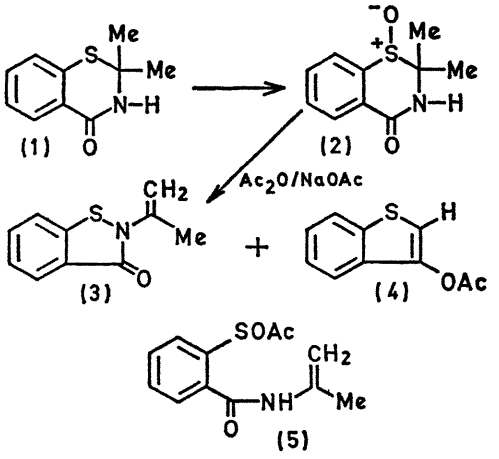
Rearrangement of Benzothiazine Sulphoxides

By ROBERT B. MORIN* and DOUGLAS O. SPRY
(*The Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana* 46206)

Summary The reaction of substituted benzothiazine sulphoxides with Ac_2O under reflux leads by an elimination reaction to a sulphenic acid derivative which undergoes subsequent addition to the generated double bond if the nitrogen is tertiary but is trapped as a cyclic sulphenamide by a secondary nitrogen.

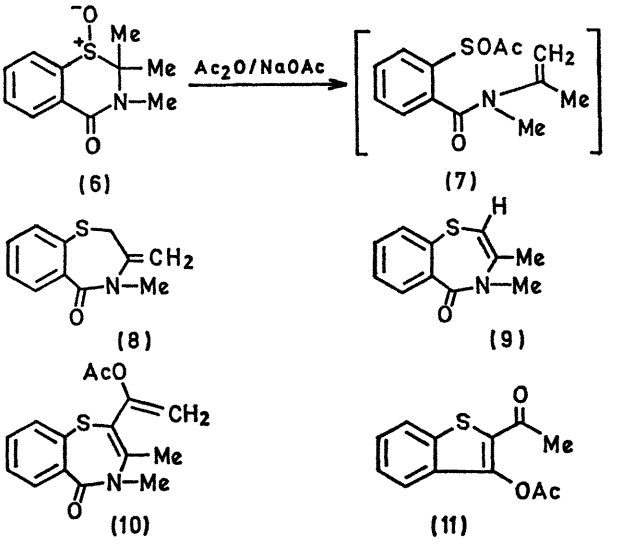
IN our work on penicillin sulphoxides[1] and 2,2-dimethylthiachroman 1-oxides,[2] we have found an internal oxidative–reductive reaction of sulphoxides in which a carbon β to the sulphur becomes oxidized. In the penicillins two products were isolated in which an N–S bond had been formed (under certain conditions these were the major products). The work we are now reporting on simple, nitrogen-containing cyclic sulphoxides indicates the generality of the reaction and provides further evidence for the formation of an intermediate sulphenic acid.



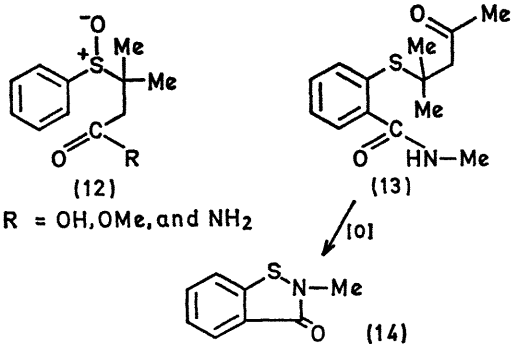
Oxidation of the dihydrobenzothiazine derivative (**1**)[3] with *m*-chloroperbenzoic acid in $CHCl_3$ at $-8°$ gave the sulphoxide (**2**), m.p. 128—129° which was used for our study. Use of more vigorous conditions or several other common oxidants did not give isolable quantities of the sulphoxide.[4] Treatment of (**2**) with Ac_2O containing 1% NaOAc under reflux gave in good yield a 3 : 2 mixture of two products which were separated by silica chromatography.

