

# SYNTHESIS OF STEROIDAL DIASTEREOMERIC OXATHIOLANES A CONFIGURATIONAL STUDY

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**Abstract---** A number of steroidal as well as non steroidal ketones have been reported to condense readily with  $\beta$ -mercaptoethanol to furnish oxathiolanes. The method for effecting the condensation of ketones with ethanedithiol or  $\beta$ -mercaptoethanol include use of zinc chloride and sodium sulphate <sup>1</sup>, hydrogen chloride in ether<sup>2</sup>, *p*-toulenesulphonic acid in benzene under azeotropic distillation employing water separator and an exchange method <sup>3,4</sup>

Keywords: Formic acid, *N*-bromosuccinimide, potassium dichromate,  $\beta$ -mercaptoethanol

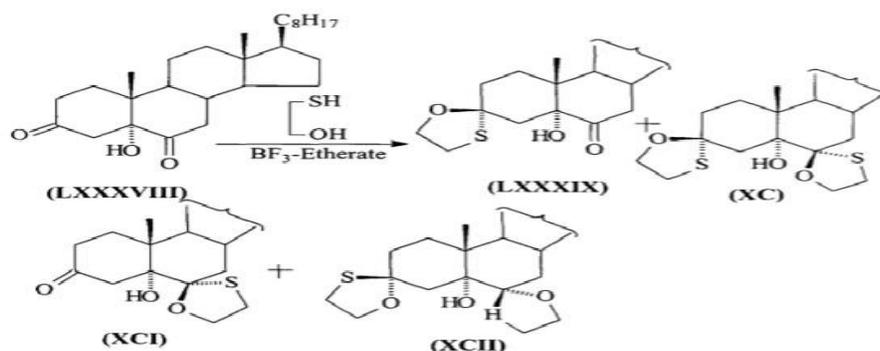
## I. Introduction

The synthesis and structure elucidation of steroidal oxathiolanes from their respective ketones need to be reported in order to provide a clear guideline for identification of some new synthesized steroidal oxathiolanes and further configurational studies in the case of isomeric oxathiolanes.

## II. Experimental

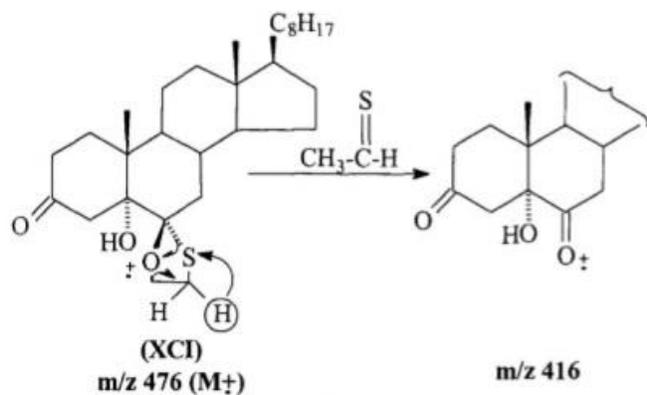
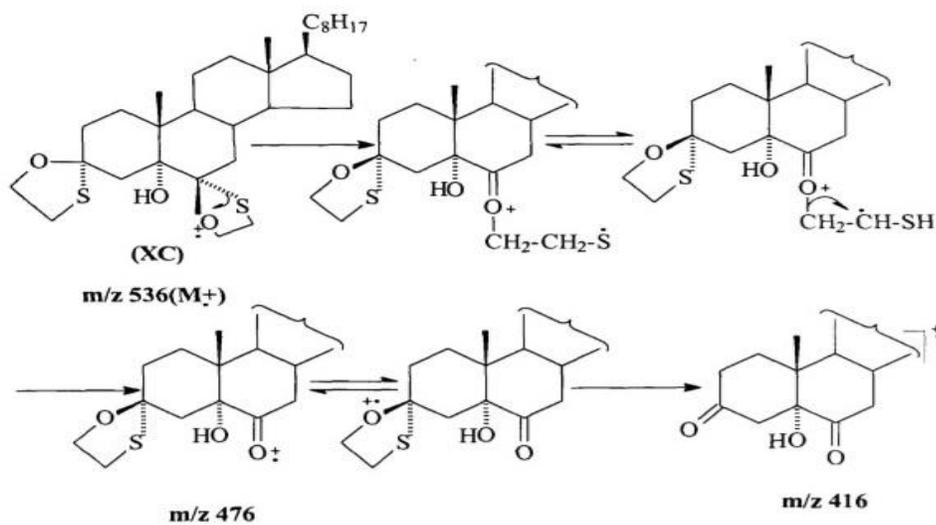
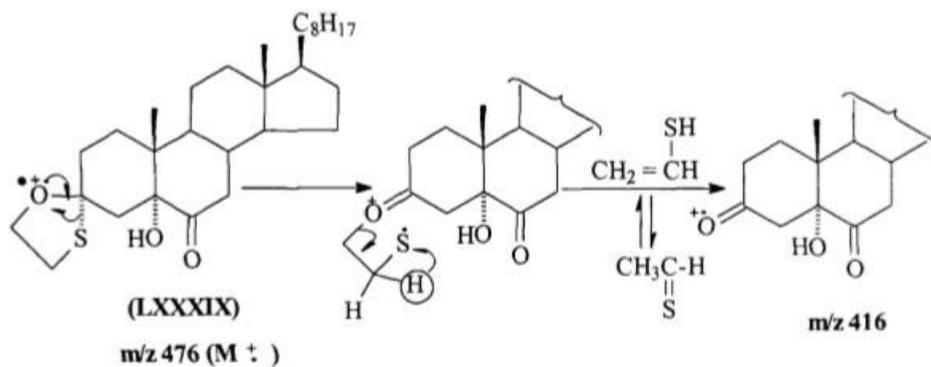
When 5-hydroxy -5 $\alpha$ - cholestane-3,6-dione <sup>5</sup> (LXXXVIII) was treated with  $\beta$ -mercaptoethanol in the presence of BF<sub>3</sub>-etherate (as catalyst) to furnish 3 $\beta$ -oxy-3 $\alpha$ -thiodimethylene-5- hydroxy-5 $\alpha$ -cholestan-6-one ( LXXXIX), bis - 3,6 -(  $\beta$ -oxy- $\alpha$ -thiodimethylene ) -5-hydroxy-5 $\alpha$ -cholestan-6-one ( XC ), 6 $\beta$ -oxy-6 $\alpha$ -thiodimethylene -5-hydroxy -5 $\alpha$ -cholestan-3-one ( XCI ) and 3 $\alpha$ -oxy-3 $\beta$ -thio,6 $\beta$ -oxy-6 $\alpha$ -thio-bisdimethylene-5-hydroxy-5 $\alpha$ -cholestan-6-one ( XCII ). The structure and stereochemistry of these steroidal oxathiolanes were established on the basis of I.R,<sup>1</sup>H-NMR, Mass and CD spectral studies.

