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Synthesis of 1,3-Oxathiolane-2-Thiones by the Reaction of Steroidal Oxiranes with Carbon Disulfide

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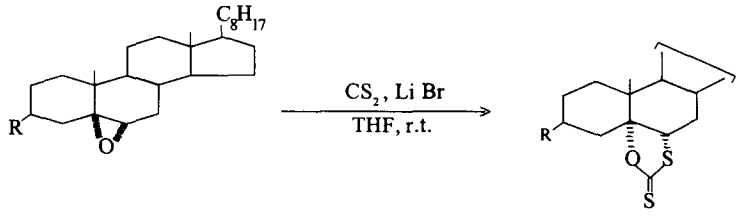
Abstract : The reaction of 5, 6α-epoxy-5α-cholestane (1), its 3β-acetoxy-(2) and 3β- chloro-(3) analogues with carbon disulfide in THF at room temperature in the presence of Li Br as catalyst afford selectively the corresponding 1,3-oxathiolane-2-thiones (steroidal cyclic *cis*-dithiocarbonates) (4-6) in high yields.

In the literature, there have been many reports on the reaction of epoxides with carbon disulfide in different reaction conditions[1-9]. Depending upon the catalysts and reaction conditions, five-membered cyclic dithiocarbonates, its regioisomers, trithiocarbonates and episulfides have been reported to be formed. Kihara *et al*[1] have recently reported a selective method for the preparation of *trans*-1,3-oxathiolane-2-thiones by using alkali metal halides.



(1) R, H
(2) R, OAc
(3) R, Cl

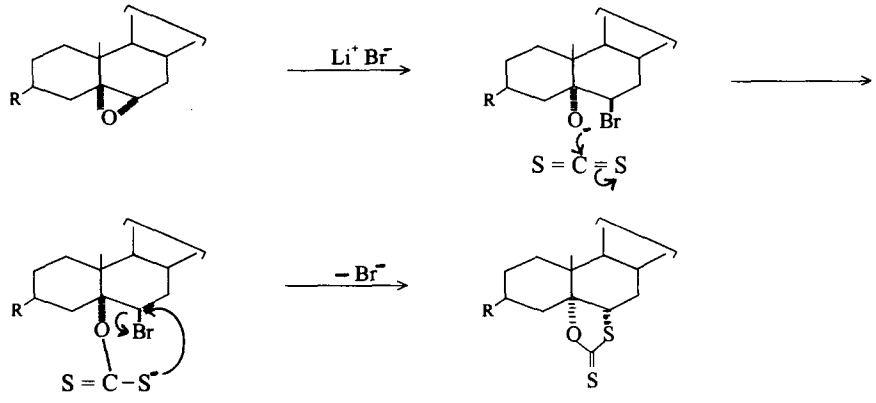
(4) R, H
(5) R, OAc
(6) R, Cl

Here we wish to report a novel and convenient preparation of steroidal 1,3-oxathiolane-2-thiones (*cis*-cyclic dithiocarbonates) at room temperature in high yields by the reaction of steroidal 5α, 6α-epoxides with carbon disulfide in THF using lithium bromide as catalyst. Here the *cis* products were obtained selectively as the single product.

Table : Physical, Analytical and Spectral data of Compound (4-6).

Compound	M.P. °C	Yield (%)	IR (KBr/Neat) (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) (δ,ppm,60MHz)	Mass m/z
4	Oil	70	1185 (C=S) and 1049 (C-O)	3.9 m (1H, C6β-H) 1.10 (C10 - CH_3) 0.68 (C13 - CH_3) 0.91, 0.80 (other methyl protons)	462 (M^+), 418 (M - CS), 402 (M -COS), 386 (M - CS_2), 370 (M - COS_2)
5	87	83	1735 ($OCOCH_3$), 1190 (C=S) and 1040 (C-O)	4.70 m (1H, C3α-H $w½$=17 Hz, axial), 3.93 m (1H, C6β-H), 2.01 s (3H,$OCOCH_3$) 1.14 (C10 - CH_3) 0.76 (C13 - CH_3) 0.90, 0.85 (other methyl protons)	520 (M^+), 476 (M-CS), 460 (M-COS), 459 (M- OAc), 444 (M-CS_2), 428 (M - COS_2)
6	95	78	1180(C=S), 1045 (C - O) and 710 (C - Cl)	4.10 m (1H, C3α-H, $w½$=15 Hz, axial), 3.85 m (1H, C6β-H) 1.05 (C10-CH_3) 0.69 (C13 - CH_3) 0.97, 0.81 (other methyl protons)	496/498 (M^+), 460(M-HCl), 452/454 (M-CS), 436/438(M-COS), 420/422 (M-CS_2), 404/406 (M- COS_2)

It is proposed that this reaction proceeds *via* nucleophilic attack of bromide ion at the less substituted (C-6) position of the steroidal epoxides and cyclization of the resulting dithiocarbonate anion (Scheme 1), the reaction of epoxide with lithium bromide which is the rate-determining step for the reaction of epoxide with carbon disulfide may proceed at room temperature. These *cis*-dithiocarbonates (4-6) were obtained selectively from the reaction of epoxides (1-3) with carbon disulfide by double S_N^2 inversion on the epoxide ring at C-6.



Scheme 1

The structures of these steroidal cyclic dithiocarbonates (1,3-oxathiolane-2-thiones) (4-6) have been established on the basis of their physical, analytical and spectral data (Table).

To obtain the desired cyclic dithiocarbonates (4-6), a sloution of lithium bromide (0.05 mmol) and steroidal epoxide (1.0 mmol) in THF (25 ml) was stirred at room temperature for 5-6 min., then carbon disulfide (1.2 mmol) was added to the solution and the resulting mixture was stirred at room temperature for 5-6 h. Progress of the reaction was monitored by the TLC. After completion of reaction the solvents were removed under reduced pressure and the residue was purified by column chromatography over a silica gel column (petroleum ether-diethyl ether, 13 : 1) to give the respective steroidal cyclic dithiocarbonates (4-6) (Table).

Thus the above method is useful to prepare selectively steroidal cyclic dithiocarbonates having *cis* geometry at C-5 and C-6 from the respective epoxides.

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