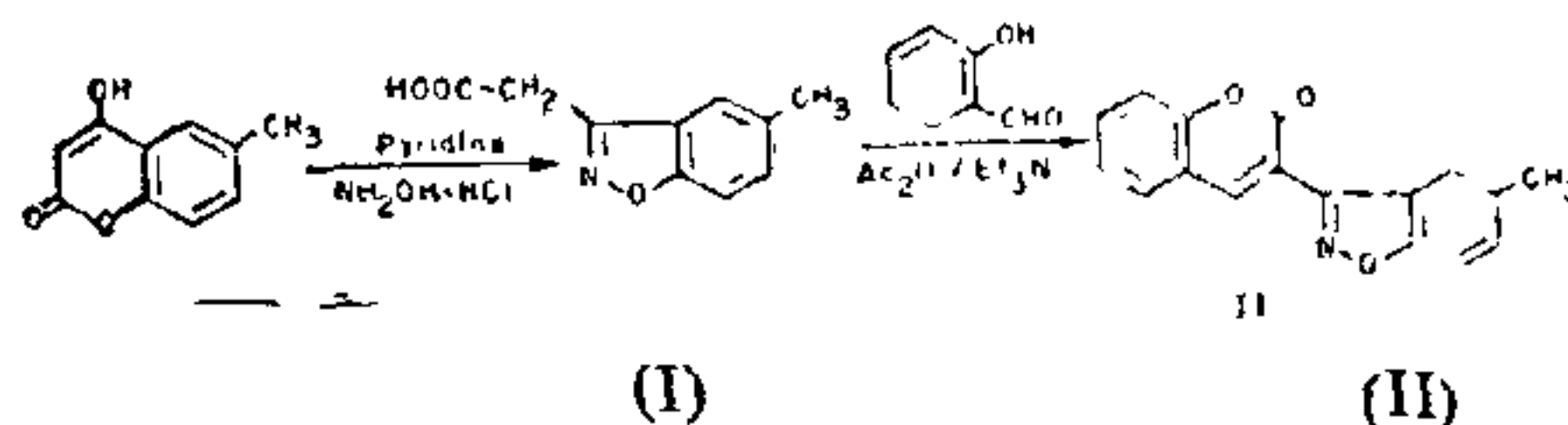


**SYNTHESIS OF 3-(3'-BENZISOXAZOLYL)
COUMARINS**

IN continuation of our earlier work on the synthesis of 3-heteryl coumarins¹⁻⁴, we now report the synthesis of 3-(3'-benzisoxazolyl) coumarins, in view of the reported physiological properties of 3-substituted benzisoxazoles^{5,6} and coumarin.

The synthesis of the title compounds involves the condensation of 1, 2-benzisoxazole-3-acetic acid with salicylaldehyde or *o*-hydroxy acetophenones in acetic anhydride and triethylamine. The required 1, 2-benzisoxazole-3-acetic acids have been prepared by refluxing 4-hydroxycoumarin with hydroxylamine in pyridine⁷.

The compound obtained by condensing salicylaldehyde with 5-methyl-1, 2-benzisoxazole-3-acetic



Following this procedure the compounds synthesized are given in Table I with the relevant data.

