THIOL-ESTER-THIONO-ESTER REARRANGEMENTS INDUCED BY ALKYLATING REAGENTS, PERACIDS, OR N-HALOSUCCINIMIDE IN THE 3-ACYLTHIO-4-ARYL-3-ISOTHIAZOLINE-5-THIONE SYSTEM

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Alkylations of 3-acylthio-4-aryl-3-isothiazoline-5-thiones with diazomethane, triethyloxonium tetrafluoroborate, or alkyl iodide afford 5-alkylthio-4-aryl-3-thioacyloxyisothiazoles, whereas the reactions of these isothiazolines with peracids or N-halosuccinimide produce bis(4-aryl-3-thioacyloxyisothiazol-5-yl) disulfides.

Thiono-esters rearrange to thiol-esters not only by the action of chemical reagents (e.g. triethyloxonium tetrafluoroborate¹ and boron trifluoride-etherate²), but also by thermolysis³ and electron impact.⁴ These rearrangements are considered to take place by virtue of the nucleophilic character of the C=S group. However, their reverse process, namely, the rearrangements from thiol-esters to thiono-esters have not been studied.⁵ We wish to report that the latter rearrangements take place readily for a series of 3-acylthio-4-aryl-3-isothiazoline-5-thiones (1), which are initiated by the attack of alkylating reagents, peracids, and N-halosuccinimide on a remote and nucleophilic C=S group.

When the isothiazoline <u>la</u> $(Ar^1=p-MeC_6H_4, Ar^2=Ph)$ was allowed to react with diazomethane in tetrahydrofuran, 5-methylthio-3-thiobenzoyloxy-4-p-tolylisothiazole <u>3a</u> $(Ar^1=p-MeC_6H_4, Ar^2=Ph, R=Me; 93 %, mp 198-199^{\circ})$ was obtained. Its structure was assigned on the basis of spectral data $[UV_{max} (CHCl_3) 263 (\log \varepsilon 4.38), 320 (3.77), and 397 nm (4.52); IR (KBr) 1325 (SMe) and 1265 cm⁻¹ (C=S); ⁶ <math>\delta_H (CDCl_3)$ 2.48 (s, 3H), 2.68 (s, 3H), 7.36 (s, 4H), 7.46 (m, 3H), and 8.20 (m, 2H)]. No v (C=O) absorption was observed in its IR spectrum. By a similar procedure, the compound <u>3b</u> $(Ar^1=Ar^2=Ph, R=Me; 97 \%, mp 207-208^{\circ})$ and <u>3c</u> $(Ar^1=Ph, Ar^2=R=Me; 83 \%, mp 146-147^{\circ})$ were prepared. The latter compound <u>3c</u> was also synthesized in 34 % yield by the reaction of the isothiazoline <u>1c</u> $(Ar^1=Ph, Ar^2=Me)$ and methyl iodide in hot dichloromethane. As an alternative alkylation method, the reactions of <u>1b</u> $(Ar^1=Ar^2=Ph)$ and <u>1d</u> $(Ar^1=p-ClC_6H_4, Ar^2=Ph)$ with triethyloxonium tetrafluoroborate were studied, from which 4-aryl-5-ethylthio-3-thioacyloxyisothiazole <u>3d</u> $(Ar^1=Ar^2=Ph, R=Et; 83 \%, mp 183-185^{\circ})$ and <u>3e</u> $(Ar^1=p-ClC_6H_4, Ar^2=Ph, R=Et; 88 \%, mp 205-206^{\circ})$ were obtained, respectively.

When an equimolecular mixture of the isothiazoline <u>la</u> and <u>m</u>-chloroperbenzoic acid was stirred at room temperature for l h, a compound $[C_{34}H_{24}N_2O_2S_6; mp$ 232-233^O (decomp.)] was isolated in 84 % yield. The structure of bis(3-thiobenzoyloxy-4-<u>p</u>-tolylisothiazol-5-yl) disulfide <u>4a</u> (Ar¹=<u>p</u>-MeC₆H₄, Ar²=Ph) was assigned from the spectral data [UV (CHCl₃) 267 (log ε 4.56), 320sh (3.82), and 403 nm (4.65); IR (Nujol) 1260 cm⁻¹ (C=S); ⁶ $\delta_{\rm H}$ (CF₃CO₂D) 2.58 (s, 6H) and 7.40-7.93 (m, 18H)]. Again, there was no ν (C=O) absorption. By a similar method, the disulfide <u>4b</u> [Ar¹=Ar²=Ph; 100 %, mp 208-209^O (decomp.)] was prepared. Alternatively, this disulfide <u>4b</u> was obtained in 67 % yield, when an equimolecular mixture of <u>1b</u> and N-bromosuccinimide was stirred at room temperature in acetic acid.

The S+O migration in the reaction of $\underline{1}$ giving the thiono-ester $\underline{3}$ may be accounted for by postulating the intermediacy of a resonance-stabilized ion $\underline{2}$, but a mechanistic explanation for the formation of the thiono-ester $\underline{4}$ from $\underline{1}$ can not be advanced at present.

The isothiazolines <u>1</u> were synthesized in high yields by the reaction of 4-aryl-3-mercapto-3-isothiazoline-5-thione with acyl chloride in pyridine. Satisfactory micro-analyses have been obtained for the compounds described herein.



(i) CH_2N_2 ; (ii) MeI; (iii) $Et_3O^+ \cdot BF_4^-$; (iv) <u>m</u>-Chloroperbenzoic acid; (iv) NBS

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