

A NOVEL RING TRANSFORMATION OF BENZOTHIAZOLINE SULFOXIDES¹

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Reaction of 3-acetylbenzothiazoline sulfoxides with acetic anhydride gave novel ring expansion products, benzothiazine derivatives.

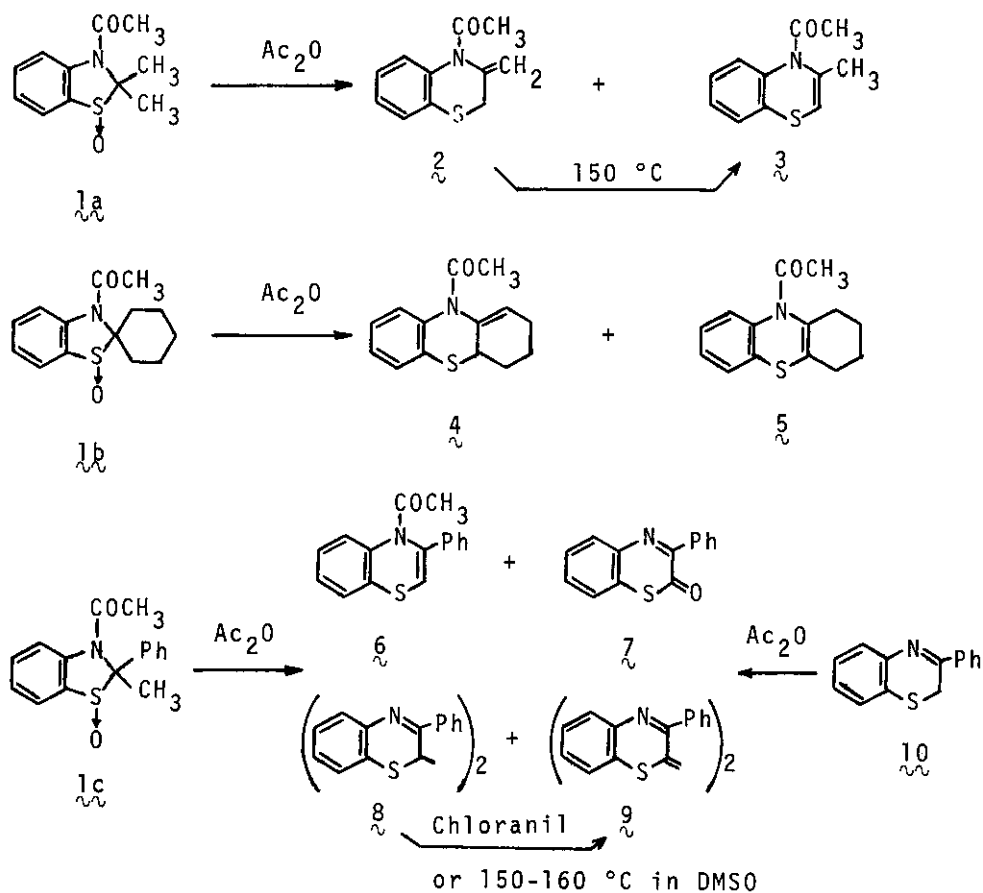
There is a fair number of reports on the chemistry of benzothiazolines so far. On the other hand, investigations on benzothiazoline sulfoxides are little known.² In this communication, we wish to report a novel ring transformation of benzothiazoline sulfoxides to benzothiazines by the reaction with acetic anhydride.

The 3-acetylbenzothiazoline sulfoxides (1a-e)^{*}, required in the present study, were conveniently prepared by oxidation of the corresponding 3-acetylbenzothiazolines with m-chloroperbenzoic

* NMR spectroscopic studies of 1c and 1e have revealed that the relative configuration of the sulfoxide to methyl group is cis in 1c and trans in 1e. The details will be reported in the full paper in the near future. All new compounds had satisfactory analytical data to support the assignment.

acid in chloroform at room temperature in high yield.

Refluxing 3-acetyl-2,2-dimethylbenzothiazoline 1-oxide (**1a**) in acetic anhydride for 1 hr resulted in the formation of 4-acetyl-3-methylene-2,3-dihydro-4H-1,4-benzothiazine (**2**) and 4-acetyl-3-methyl-4H-1,4-benzothiazine (**3**) in yields of 31.5 % and 48.6 %, respectively. These compounds have the following physico-chemical data ; **2** : mp 93-94 °C as colorless plates (ether- n-hexane) : ir (KBr) ν max cm^{-1} 1660 (CO), 925 (=CH₂) : nmr (CDCl₃) δ 2.20 (3H, s, COCH₃), 3.89 (2H, br.s, C₂-H₂), 5.33 (1H, s, =CH),



5.42 (1H, br.s, =CH), 7.00-7.90 (4H, m, ArH) : UV (EtOH) max nm 300, 290, 255, 229, 205 : mass (m/e) 205 (M^+), 163 (base peak) ; λ : bp 120 °C (0.3 mmHg) as colorless oil : ir (neat) ν max cm^{-1} 1670 (CO) : nmr ($CDCl_3$) δ 2.11 (3H, s, $COCH_3$), 2.25 (3H, d, $J=1$ Hz, C_3-CH_3), 6.28 (1H, q, $J=1$ Hz, C_2-H), 7.10-7.50 (4H, m, ArH). Compound (2) was isomerized to 3 quantitatively, on heating at 150 °C for 3 hr.