The principal product was the expected compound (**3**): m.p. 38—39°, n.m.r. δ 2·33 (s,3), 5·00 (s,1), 5·30 (s,1), 7·25—8·0 (m,4). The second material did not contain nitrogen. Physical data indicated that the substance can be represented by structure (**4**), an assignment which was confirmed by comparison with authentic, independently synthesized material.[5] Compound (**4**) can be obtained from (**3**) under Ac_2O–NaOAc conditions, a reaction known for some years.[5]

We envision the transformation of (**1**) to (**3**) as an initial elimination to the intermediate (**5**), and now in contrast with the dimethylthiachroman system the sulphenic acid moiety does not add to the generated double bond but is trapped by the neighbouring nitrogen atom forming a stable cyclic sulphenamide. No products of double bond addition were detected.



Treatment of the *N*-methyldihydrobenzothiazine sulphoxide (**6**), m.p. 80—82°, with Ac_2O–NaOAc under reflux gave four products, (**8**)—(**11**). The principal product, m.p. 90—91°, formed in approximately 50% yield, was assigned structure (**10**) on the basis of physical data: i.r. 1775, 1650 cm^{-1}; n.m.r. δ 2·08 (s,3), 2·36 (s,3), 3·11 (s,3), 5·31 (s,1), 5·70 (s,1), 7·4 (m,4); mass spectrum 289, 247 (*m* — 42), 205 (*m* — 84). Mild basic hydrolysis of (**10**) gave a substance lacking the 1775 peak in the i.r. The yields of (**8**), n.m.r. δ 3·30 (s,3), 3·88 (s,2), 5·01 (br.s,2), 7·4 (m,4), and (**9**), n.m.r. δ 1·95 (s,3), 3·25 (s,3), 6·01 (br.s,1), 7·5 (m,4), were variable, partly a result of the fact that (**8**) can be converted into (**9**) under the conditions of the rearrangement. Compound (**11**), i.r. ($CHCl_3$) 1786, 1667 cm^{-1}; n.m.r. δ 2·45 (s,3),



2·53 (s,3), 7·5 (m,4), was formed in approximately 10% yield. Compounds (**8**) and (**9**) result from addition of the sulphenyl derivative to the double bond in the intermediate (**7**). Treatment of either (**8**) or (**9**) under the conditions of the reaction does not produce (**10**). As a consequence, the

intermediate (**7**) must have sufficient stability to undergo acylation of the enamide moiety. Subsequent addition of the sulphenic group to the substituted double bond and enol acetylation will provide (**10**). Compound (**11**) results from the action of Ac_2O–NaOAc on the quaternary derivative corresponding to (**3**) or on the intermediate (**7**).

In the acyclic sulphoxides (**12**; R = OH, OMe, and NH_2), elimination occurs on treatment with Ac_2O under reflux; however, the derived phenylsulphenic acid reacts with itself, ultimately providing diphenyl disulphide, the only sulphur-containing product isolated.[6] We have been unable to obtain the sulphoxide of the sulphide (**13**), m.p. 82—83°; however, we have obtained (**14**) as the sole product of the oxidation of (**13**) with ozone at −70° or with *m*-chloroperbenzoic acid at room temperature. Apparently the sulphoxide is formed, followed by an elimination facilitated by the β-keto-group; and the generated sulphenic acid reacts with the neighbouring amide group. Neither the reactions of (**12**) nor of (**13**) afforded products which correspond to an oxidation of the methyl groups or the methylene function.

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[4] We are indebted to K. L. Kannan, Eli Lilly and Company for some of these data.
[5] R. G. Bartlett and E. W. McClelland, *J. Chem. Soc.*, 1934, 818.
[6] We are indebted to T. M. McGrath, Eli Lilly and Company, for some of these data.