=6.0 Hz). Therefore, XI-A was oxidized to the corresponding 3-oxo compound XII-A with chromium trioxide in pyridine. XII-A: colorless rods (acetone), mp 145—146°. *Anal.* Calcd. for $C_{33}H_{54}O_3$: C, 79.46; H, 10.92. Found: C, 79.58; H, 11.18. IR ν_{max}^{KBr} cm^{-1}: 1705, 1378, 1368. NMR $\delta_{ppm}^{CDCl_3}$: 0.59, 0.82 (each 1H, ABq. J=4.0 Hz, cyclopropane methylene proton), 0.91 (3H, s, C–CH_3), 0.93 (3H, d, J=6.0 Hz, CH–C$\underline{H}_3$), 1.02, 1.06 (each 3H, s, C–CH_3), 1.12 (6H, s, C–$CH_3\times2$), 1.27, 1.38, 1.42 (each 3H, s, C–CH_3), 3.66 (1H, br. d, J=7.0 Hz, C24-H). Mass Spectrum m/e: 498 (M^+).

The carbonyl group of XII-A was then reduced under the Meerwein-Ponndorf conditions to yield a 3α-hydroxy derivative: colorless needles (methanol–acetone), mp 179—182°. *Anal.* Calcd. for $C_{33}H_{56}O_3$: C, 79.14; H, 11.27. Found: C, 79.36; H, 11.48. IR ν_{max}^{KBr} cm^{-1}: 3500. Mass Spectrum m/e 500 (M^+). The final product was identified with VIII by mixed melting point determination, IR and mass spectrometry.

Finally, the position of the carboxyl function in protolyofoligenic acid (II) is considered to be at C-14 on the basis of the recent X-ray analysis of a derivative of lyofoligenic acid,[5] since lyofoligenic acid was already shown to possess the carboxyl function at the same position as II.[1]

Based on the accumulated evidence the stereostructure II has been established for protolyofoligenic acid.

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Received August 15, 1974

5) J. Sakakibara, Y. Hotta, M. Yasue, Y. Iitaka, and K. Yamazaki, *Chem. Commun.*, **1974**, 839.

[Chem. Pharm. Bull. 23(2) 462—464 (1975)]

UDC 547.92.04

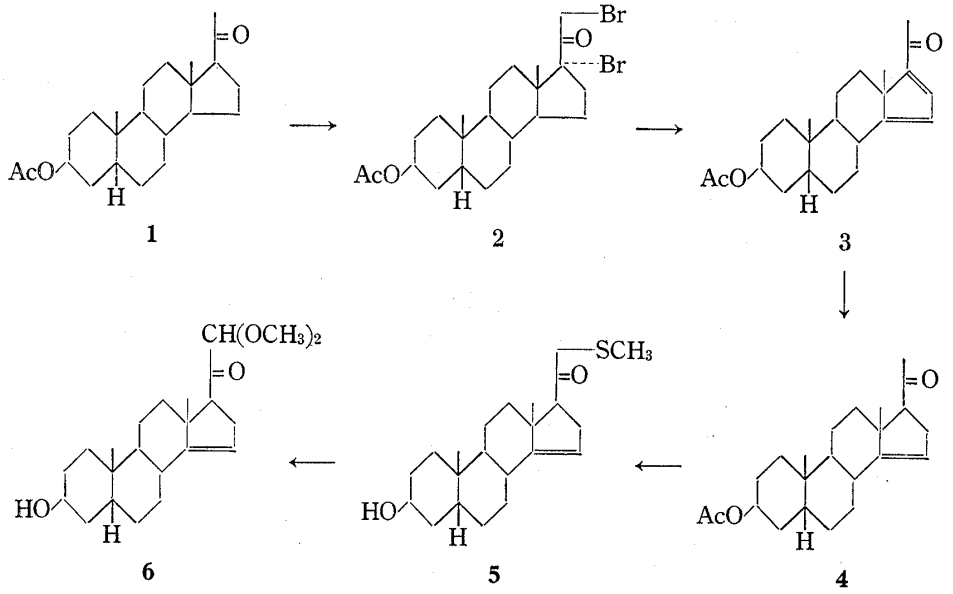
Facile Preparation of Pregn-14-ene-20,21-diones

A practical synthetic method of 21-dimethoxypregn-14-en-20-ones which are key intermediates in bufadienolide syntheses is described. It involves 21-thiomethylation of pregn-14-en-20-ones followed by oxidation with N-chlorosuccinimide in methanol.

