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Synthesis of Sulfur-Bridged Uracil Anhydronucleosides

Anhydronucleosides are the useful intermediates for the chemical transformation of nucleosides. Of the pyrimidine nucleosides a large number of oxygen–bridged anhydronucleosides has been prepared.[1] In this paper the synthesis of sulfur–bridged anhydronucleosides is presented. Two such compounds have so far been prepared. Shaw and Warrener synthesized a (*S*)-2,2′-anhydronucleoside (I) as an intermediate to thymidine starting from 1-β-D-ribofuranosyl-2- thiothymine.[2] Recently Wempen and Fox prepared a (*S*)-2,3′-anhydronucleoside (II) from 2,5′-anhydro-3′-mesylthymidine.[3] The present synthesis of (*S*)-2,2′- and (*S*)-2,5′-anhydrouridines involves the use of anhydrouridine as the starting materials.

2,2′-Anhydro-3′,5′-di-O-acetyluridine (III)[4] was treated with hydrogen sulfide in pyridine to afford 1-(3,5-di-*O*-acetyl-β-D-arabinofuranosyl)-2-thiouracil (IV); mp 149—151°. *Anal.* Calcd. for $C_{13}H_{16}O_7N_2S$: C, 45.39; H, 4.69; N, 8.14; S, 9.32. Found: C, 45.42; H, 4.65; N, 8.11; S, 9.48 in 73% yield. Deacetylation of IV gave the known 1-(β-D-arabinofuranosyl)-2-thiouracil.[5] Methanesulfonylation of IV in pyridine afforded (V); mp 181—182°. Compound (V) was treated with 5 molar excess of sodium methoxide in methanol at room temperature followed by neutralization with ion exchange resin (Dowex 50, H^+ from). After the work-up the product, (*S*)-2,2′-anhydro-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)-2-thiouracil (VI), was obtained in 93% yield: mp 189—191° (from aq. EtOH); Mass Spectrum *m/e*: 242 (M^+); *Anal.* Calcd. for $C_9H_{10}O_4N_2S$: C, 44.63; H, 4.16; N, 11.57; S, 13.19. Found C, 44.41; H, 4.19; N, 11.67; S, 13.22. The compound (VI) showed ultraviolet (UV) spectra (λ_{max} 230 mμ, ε 27000) which resembled with those for 2-methylthiouridine.[6] Desulfurization of VI with Raney-Ni and successive acid treatment afforded 4-pyrimidone and 2-deoxy-D-ribose. Nuclear magnetic

Table I. NMR Chemical Shift of (*S*)-Anhydronucleosides.

	Coumpound (VI)		Compound (XI)	
	(ppm)	*J* (cps)	(ppm)	*J* (cps)
C_5–H	5.88 d	$J_{5,6}$ 8	5.92 d	$J_{5,6}$ 8
C_6–H	7.82 d	$J_{5,6}$ 8	8.05 d	$J_{5,6}$ 8
C_1'–H	6.33 d	$J_{1',2'}$ 7	5.83 s	
C_2'–H	4.28 m		5.34 d	$J_{2',3'}$ 6
C_3'–H	4.34 m	$J_{3',4'}$ 3	4.95 d	$J_{2'2,'}$ 6
C_4'–H	3.98 ps.q	$J_{3',4'}$ 3	4.92 q	$J_{4',a}$ 2
		$J_{4',5'}$ 5		$J_{4',b}$ 4
C_5'–H	3.44 d	$J_{4',5'}$ 5	3.50 (Ha q)	$J_{a,b}$ 14
			3.16 (Hb q)	$J_{4',a}$ 2
				$J_{4',b}$ 4

NMR Spectra were taken on a Hitachi H-60 recording spectrometer in d-DMSO and TMS as an internal standard. Compound (XI) exhibits signals of isopropylidene group -H at 1.32 and 1.46 ppm.