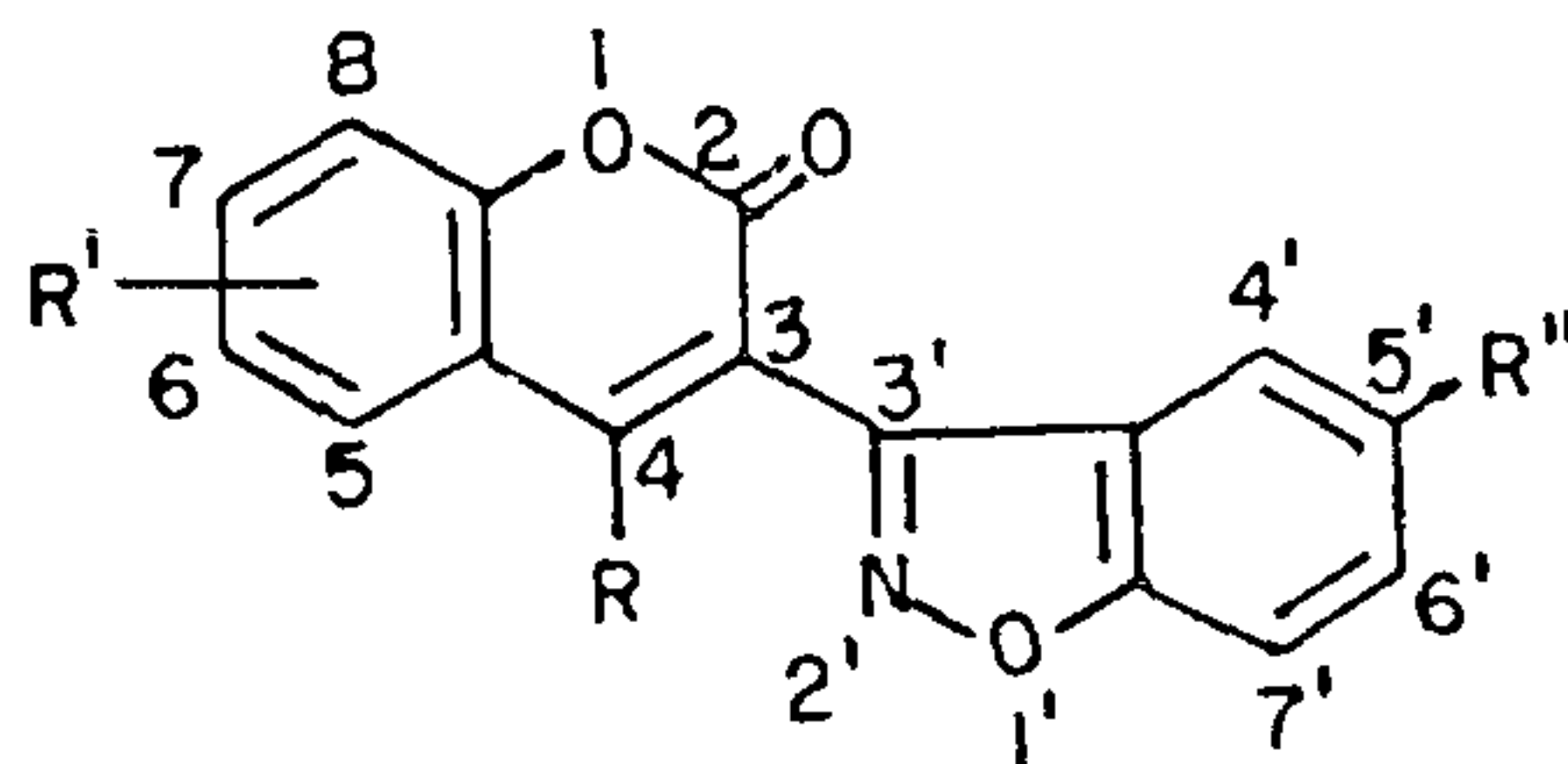


TABLE I

Sl. No.	Substituent			Solvent of Crystallisation	m.p. °C	Yield %
	R	R'	R''			
1.	H	H	methyl	Methanol	187	90
2.	H	6-nitro	methyl	Benzene	280	85
3.	H	8-nitro	methyl	Benzene	256	80
4.	Methyl	H	methyl	Pet. ether	92	90
5.	H	6-methyl	methyl	Methanol	162	90
6.	Methyl	6-methyl	methyl	Methanol	192	90
7.	H	6, 8-dichloro	methyl	Ethyl acetate	264	85
8.	H	H	H	Methanol	127	90
9.	H	6-nitro	H	Benzene	282	85
10.	H	8-nitro	H	Benzene	254	85

acid (I) using acetic anhydride and triethylamine, was a colourless product (II) (m.p. 187°C). This was insoluble in sodium bicarbonate and 5% sodium hydroxide and gave a single spot on T.L.C. (ethyl acetate, benzene, 1:1). The compound (II) contained nitrogen and from the mass spectrum the molecular weight of the compound was found to be 277 corresponding to the molecular formula C₁₇H₁₁O₃N. The IR spectrum (KBr pellet) of the compound showed peaks at 1710 cm⁻¹ (lactone >C=O) and 1600 cm⁻¹ (assignable for >C=N-). The NMR spectrum (CDCl₃) of the compound showed sharp signals at δ 2.32 (s, 3H), δ 7.29 (m, 7H) for aromatic protons and δ 8.1 (s, 1H) corresponding to the C₄ proton of coumarin.