As demonstrated by Stache, *et al.*[1] in their syntheses of scillarenin and 5α-bufalin, facile synthesis of the title compounds is a crucial requirement for establishing practical synthetic method of natural bufadienolides.[2] We herein describe an effective method for the preparation of pregn-14-ene-20,21-diones from readily available pregnan-20-ones or pregn-16-en-20-ones. It involves in the key step a new oxidation method of methylketone to α-ketoaldehyde *via* thiomethyl derivative which will find general applicability. Exemplified below are the con-

1) U. Stache, K. Radscheit, W. Fritsch, H. Kohl, W. Haede, and H. Ruschig, *Tetrahedron Letters*, **1969**, 3033; *Ann. Chem.*, **750**, 149 (1971). See also, W. Haede, W. Fritsch, K. Radscheit, U. Stache, and H. Ruschig, *ibid.*, **741**, 92 (1970).
2) F. Sondheimer, *Chemistry in Britain*, **1965**, 454.

version of 5β-pregnan-3β-ol-20-one acetate (**1**) into 5β-pregn-14-en-3β-ol-20,21-dione dimethylacetal (**6**), from which bufalin (3β,14-dihydroxy-5β,14β-bufa-20,22-dienolide) could be synthesized by known methods.[1,3]



17α,21-Dibromo-5β-pregnan-3β-ol-20-one acetate[4] obtained from commercially available **1** was dehydrobrominated[5] by heating (90—95°) in dimethylformamide in the presence of lithium bromide (2 eq) to afford dienone **3**,[6,7] mp 110—112°, in 76—82% yield from **1**.[9] Partial hydrogenation of **3** was performed with triethylsilane as reported previously[10] and non crystallizable enone **4** which has potential double bond for 14-oxygenation was obtained in 70—75% yields after silica gel chromatography. The 14-en-20-one **4** was then condensed with diethyl oxalate in the presence of sodium ethoxide and the resulting crude oxalylketone was reacted with methyl thiotosylate[11] (1.1 eq) in refluxing ethanol containing excess potassium acetate (*ca.* 5 eq) for 2.5 hr to give 66% yield of monosulfenylated product **5**, mp 96—98°. The methylthiomethylketone **5** (1.79 g) was oxidized with N-chlorosuccinimide (2.2 eq) in 2% methanolic sulfuric acid (30 ml) at 0° for 15 min. The reaction product was purified by chromatography on silver nitrate impregnated silica gel to give 86% yield of 5β-pregn-14-en-

3) W. Kreiser and H.U. Warnecke, *Ann. Chem.*, **1973**, 2078.
4) R.E. Marker, H.M. Crooks, Jr., and R.B. Wagner, *J. Am. Chem. Soc.*, **64**, 213 (1942).
5) R. Joly and J. Warnant, Fr. Patent addn. 71333 (1959) [*Chem. Abstr.*, **55**, 20008 (1961)]; R. Deghenghi, *Pure and Applied Chemistry*, **21**, 153 (1970).
6) Dienone **3** was also obtained from 5β-pregn-16-en-3β-ol-20-one acetate by the following methods that proved not to be practically usable. i) Allylic bromination with N-bromosuccinimide or molecular bromine and subsequent dehydrobromination. Though the conversion was acceptable (50—60% by NMR), great difficulty was encountered in isolating **3** from the reaction mixture. Even by careful chromatography pure **3** free from the starting material could not have been obtained. ii) 21-Bromination by cupric bromide after the method of E.R. Glazier [*J. Org. Chem.*, **26**, 4397 (1962)] followed by lithium salt catalyzed dehydrobromination. The low yield (30% overall) was proved to be responsible for the formation of 21,21-dibromo compound that could not be suppressed.
7) Usefulness of such dienone for the synthesis of cardenolides had already been shown by us[8] and pointed out by G.R. Pettit, *et al.* [*J. Org. Chem.*, **35**, 1367 (1970)].
8) E. Yoshii and K. Ozaki, *Chem. Pharm. Bull.* (Tokyo), **20**, 1585 (1972).
9) Isolated yields are given throughout this paper. Infrared, nuclear magnetic and mass spectral data were consistent with the assigned structures.
10) E. Yoshii, H. Ikeshima, and K. Ozaki, *Chem. Pharm. Bull.* (Tokyo), **20**, 1827 (1972).
11) Reaction of methyl thiotosylate with 2-hydroxymethylenecyclohexanone derivatives: R.L. Autrey and P.W. Scullard, *J. Am. Chem. Soc.*, **90**, 4917, 4924 (1968); Y. Shimizu, *Tetrahedron Letters*, **1972**, 2919.