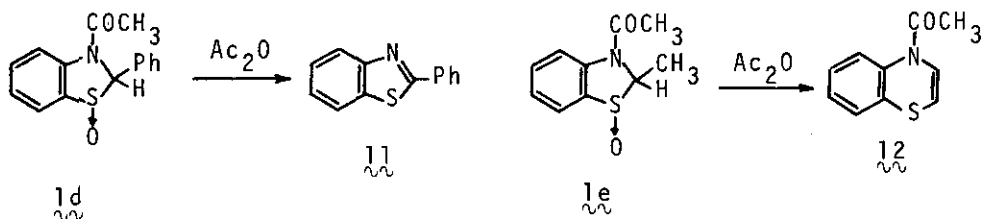
Similarly, reaction of 3-acetylbenzothiazoline-2-spirocyclohexane 1-oxide (1b) with acetic anhydride gave N-acetyltetrahydrophenothiazine derivatives (4) and (5) in yields of 72.1 % and 13.8 %, respectively. Compound (4) : mp 100-101 °C as colorless prisms (EtOH- n-hexane) : ir (KBr) ν max cm^{-1} 1660 : nmr ($CDCl_3$) δ 1.50-2.50 (6H, m, C_2-H_2 , C_3-H_2 , C_4-H_2), 2.17 (3H, s, $COCH_3$), 4.25 (1H, m, $C_{4a}-H$), 6.00 (1H, t.d, $J=4$ Hz, 2 Hz, C_1-H), 7.00-7.70 (4H, m, ArH) : UV (EtOH) λ max nm 300, 290, 255, 230, 215 : mass (m/e) 245 (M^+), 203 (base peak) ; Compound (5) : mp 146-147 °C as colorless prisms (EtOH- n-hexane) : ir (KBr) ν max cm^{-1} 1660 (CO) : nmr ($CDCl_3$) δ 1.50-2.00 (4H, m, C_2-H_2 , C_3-H_2), 2.08 (3H, s, $COCH_3$), 2.15-2.70 (4H, m, C_1-H_2 , C_4-H_2), 7.00-7.80 (4H, m, ArH) : UV (EtOH) λ max nm 253.5, 212.5 : mass (m/e) 245 (M^+), 202 (base peak). On heating, compound (4) was not isomerized to form 5, but decomposed, different from the case of compound (2).

When 3-acetyl-2-methyl-2-phenylbenzothiazoline 1-oxide (1c) was refluxed in acetic anhydride, 4-acetyl-3-phenyl-4H-1,4-benzothiazine (6) was afforded in 37.8 % yield with 2-oxo-3-phenyl-2H-1,4-benzothiazine (7), 2-[3-phenyl-2H-1,4-benzothiazin-2-yl]-

3-phenyl-2H-1,4-benzothiazine (8)³ and $\Delta^{2,2'}$ -bi-(3-phenyl-2H-1,4-benzothiazine) (9) as by-products. Compound (6) : bp 196 °C (0.5 mmHg) : ir (neat) ν max cm^{-1} 1680 (CO) : nmr (CDCl_3) δ 1.95 (3H, s, COCH_3), 6.85 (1H, s, $\text{C}_2\text{-H}$), 7.00-8.20 (9H, m, ArH) ; Compound (7) : mp 100-101 °C as yellow needles (n-hexane) : ir (KBr) ν max cm^{-1} 1610 (CO) : nmr (CDCl_3) δ 7.20-7.80 (5H, m, ArH), 7.80-8.35 (4H, m, ArH) : mass (m/e) 239 (M^+), 211 (base peak) ; Compound (9) : mp 264 °C as red needles (EtOH- n-hexane) : nmr (CDCl_3) δ 6.85-8.15 (m, ArH) : mass (m/e) 446 (M^+).

