

RING TRANSFORMATIONS OF 4-ARYL-3-HALOACYLTHIO-3-ISOTHIAZOLINE-5-THIONES AS A NEW ACCESS TO THE 4(5H)-THIAZOLONE AND 5,6-DIHYDRO-4H-1,3-THIAZIN-4-ONE RINGS

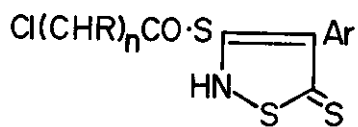
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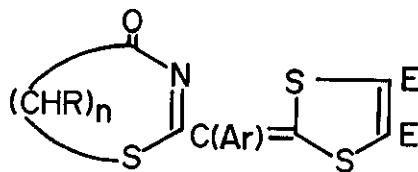
Abstract- The reactions of 4-aryl-3-haloacylthio-3-isothiazoline-5-thiones with reactive acetylenes (e.g. dimethyl acetylenedicarboxylate and dibenzoylacetylene) afford 2-[1,3-dithiol-2-ylidene(aryl)methyl]-4(5H)-thiazolones and 5,6-dihydro-2-[1,3-dithiol-2-ylidene(aryl)methyl]-4H-1,3-thiazin-4-ones mostly in high yields.

RING transformations of isothiazoles have received only scattered attention<sup>1,2</sup> in contrast to those of isoxazoles.<sup>3</sup> Recently we have found that the reactions of 4-aryl-3-benzoylthio-3-isothiazoline-5-thiones with dialkyl acetylenedicarboxylate are accompanied by an S+N acyl migration to produce N-benzoyl-[4,5-bis(alkoxy-carbonyl)-1,3-dithiol-2-ylidene]-arylethanethioamides.<sup>1</sup> If a similar S+N acyl migration takes place for the reactions of 4-aryl-3-haloacylthio-3-isothiazoline-5-thiones (1) with reactive acetylenes, heterocyclisations of the resulting N-haloacylthioamides (2) would be feasible. We now report that 2-[1,3-dithiol-2-ylidene(aryl)methyl]-4(5H)-thiazolones (3-5) and 5,6-dihydro-2-[1,3-dithiol-2-ylidene(aryl)methyl]-4H-1,3-thiazin-4-ones (7-9) are accessible, mostly in high yields, by utilising this strategy.

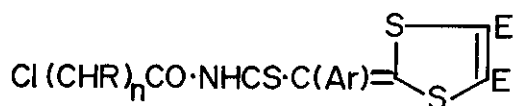
When the isothiazoline (1a)<sup>4</sup> was heated under reflux with dimethyl acetylenedicarboxylate (DMAD) (1 mol equiv.) in acetonitrile for a few hours, hydrogen chloride copiously evolved and evaporation of the reaction mixture left the thiazolone (3)<sup>4</sup> [91 % yield, brown prisms (from Me<sub>2</sub>CO), m.p. 209-210°C (decomp.),  $\nu_{\max}$ . (CHCl<sub>3</sub>) 1730 and 1700 cm<sup>-1</sup> (C=O)]. Its <sup>1</sup>H n.m.r. spectrum [(CD<sub>3</sub>)<sub>2</sub>SO] displays a singlet at  $\delta$  4.00 (2H) in addition to signals at  $\delta$  3.75 (s, 3H), 3.85



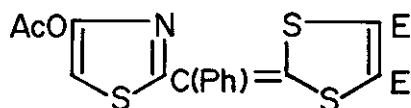
- (1) a; n=1, R=H, Ar=Ph  
 b; n=1, R=Me, Ar=Ph  
 c; n=2, R=H, Ar=Ph  
 d; n=2, R=H, Ar=p-ClC<sub>6</sub>H<sub>4</sub>  
 e; n=3, R=H, Ar=Ph



- (3) n=1, R=H, Ar=Ph, E=CO<sub>2</sub>Me  
 (4) n=1, R=H, Ar=Ph, E=CO·Ph  
 (5) n=1, R=Me, Ar=Ph, E=CO<sub>2</sub>Me  
 (7) n=2, R=H, Ar=Ph, E=CO<sub>2</sub>Me  
 (8) n=2, R=H, Ar=Ph, E=CO·Ph  
 (9) n=2, R=H, Ar=p-ClC<sub>6</sub>H<sub>4</sub>,  
 E=CO<sub>2</sub>Me



(2)



(6) E=CO<sub>2</sub>Me

(s, 3H), and 7.38-7.65 (m, 5H). In the light of the reports that the methylene signal of 2-phenyl-4(5H)-thiazolone appears at  $\delta$  4.3<sup>5</sup> and that of 2-phenyl-5(4H)-thiazolone at  $\delta$  4.84,<sup>6</sup> our product must have a 4(5H)-thiazolone structure.