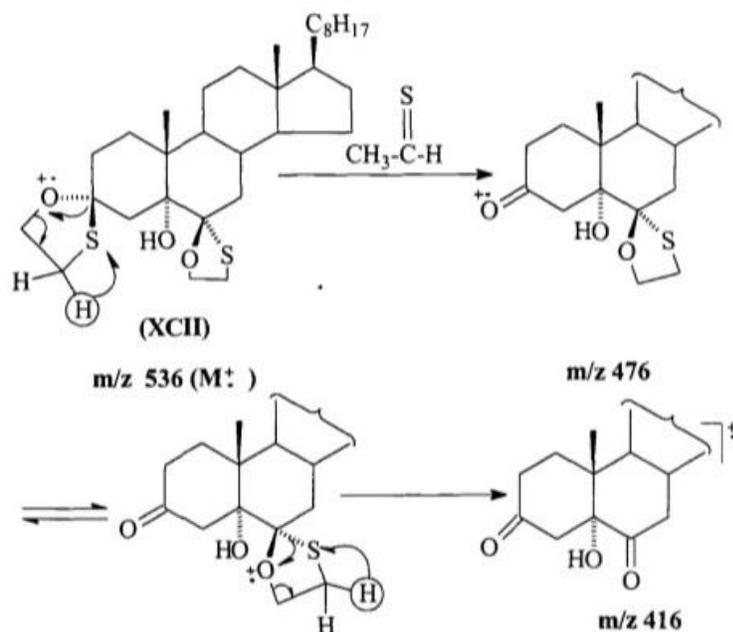
A solution of 5-hydroxy -5 $\alpha$ - cholestane-3,6-dione (LXXXVIII) (4.0g) in acetic acid (120ml) was treated with  $\beta$ -mercaptoethanol (4 ml) and BF<sub>3</sub>-etherate (2 ml) and the reaction mixture was allowed to stand at room temperature for 2 hours. On completion of the reaction, methanol (120 ml) was added to it, the resultant solution thus obtained was poured into water and extracted with ether. The ethereal layer was washed successively with water, sodium bicarbonate solution (5%) and water and dried over anhydrous sodium sulphate. The solvent was distilled under reduced pressure to yield an oily product which was chromatographed over silica gel (80g) to provide compounds LXXXIX, XC, XCI and XCII.



Schematic Plan of synthesis

**Proposed Mass Fragmentation of Moieties :**





### III. Result and Discussion

The structure and stereochemistry of these steroidal oxathiolanes (LXXXIX, XC, XCI and XCII) were established on the basis of I.R,  $^1\text{H-NMR}$ , Mass and CD spectral studies.