In order to elucidate the mechanism for the formation of 7, 8 and 9, the reactivities of 3-phenyl-2H-1,4-benzothiazine (10) presumed as an intermediate in the reaction path were investigated. Refluxing 10, synthesized by the alternative method³, in acetic anhydride gave 6, 7, 8 and 9. And further, stirring 10 in chloroform in the presence of benzoyl peroxide at room temperature for 3 days afforded 7, 8 and 9 in yields of 37.1 %, 13.1 % and 13.2 %, respectively. By the treatment with chloranil in refluxed xylene or heating at 150-160 °C in DMSO 8 was converted into 9 in high yield. These results show that 7, 8 and 9 might be formed by autoxidation of 10.

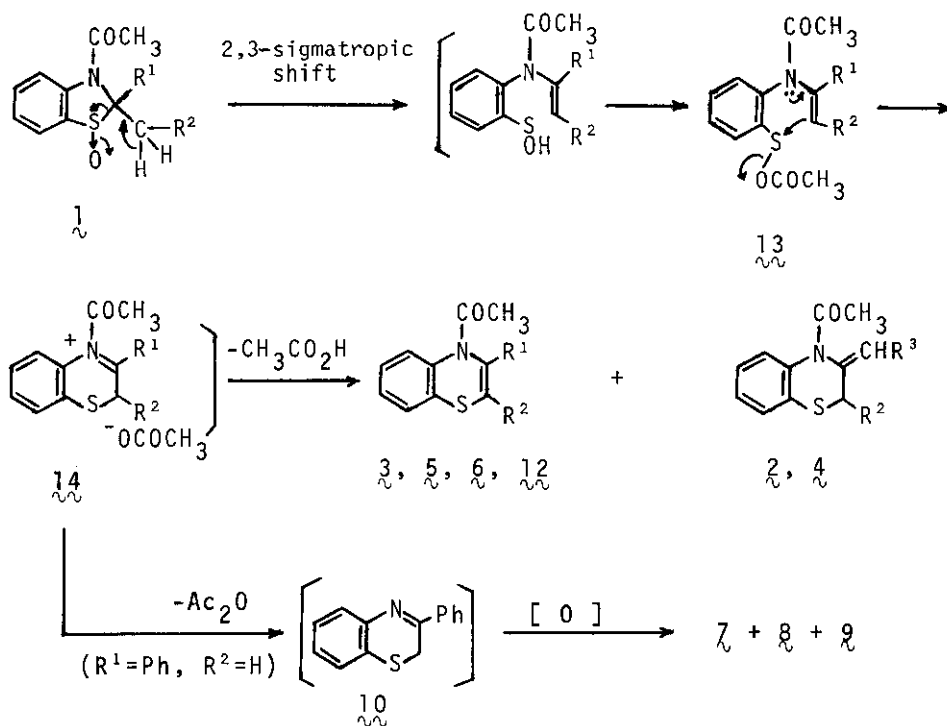
In the reaction of 2-monosubstituted benzothiazoline sulfoxides with acetic anhydride, 3-acetyl-2-phenylbenzothiazoline 1-oxide (1d) gave 2-phenylbenzothiazole (11)⁴ in 57.1 % yield. However, 3-acetyl-2-methylbenzothiazoline 1-oxide (1e) gave only the ring expansion product, 4-acetyl-4H-1,4-benzothiazine (12) in 39.3 % yield : mp 92-93.5 °C as colorless prisms (n-hexane) : ir (KBr) ν max cm^{-1} 1670 (CO) : nmr (CDCl_3) δ 2.30 (3H, s, COCH_3), 6.13



(1H, d, $J=6.5$ Hz, $\text{C}_2\text{-H}$), 6.90 (1H, br.d, $J=6.5$ Hz, $\text{C}_3\text{-H}$), 7.15-7.65 (4H, m, ArH) : UV (EtOH) λ max nm 290, 265, 238, 212.5 : mass (m/e) 191 (M^+), 149 (base peak), but 2-methylbenzothiazole was not formed. This reaction is quite different from the reaction of cyclic sulfoxides, having at least one proton at α -position, with acetic anhydride, since the sulfoxides gave the products of a normal Pummerer-type rearrangement which decomposed to olefinic products in the course of the reaction, but not any ring expansion product.⁵ Therefore, this is the first example that α -monosubstituted cyclic sulfoxide underwent the ring expansion reaction in the reaction with acetic anhydride.

From the results mentioned above, the novel ring transformation of benzothiazoline sulfoxides to benzothiazines might be explained by the mechanism postulating formation of a sulfenic anhydride (**13**)⁶, via the sulfenic acid intermediate resulted from 2,3-sigmatropic rearrangement of the sulfoxide^{*}, followed by formation of the immonium ion (**14**) as shown in Scheme I. Collapse of the immonium ion (**14**) leads to the observed products.

^{*} It is reasonable to consider that trans-**1e** probably epimerized to cis form before ring opening under the reaction conditions.



Scheme I

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Received, 30th August, 1978