The reaction of 3 with acetic anhydride afforded 93 % yield of an enol acetate (6)<sup>4</sup> [reddish brown needles (from benzene-ligroin), m.p. 180-181°C (decomp.),  $\nu_{\max}$ . (nujol) 1770 and 1735  $\text{cm}^{-1}$  (C=O),  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 2.37 (s, 3H), 3.78 (s, 3H), 3.90 (s, 3H), 6.72 (s, 1H), and 7.47 (s, 5H)]. Its off-resonance proton decoupled <sup>13</sup>C n.m.r. spectrum [ $(\text{CD}_3)_2\text{SO}$ ] shows signals of thiazole ring carbons at  $\delta$  103.1 (d), 159.9 (s), and 162.3 (s), the first being assigned to the C-5.<sup>7</sup> From these observations the structure of 3 could be firmly established.

The thiazolones (4)<sup>4</sup> [80 % yield, m.p. 249-250°C (decomp.)] and (5) were similarly prepared from 1a and 1b,<sup>4</sup> respectively, among which the latter [66 % yield, m.p. 153-155°C (decomp.),  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 1.58 (d,  $\underline{J}$  7 Hz, 3H), 3.82 (s, 3H), 3.92 (s, 3H), 4.08 (q,  $\underline{J}$  7 Hz, 1H), and 7.27-7.60 (m, 5H)]<sup>8</sup> was thermally unstable and decomposed into known<sup>1</sup> dimethyl 2-[cyano(phenyl)methylene]-1,3-dithiole-4,5-dicarboxylate during the course of recrystallisation.

The reaction of the isothiazoline (1c)<sup>4</sup> with DMAD proceeded in a similar way to give 88 % yield of the thiazinone (7)<sup>4</sup> [yellowish brown needles (from AcOEt), m.p. 203-204°C (decomp.),  $\nu_{\max}$ . ( $\text{CHCl}_3$ ) 1740 and 1670  $\text{cm}^{-1}$  (C=O),  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ) 2.64 (m, 2H), 3.17 (m, 2H), 3.76 (s, 3H), 3.88 (s, 3H), 7.18-7.40 (m, 2H), and 7.43-7.57 (m, 3H)], whose off-resonance proton decoupled <sup>13</sup>C n.m.r. spectrum [ $(\text{CD}_3)_2\text{SO}$ ] revealed two triplets at  $\delta$  28.8 and 25.2 and two singlets at  $\delta$  175.0 and 172.5 assignable to the 1,3-thiazinone ring carbons.<sup>9</sup>

Likewise, the thiazinones (8)<sup>4</sup> [91 % yield, m.p. 219-220°C (decomp.)] and (9)<sup>4</sup> [70 % yield, m.p. 213-214°C (decomp.)] were synthesized from 1c and 1d,<sup>4</sup> respectively.

During the course of the reactions of 1a-d with DMAD or dibenzoylacetylene, the corresponding thioamide (2) was not isolated. However, the reaction of 1e<sup>4</sup> with DMAD gave the thioamide (2; n=3, R=H, Ar=Ph, E=CO<sub>2</sub>Me) alone, which has defied variously attempted heterocyclisations (e.g. heating in a high-boiling solvent).

REFERENCES AND FOOTNOTES

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- <sup>3</sup> T. Nishiwaki, Synthesis, 1975, 20.
- <sup>4</sup> Satisfactory microanalytical results have been obtained for the new compounds (1-4, 6-9) and the molecular weights of the compounds (3-9) were determined by field desorption mass spectrometry. The isothiazolines (1a-e) were prepared by the reactions of 4-aryl-3-mercapto-3-isothiazoline-5-thione with the corresponding chlorocarboxylic acid in the presence of dicyclohexylcarbodiimide in dry tetrahydrofuran.
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- <sup>8</sup> Determined for a crude product which was homogeneous as revealed by t.l.c..
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