#### **3 $\beta$ -oxy-3 $\alpha$ -thiodimethylene-5- hydroxy-5 $\alpha$ -cholestan-6-one (LXXXIX)**

The oxathiolane (II) m. p  $120^\circ\text{C}$  was analyzed for  $\text{C}_{29}\text{H}_{48}\text{O}_3\text{S}$  (positive sodium nitroprusside test). In the IR Spectrum, bands appeared at  $3440(\text{OH})$ ,  $1710(\text{C}=\text{O})$ ,  $1225(-\text{S}-\text{CH}_2)$ ,  $1145(-\text{C}-\text{O})$  and  $1055\text{cm}^{-1}$  (oxathiolane ring).  $^1\text{H-NMR}$  spectrum of the compound exhibited a triplet at  $\delta$  4.18 integrating for two protons assigned to  $-\text{O}-\text{CH}_2$ . Another triplet at  $\delta$  3.05 integrating for two protons can be ascribed to  $-\text{S}-\text{CH}_2$ . The mass spectrum of oxathiolane gave molecular ion peak at  $m/z$  476 and its ketonic ion peak is at  $m/z$  416. The compound showed negative cotton effect<sup>6</sup>. On the basis of these analytical and spectral evidences the oxathiolane is characterized as 3 $\beta$ -oxy-3 $\alpha$ -thiodimethylene-5- hydroxy-5 $\alpha$ -cholestan-6-one (II).

#### **bis-3,6-( $\beta$ -oxy- $\alpha$ -thiodimethylene)-5-hydroxy-5 $\alpha$ -cholestane (XC)**

The Compound (III), m.p  $157^\circ\text{C}$  was analyzed for  $\text{C}_{31}\text{H}_{52}\text{O}_3\text{S}_2$ . IR bands appeared at  $3500(\text{OH})$ ,  $1220(-\text{S}-\text{CH}_2)$ ,  $1145(\text{C}-\text{O})$  and  $1055\text{cm}^{-1}$  (Oxathiolane ring). The  $^1\text{H-NMR}$  Spectrum showed two distorted triplet at  $\delta$  4.22 and  $\delta$  3.05 integrating for four protons each of two  $-\text{O}-\text{CH}_2$  and  $-\text{S}-\text{CH}_2$  moieties. The mass spectrum of compound (III) gave molecular ion peak at  $m/z$  536, 3-oxathiolane-6- ketonic fragment ion peak at  $m/z$  476 and 3,6 diketonic peak at  $m/z$  416. This compound gave negative cotton effect<sup>6</sup>

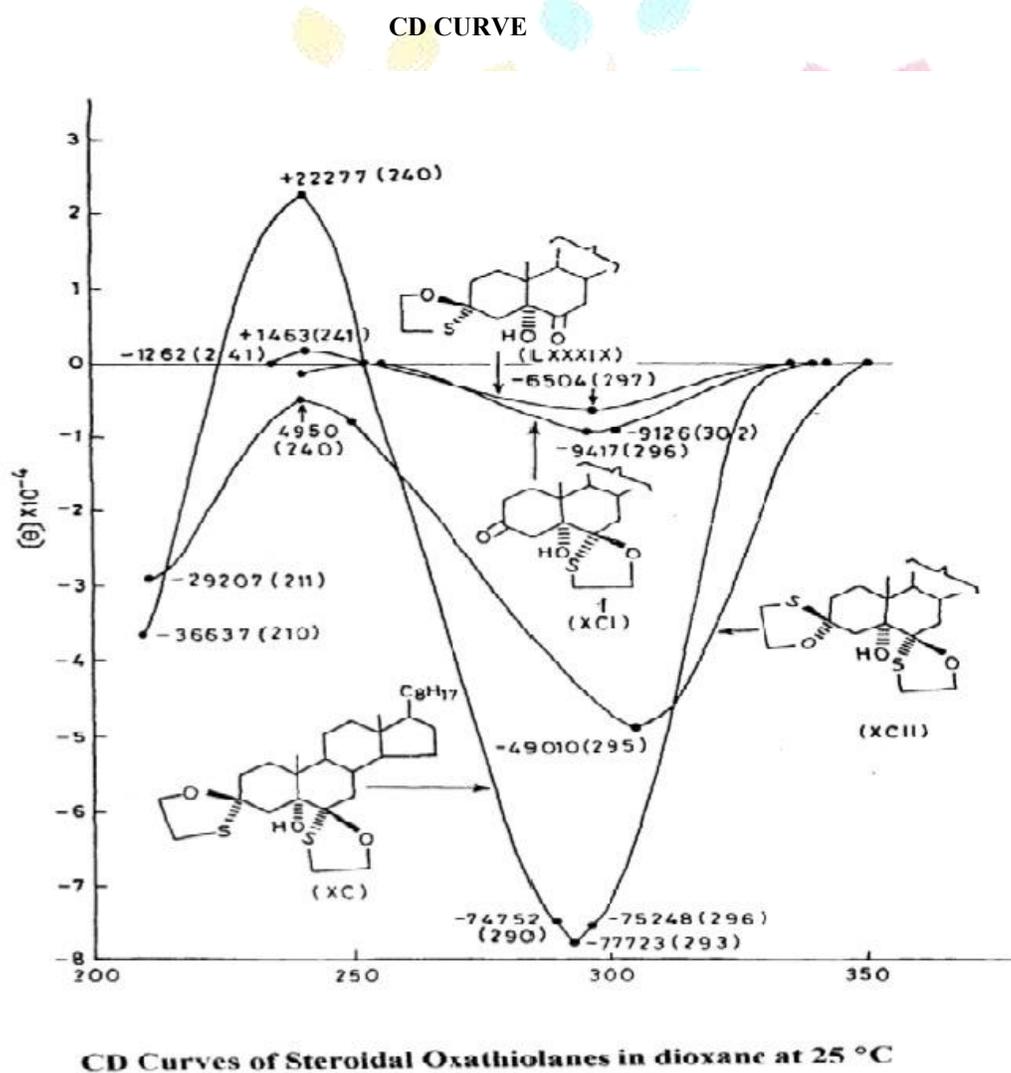
#### **6 $\beta$ -oxy-6 $\alpha$ -thiodimethylene -5-hydroxy -5 $\alpha$ -cholestan-3-one (XCI)**