From the above physical and chemical data the product (II) has been assigned as 3-(3', 5'-methyl-benzisoxazolyl) coumarin.

Further work is in progress and full details regarding their antibacterial and antifungal activities will be reported in due course.

The authors are thankful to Prof. T. Navaneeth Rao, Head, Department of Chemistry, for providing facilities, Department of Chemistry, A. SRIE LAKSHMI, Osmania University, K. VENKATESWARA RAO, Hyderabad 500 007, V. SUNDARAMURTHY, Andhra Pradesh, September 22, 1978.

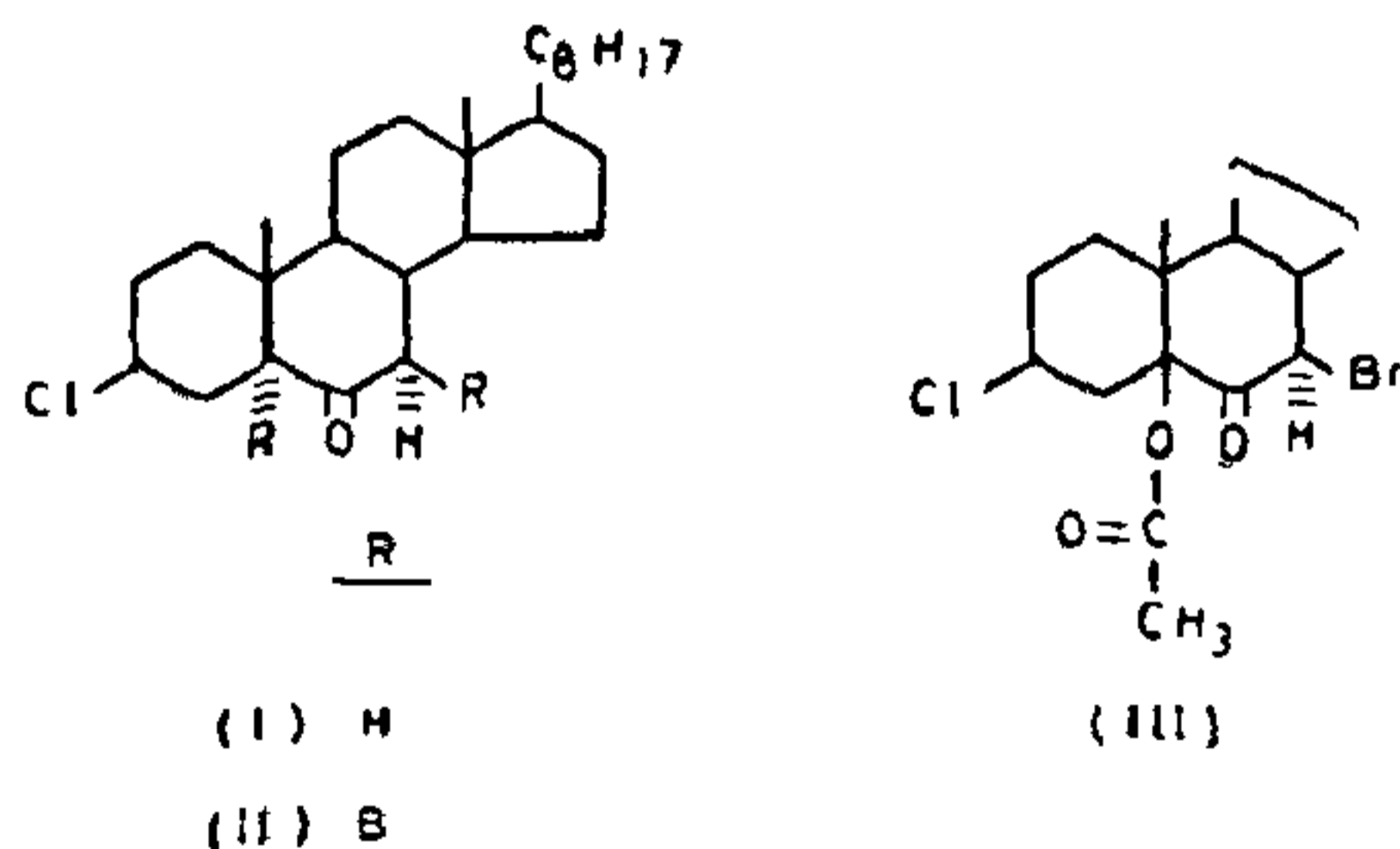
1. Sreenivasulu, B., Sundaramurthy, V. and Subba Rao, N. V., *Curr. Sci.*, 1969, 38, 240.
2. —, — and —, *Convention of Chemists*, University of Bombay, 1971, p. 88.
3. —, — and —, *Proc. Indian Acad. Sci.*, 1974, 79A, 41.