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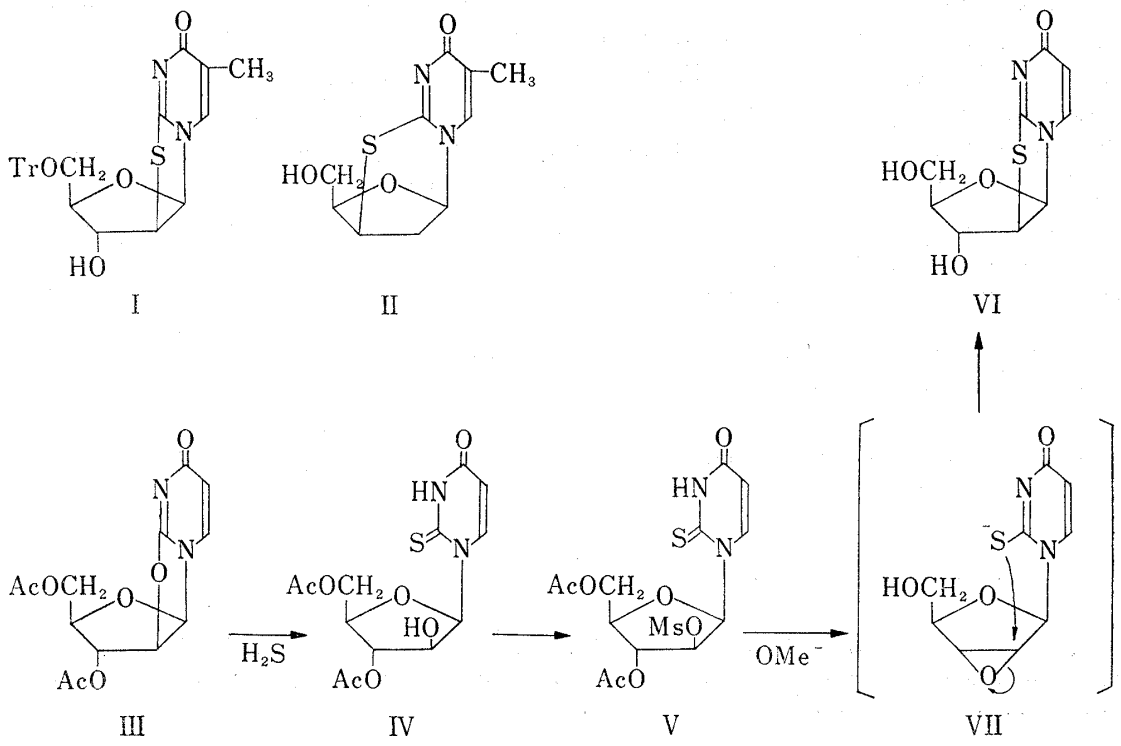
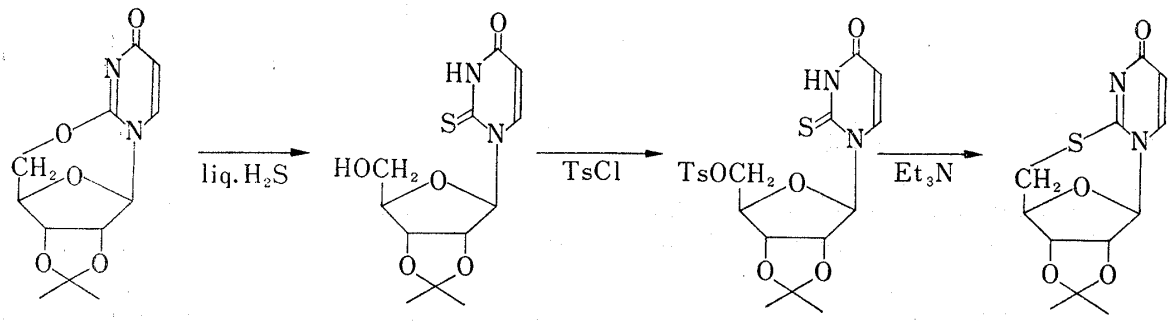
2) G. Shaw and R.N. Warrener, *J. Chem. Soc.*, **50** (1959).
3) I. Wempen and J.J. Fox, *J. Org. Chem.*, **34**, 1020 (1969).
4) *a*) D.M. Brown, D.B. Parihar, and A. Todd, *J. Chem. Soc.*, **1958**, 4242; *b*) Y. Furukawa and M. Honjo, *Chem. Pharm. Bull.* (Tokyo), **16**, 2286 (1968).
5) *a*) T. Sekiya and T. Ukita, *Chem. Pharm. Bull.* (Tokyo), **15**, 1497 (1967); *b*) W.V. Ruyle and T.Y. Shen, *J. Med. Chem.*, **10**, 331 (1967).
6) T. Ueda and H. Nishino, *Chem. Pharm. Bull.* (Tokyo), **17**, 920 (1969). For the UV spectra of substituted 2-thiouracils, see D. Shugar and J.J. Fox, *Bull. Soc. Chim., Belg.*, **61**, 293 (1952).



resonance (NMR) spectra of VI are in good accordance with those expected for the structure (VI) (Table I).

