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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 tetrafluoroborate[1] and boron trifluoride-etherate[2]), but also by thermolysis[3] 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.

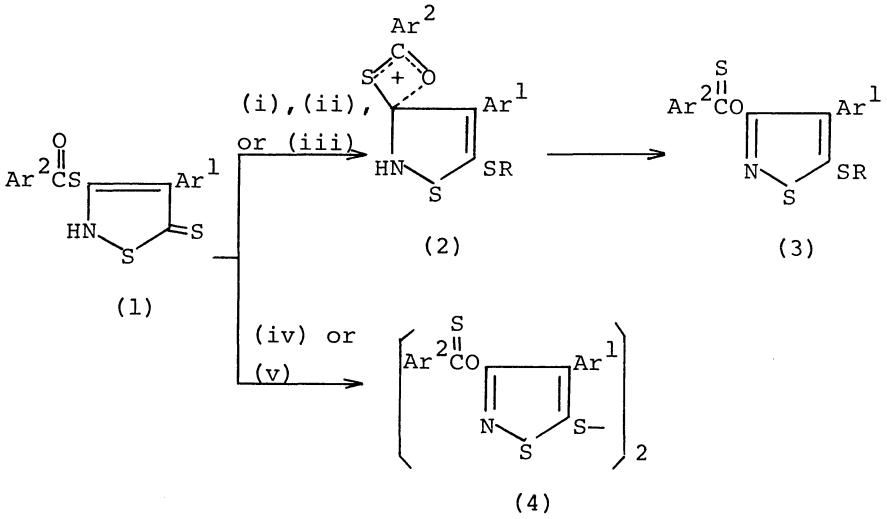
When the isothiazoline 1a (Ar^1=p-MeC_6H_4, Ar^2=Ph) was allowed to react with diazomethane in tetrahydrofuran, 5-methylthio-3-thiobenzoyloxy-4-p-tolylisothiazole 3a (Ar^1=p-MeC_6H_4, Ar^2=Ph, R=Me; 93 %, mp 198-199°) was obtained. Its structure was assigned on the basis of spectral data [UV_{max} ($CHCl_3$) 263 (log ε 4.38), 320 (3.77), and 397 nm (4.52); IR (KBr) 1325 (SMe) and 1265 cm^{-1} (C=S);[6] δ_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 ν(C=O) absorption was observed in its IR spectrum. By a similar procedure, the compound 3b (Ar^1=Ar^2=Ph, R=Me; 97 %, mp 207-208°) and 3c (Ar^1=Ph, Ar^2=R=Me; 83 %, mp 146-147°) were prepared. The latter compound 3c was also synthesized in 34 % yield by the reaction of the isothiazoline 1c (Ar^1=Ph, Ar^2=Me) and methyl iodide in hot dichloromethane. As an alternative alkylation method, the reactions of 1b (Ar^1=Ar^2=Ph) and 1d (Ar^1=p-ClC_6H_4, Ar^2=Ph) with triethyloxonium tetrafluoroborate were studied, from which 4-aryl-5-ethylthio-3-thioacyloxyisothiazole 3d (Ar^1=Ar^2=Ph, R=Et; 83 %, mp 183-185°) and 3e (Ar^1=p-ClC_6H_4, Ar^2=Ph, R=Et; 88 %, mp 205-206°) were obtained, respectively.

When an equimolecular mixture of the isothiazoline 1a and m-chloroperbenzoic acid was stirred at room temperature for 1 h, a compound [$C_{34}H_{24}N_2O_2S_6$; mp 232-233° (decomp.)] was isolated in 84 % yield. The structure of bis(3-thiobenzoyloxy-4-p-tolylisothiazol-5-yl) disulfide 4a (Ar^1=p-MeC_6H_4, Ar^2=Ph) was

assigned from the spectral data [$UV_{max}^{CHCl_3}$ 267 (log ε 4.56), 320sh (3.82), and 403 nm (4.65); IR (Nujol) 1260 cm^{-1} (C=S);[6] δ_H (CF_3CO_2D) 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 4b [Ar^1=Ar^2=Ph; 100 %, mp 208-209° (decomp.)] was prepared. Alternatively, this disulfide 4b was obtained in 67 % yield, when an equimolecular mixture of 1b and N-bromosuccinimide was stirred at room temperature in acetic acid.

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

The isothiazolines 1 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) $Et_3O^+.BF_4^-$; (iv) m-Chloroperbenzoic acid; (iv) NBS

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