4. Someswari, N., Sundaramurthy, V. and Subba Rao, N. V., *Convention of Chemists, Madurai, Org. II, 1974, p. 52.*
5. Seiyanaku, T., *Japan, 1966, 16, 168; Chem. Abst., 1967, 66, 10924.*
6. Nishimura, H., Shimizu, M., Uno, H., Hirooka, T., Masuda, Y. and Kurokawa, M., *Japan, Kokai, 1976, 76, 136, 666; Chem. Abst., 1977, 87, 394590 C.*
7. Mustafa, A., Hsihmat, O. H., Zayed, S. M. A. D. and Ahmed Nawar, A., *Tetrahedron, 1963, 19, 1831.*

STEREOCHEMICAL STUDY OF α -BROMOKETONE: ACETOLYSIS OF

3 β -CHLORO-5, 7 β -DIBROMO-5 α -CHOLESTAN-6-ONE (II) WITH SODIUM ACETATE-ALCOHOL

DURING the course of our study on bromination of steroidal ketones and subsequent reactions of α -bromoketones, we subjected II obtained from bromination of 3 β -chloro-5 α -cholestan-6-one (I) (Br_2 -HBr at room temperature) to acetolysis using CH_3COONa - $\text{C}_2\text{H}_5\text{OH}$ and obtained 3 β -chloro-5-acetoxy, 7 β -bromo-5 β -cholestan-6-one (III), the structures and stereochemistry of which are discussed.