The conversion of V to VI in methoxide solution should proceed by: a) deacetylation and "down" epoxide formation with the release of mesyloxy group to VII; b) cleavage of "down" epoxide at C-2′ by the attack of 2-thiolate ion to furnish VI. The absence of 2,3′-anhydronucleoside shows that the cleavage of the epoxide occurs exclusively at C-2′ as have been indicated in the similar type of reaction in a purine nucleoside.[7]

Treatment of 2′,3′-O-isopropylidene-2,5′-anhydrouridine (VIII)[8a] with liquid hydrogen sulfide in pyridine (1:1, by volume) in a seale dtube at room temperature for 4 days afforded 2′,3′-O-isopropylidene-2-thiouridine (IX) in 93% yield. It is to be noted that the cleavage of 2,5′-anhydro linkage of VIII with hydrogen sulfide in triethylamine–dimethylformamide occurred by alkyl-*S* fission as well as aryl-*S* fission.[6,8] Therefore the present modification provides a simple preparation of 2-thiouridine from uridine. Compound (IX) was converted to the 5′-tosylate (X); mp 175—177° (decomp.), which was treated with 2 equivalents of triethylamine in dioxan under reflux for one hour. The product, (*S*)-2,5′-anhydro-1-(5-deoxy-2,3-O-isopro-



7) M. Ikehara and H. Tada, *J. Am. Chem. Soc.*, **87**, 606 (1965).
8) *a*) D.M. Brown, D.B. Parihar, A. Todd, and S. Varadarajan, *J. Chem. Soc.*, 3028 (1958); *b*) R.W. Chambers and V. Kurkov, *J. Am. Chem. Soc.*, **85**, 2160 (1963).

pylidene-β-D-ribofuranosyl)-2-thiouracil (XI), was obtained from benzene–ethanol as a crystalline form; mp 246—247°: Mass Spectrum *m/e*: 282 (M^+): *Anal.* Calcd for $C_{12}H_{14}O_4N_2S$: C, 51.06; H, 5.00; N, 9.93; S, 11.37. Found: C, 51.05; H, 4.91; N, 10.00; S, 11.29. UV spectra (λ_{max} 243 mμ, ε 18660) are closely similar to those of 2-methylthiouridine[6] and NMR spectra are characteristic for the structure (XI) (Table I). The comparison of NMR spectra of *O*- and *S*-anhydronucleosides reveals that the signals of the proton(s) at the carbon bearing sulfur bridge are shifted to higher magnetic field by ~1 ppm.[9]

The studies of optical properties and cleavage reaction of sulfur bridge of (*S*)-anhydronucleosides are presently being undertaken.

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9) For the NMR spectra of 2,2′- and 2,5′-anhydrouridines, see M. Honjo, Y. Furukawa, M. Nishikawa, K. Kamiya, and Y. Yoshioka, *Chem. Pharm. Bull.* (Tokyo), **15**, 1076 (1967) and J. Zemlicka and F. Sorm, *Collection Czech. Chem. Commun.*, **32**, 576 (1967), respectively.

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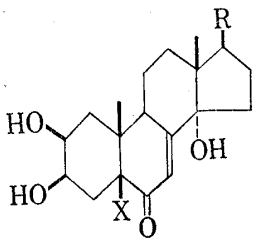
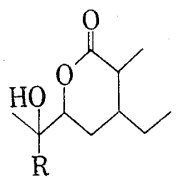
Structure of Precyasterone, A Novel C_{29} Insect-Moulting Substance from *Cyathula capitata*

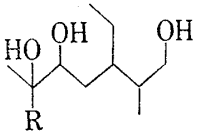
During our investigation on the roots of *Cyathula capitata* MOQUIN-TANDON (Amaranthaceae), five C_{29} phytoecdysones, sengosterone (III),[1] cyasterone (IV),[2] capitasterone (V),[3] amarasterone A (VI), and amarasterone B (VII)[4] have hitherto been isolated. In addition,



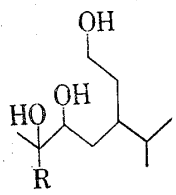
III : X=OH
IV : X=H



V : X=H



VI : X=H



VII : X=H

there has been obtained another active C_{29} congener now named precyasterone. The present communication describes evidence which indicates the structure I for precyasterone.

1) H. Hikino, K. Nomoto, and T. Takemoto, *Tetrahedron Letters*, **1969**, 1417; *idem*, *Tetrahedron*, **26**, 887 (1970).
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3) T. Takemoto, K. Nomoto, Y. Hikino, and H. Hikino, *Tetrahedron Letters*, **1968**, 4929.
4) T. Takemoto, K. Nomoto, and H. Hikino, *Tetrahedron Letters*, **1968**, 4953.