

were identical to those of the reference compounds. The methyl esters were detected by reagents b, c, and d, the dilactones by reagent d.

Reduction. An aliquot of the esterification product (20 mg) was reduced with lithium aluminium hydride (0.3 g) in tetrahydrofuran (30 ml) by gentle reflux for 2 h. The reaction product (13 mg) furnished an alcohol, indistinguishable from D-glucitol by chromatographic investigation in the solvent systems A, B, and D. The alcohol was detected by reagent c.

De-O-methylation¹⁰ failed to cause a change in chromatographic mobility of the alcohol.

Acknowledgements. The authors are greatly indebted to the head of the Department of Pharmacognosy, Professor Arnold Nordal, for his interest in this work and for his valuable support. Financial support was rendered to one of the authors (M.A.) by *Norges Almenvitenskapelige Forskningsråd*.

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Received October 3, 1970.

N-Quarternary Compounds

Part XX.¹ Stereochemical Studies

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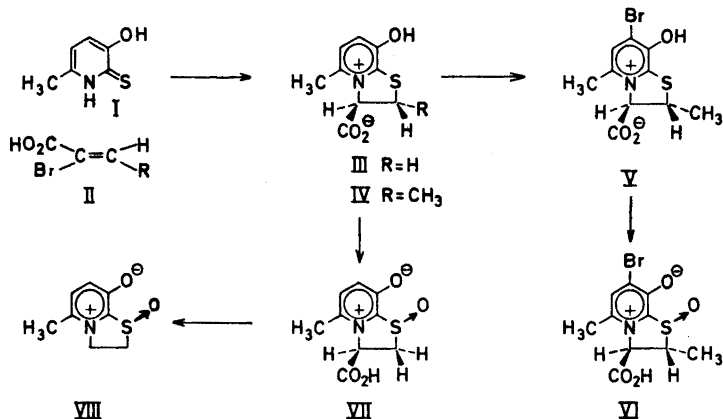
Our stereochemical studies^{2,3} in the dihydrothiazolo[3,2-a]pyridinium-8-oxide series required the establishment of relative configuration by X-ray analysis. For this purpose we have synthesized a bromo-sulphoxide (VI).

The product obtained by the addition of the thiolactam (I) to α -bromoisocrotonic acid followed by cyclisation of the adduct over the annular nitrogen has been assigned a *trans* configuration on the basis of the value of the coupling constant, $J_{2,3} < 1$, in the NMR spectrum in TFA.³ The *trans* configuration has now been confirmed by X-ray analysis of VI.⁴

Peracid oxidation of the thioether (III) gave the diastereomeric sulphoxides in the ratio 9:1. The stereoselectivity in the oxidation was further increased by having a *trans* methyl group in the 2-position (IV). In agreement with NMR arguments³ *cis* oxidation of the sulphur with respect to the carboxy group was assumed. For this assumption to be correct the carboxy group must participate in the oxidation. The mechanism proposed is either a rapid, preferential oxidation of the carboxy group, the formation of a diacylperoxide intermediate, or the formation of a hydrogen bonded complex between the peracid and the carboxy group. The actual species involved should depend on the experimental conditions. X-Ray analysis of VI confirms that the sulphanyl oxygen is *cis* with respect to the carboxy group.⁴

The sulphoxides are very readily decarboxylated. We have used this in the preparation of optically active sulphoxides of type VIII. Thus oxidation of compound III with the L-configuration followed by decarboxylation led to an optically active sulphoxide assigned the absolute *S*-configuration.³ From the discussion above it follows that this assignment is in agreement with the relative stereochemistry of VI determined by X-ray analysis.⁴

The sulphoxide (VI) is formulated as a phenolate rather than as a carboxylate since the X-ray analysis⁴ shows strong



hydrogen bonding between the phenolic oxygen and a carboxyl oxygen, the distance between the oxygens being 2.46 Å, with the hydrogen closer to the carboxyl oxygen.

The synthesis of VI is outlined above. Compound IV was synthesized as previously described³ and was brominated using bromine in acetic acid. Electrophilic substitution in 5-methyldihydrothiazolo[3,2-a]pyridinium-8-oxide systems have been shown by chemical means to take place in the 7-position.⁵ The X-ray work confirms that the bromine has entered the 7-position. The oxidation of V was carried out in formic acid by the addition of hydrogen peroxide. Chromatography showed that only traces of the *trans* sulphoxide was formed, the major product having the *cis* configuration.

Experimental. 7-Bromo-*trans*-2,5-dimethyl-8-hydroxydihydrothiazolo[3,2-a]pyridinium-3-carboxylate (V). Bromine (3.2 g, 0.02 mol) in acetic acid (100 ml) was added dropwise over 2 h to a solution at 50° of *trans*-2,5-dimethyl-8-hydroxydihydrothiazolo[3,2-a]pyridinium-3-carboxylate³ (4.0 g, 0.016 mol) and sodium acetate (2.0 g, 0.02 mol) in acetic acid (400 ml). The solution was left at room temperature and the precipitated bromo-hydrobromide (6.5 g) collected. The base was liberated by dissolution in water and passage through a DEAE Sephadex A-25-column. After washing the column with water the base was eluted with 0.05 N formic acid. Evaporation of the eluate yielded the bromo compound (4.4 g, 83%), m.p. 180° (dec.). The analytical sample was recrystallized from water. (Found: C 39.60; H 3.56; N 4.90. Calc. for C₁₀H₁₀BrNO₃S: C 39.43; H 3.29; N 4.61.)

7-Bromo-3-carboxy-*trans*-2,5-dimethyl-1-oxo-dihydrothiazolo[3,2-a]pyridinium-8-oxide (VI). 30% Hydrogen peroxide (1 ml, 0.012 mol) was added dropwise at 0° to a solution of 7-bromo-*trans*-2,5-dimethyl-8-hydroxydihydrothiazolo[3,2-a]pyridinium-3-carboxylate (1.0 g, 0.003 mol) in formic acid (80 ml). The solution was left at 5° for 3 h, the solution evaporated at reduced pressure and the residue dissolved in cold water (7 ml). The major sulphoxide isomer crystallized out on standing at 5° overnight, yield 0.8 g (76%). This compound is very susceptible to decarboxylation and gave no sharp melting point on heating.

Chromatography³ of the reaction mixture before isolation showed that the sulphoxide formed consisted of 90–95% of the one stereoisomer.

The analytical specimen was prepared by dissolving the product in warm formic acid (2 ml) followed by the addition of water (10 ml) and leaving the solution in the cold when the sulphoxide crystallized out. (Found: C 37.64; H 3.43; Br 25.40; N 4.53. Calc. for C₁₀H₁₀BrNO₄S: C 37.47; H 3.13; Br 25.00; N 4.37.)

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Received November 6, 1970.