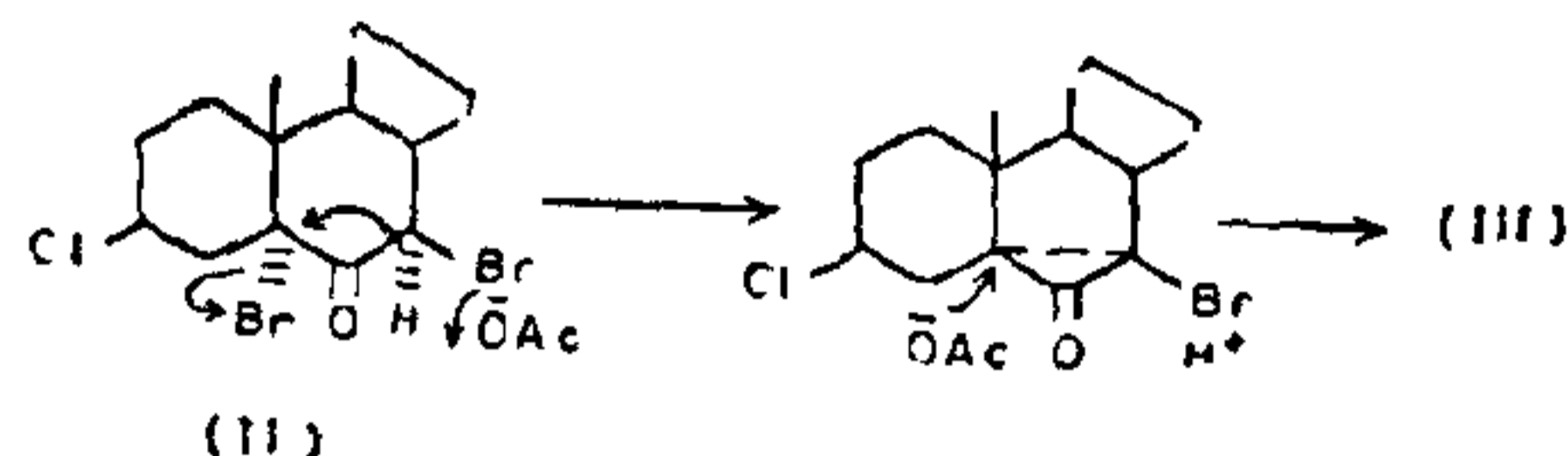


The acetoxy ketone (III) analysed for $\text{C}_{29}\text{H}_{46}\text{BrO}_3\text{Cl}$ and gave a positive Beilstein test for halogens. The i.r. spectrum of III exhibited bands at 1745 ($-\text{CO}-\text{O}-$), 1730 ($>\text{C}=\text{O}$), 1237 ($-\text{C}-\text{O}-$), 735 ($\text{C}-\text{Cl}$), 652 cm^{-1} ($\text{C}-\text{Br}$). The n.m.r. spectrum gave signals at δ 4.46 d (C_7 - αH ; J C_7 - αH , C_8 - βH = 9 Hz; axial), 3.84 br (C_3 - αH ; $W_{\frac{1}{2}} = 12$ Hz; equatorial), 2.4s (C_5 - $\text{O}-\text{CO}-\text{CH}_3$), 0.90, 0.80 and 0.68 (C_{10} - CH_3 , C_{13} - CH_3 and other methyl protons).

It is reported that on inversion of configuration at C5 from 5 α to 5 β , the C3- α proton changes from axial to equatorial. This stereochemical change during the acetolysis is revealed by i.r. and n.m.r. spectra of (II) and (III). C3- α proton in (III) is subjected to two equatorial and two axial vicinal couplings. This combination of splitting results in a broad signal at δ 3.84 with half band width = 12 Hz. This supports

equatorial orientation for C3- αH and implies cis A/B ring function. For axial C3- α proton, $W_{\frac{1}{2}}$ is reported 22 Hz as in (II)¹. The axial configuration of C3-C₄ in (III) was further substantiated by an i.r. band at 735 cm^{-1} for C-Cl band².

A tentative mechanism for the formation of (III) can be suggested as follows:



Experimental

Melting points are uncorrected. i.r. spectra were recorded with a Perkin-Elmer 237 spectrophotometer in Nujol. n.m.r. spectra were run in CDCl_3 with Varian A100 MHz instrument with TMS as the internal standard (s, singlet; d, doublet; br, broad; $W_{\frac{1}{2}}$, half band width).

3 β -Chloro-5, 7 β -dibromo-5 α -cholestan-6-one (II)

To a solution of 3 β -chloro-5 α -cholestan-6-one (I) (4.0 g, m.p. 128°) in ether (30 ml) at room temperature was added a solution of bromine in acetic acid (40 ml, 5%) which was completed over a period of half an hour. The reaction mixture (catalysed by a few drops of hydrobromic acid) was allowed to stand at room temperature for 3 days. The solid material thus obtained was filtered and air-dried. Recrystallization from pet. ether afforded the bromoketone (II), m.p. $174-75^\circ$ (Found C, 55.95; H, 7.45. $\text{C}_{27}\text{H}_{43}\text{OClBr}_2$ required C, 56.05; H, 7.44%) (positive Beilstein test); ν_{max} (Nujol) 1725 ($>\text{C}=\text{O}$), 758 ($\text{C}-\text{Cl}$), 736 and 655 cm^{-1} ($\text{C}-\text{Br}$); n.m.r. (CDCl_3); δ 5.35 (d, C_7 - αH , $J = 9$ Hz, axial), 4.39 (br, C_3 - αH , $W_{\frac{1}{2}} = 22$ Hz, axial) 1.1 (s, C_{10} - CH_3), 0.72 (s, C_{13} - CH_3), 0.95 and 0.84 (other methyl protons).

3 β -Chloro-5-acetoxy, 7 β -bromo-5 β -cholestan-6-one (III)

A mixture of bromoketone (II) (1.0 g), sodium acetate trihydrate (4.0 g) in ethanol (75 ml) was heated under reflux for 4 hrs. The solvent was removed by distillation under reduced pressure and residue poured into ice-cold water and extracted with ether. The ethereal solution was washed with water and dried over anhydrous sodium sulphate. Evaporation of ether provided an oil which was chromatographed over silica gel (20.0 g). Elution with pet. ether-ether (6:1) furnished a solid which was recrystallized from pet. ether (590 mg), m.p. 155° (Found C, 62.38; H, 8.19. $\text{C}_{29}\text{H}_{46}\text{ClBrO}_3$ requires C, 62.47; H, 8.25%).

We are thankful to Prof. W. Rahman for providing necessary facilities and to Prof. M. S. Ahmad for a helpful discussion. Financial assistance from UGC