3β-ol-20,21-dione dimethylacetal **6**,[12] mp 110—111°. By the same reaction sequence pregn-5-en-3β-ol-20-one acetate was converted to pregn-5-en-3β-ol-20,21-dione dimethylacetal in an overall yield of 71%.[13]

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Received September 26, 1974

12) During the initial stage of the present investigation, an 2-etianoyl-1,3-dithiolane was prepared in good yield by the reaction of ethane-1,2-dithiol ditosylate with 21-oxalylderivative of pregn-5-en-3β-ol-20-one with expectation that the dithioacetal group be hydrolyzed. But all attempts to hydrolysis by existing methods resulted in failure, occurring oxidation at C_2 of 2-acyl-1,3-dithiolane to give α-keto-ester or α-ketothiolester. Reported at 93th Annual Meeting of Pharmaceutical Society of Japan, Tokyo, 1973.

13) Previously this conversion has been achieved usually by three step sequence ——21-acetoxylation with lead tetraacetate,[14] hydrolysis, and cupric acetate oxidation.[1,15] However, this method has intrinsic limitation for general application in that acetoxylation of methylketone bearing reactive double bond (*e.g.* **4**) dose not afford acceptable yield. Our method has its significance in that there exists no such limitation.

14) J.D. Cocker, H.B. Henbest, G.H. Phillips, G.P. Slater, and D.A. Thomas, *J. Chem. Soc.*, **1965**, 6; G.R. Pettit, C.L. Herald, and J.P. Yardley, *J. Org. Chem.*, **35**, 1389 (1970).

15) M.L. Lewbart and V.R. Mattox, *J. Org. Chem.*, **28**, 2001 (1963).

[Chem. Pharm. Bull. 23(2) 464—466 (1975)]

UDC 547.857.7'457.1.04

Chemical Conversion of Adenosine to Guanosine (Nucleosides and Nucleotides. XI)[1]

A versatile chemical conversion of adenosine to guanosine is described. Treatment of adenosine-1-oxide with cyanogen bromide afforded hydrobromide salt of 2-imino-6-β-D-ribofuranosyl-(1,2,4-oxadiazolo[2,3-*f*]purine), which existed as N^6-cyanoadenosine-1-oxide on neutralization. Methylation of the latter followed by treatment with alkali afforded N^6-methoxy-2-aminoadenosine. The solvolysis of the product with liquid hydrogen sulfide gave 6-thioguanosine in high yield. Thioguanosine can be oxidatively hydrolyzed to guanosine by the known procedure. Catalytic hydrogenation of the oxadiazolopurine riboside in the presence of acetic acid gave 6-ureidopurine riboside.

One of the most interesting chemical reactions in nucleic acid chemistry is a conversion of a certain nucleobase to another in nucleoside, nucleotide and polynucleotide levels. Such conversions have sofar been limited in the hydrolytic deamination of adenine- or cytosine- to hypoxanthine- or uracil-moiety.

We present here a versatile chemical conversion of adenosine to guanosine, through 6-thioguanosine, in relatively mild reaction conditions.

To a suspension of adenosine-1-oxide (I, 5 g)[2] in 400 ml of MeOH cyanogen bromide (2 g) was added and the mixture was stirred for one hour. The product, obtained in almost quantitative yield, was found to be 2-imino-6-β-D-ribofuranosyl(1,2,4-oxadiazolo [2,3-*f*] purine) hydrobromide(II, 6.3 g, 92%; *Anal.* Calcd. for $C_{11}H_{13}O_5N_6Br \cdot 1/3H_2O$: C, 33.43;

1) Part X: T. Ueda, K. Miura, M. Imazawa and K. Odajima, *Chem. Pharm. Bull.* (Tokyo), **22**, 2377 (1974).

2) M.A. Stevens, D.I. Magrath, H.W. Smith, and G.B. Brown, *J. Am. Chem. Soc.*, **80**, 2755 (1958).