The compound (IV) m.p.  $101^\circ\text{C}$  was analyzed for  $\text{C}_{29}\text{H}_{48}\text{O}_3\text{S}$ . The IR band appeared at  $3430(\text{OH})$ ,  $1715(\text{C}=\text{O})$ ,  $1225(-\text{S}-\text{CH}_2)$ ,  $1140(\text{C}-\text{O})$  and  $1055\text{cm}^{-1}$  (oxathiolane ring).  $^1\text{H-NMR}$  spectrum of compound gave triplet at  $\delta$  4.1 integrating for two protons assigned to  $-\text{O}-\text{CH}_2$ . Another triplet at  $\delta$  3.15 integrating for two protons

was assigned to  $-S-CH_2$ . The mass spectrum of the compound (IV) gave molecular ion peak at  $m/z$  476 and its ketonic ion peak at  $m/z$  416. The compound (IV) showed negative cotton effect <sup>6</sup>.

### 3 $\alpha$ -oxy-3 $\beta$ -thio,6 $\beta$ -oxy-6 $\alpha$ -thio-bisdimethylene -5-hydroxy-5 $\alpha$ -cholestane (XCII)

The compound (V) m.p.170 °C was analyzed for  $C_{31}H_{52}O_3S_2$ . The I.R spectrum of the oxathiolane gave bands at 3490(OH),1215(S-CH<sub>2</sub>), 1140 (C-O) and 1050  $cm^{-1}$  (oxathiolane ring). <sup>1</sup>H-NMR Spectrum of the compound gave two distorted triplets at  $\delta$  4.15 and  $\delta$  3.2 each integrating for four protons assigned to (2x-O-CH<sub>2</sub>) and (2x-S-CH<sub>2</sub>). The mass spectrum of the compound (XCII) showed the molecular ion peak at  $m/z$  536 followed by C<sub>6</sub>-Oxathiolane -3-Ketonic ion peak at  $m/z$  476 and 3,6 -diketonic peak at  $m/z$  416.



#### IV. Conclusions

The main aim of the above study is to explain the stereochemistry of oxathiolane moieties at C<sub>3</sub> and C<sub>6</sub> by the CD spectra. The structure is also studied by IR, <sup>1</sup>H-NMR, Mass Spectral evidences.

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### References

- [1] J. Ramo, G.Rosenkranz and C.Djerassi , J.Am.Chem.Soc; ( 1951) 73:4961.
- [2] P.Kipnis and J. Ornfelt , J.Am. Chem. Soc; (1949) 71:3555.
- [3] C . Djerassi and M.Gormam , J.Am. Chem .Soc; (1953)75:3704.
- [4] E.P Oliveto, T.Clayton and E.B Hershberg, J.Am.Chem .Soc; (1953)75:486.
- [5] L.F . Fieser,J.Am.Chem.Soc; ( 1953) 75:4386
- [6] Shafiullah, H.Ali, H.ogura and H. Takayanagi, Bull .Chem.Soc ( Japan); (1981) 54:3006

