

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

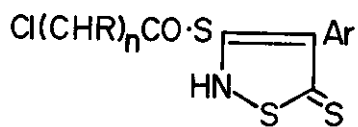
Tarozaemon Nishiwaki,^{*} Etsuko Kawamura, Noritaka Abe, Hirafumi Kochi, Yoshiro Sasaoka, and Kazumi Soneda

Department of Chemistry, Faculty of Sciences, Yamaguchi University, Yamaguchi City 753, Japan

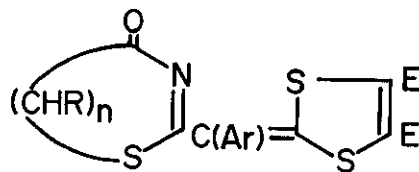
Abstract- The reactions of 4-aryl-3-haloacylthio-3-isothiazoline-5-thiones with reactive acetylenes (e.g. dimethyl acetylenedicarboxylate and dibenzoylacetylene) afford 2-[1,3-dithiol-2-ylidene(aryl)methyl]-4(5H)-thiazolones and 5,6-dihydro-2-[1,3-dithiol-2-ylidene(aryl)methyl]-4H-1,3-thiazin-4-ones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

RING transformations of isothiazoles have received only scattered attention^{1,2} in contrast to those of isoxazoles.³ 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.¹ 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.

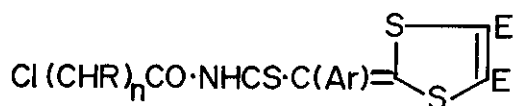
When the isothiazoline (1a)⁴ was heated under reflux with dimethyl acetylenedicarboxylate (DMAD) (1 mol equiv.) in acetonitrile for a few hours, hydrogen chloride copiously evolved and evaporation of the reaction mixture left the thiazolone (3)⁴ [91 % yield, brown prisms (from Me₂CO), m.p. 209-210°C (decomp.), ν_{max} (CHCl₃) 1730 and 1700 cm⁻¹ (C=O)]. Its ¹H n.m.r. spectrum [(CD₃)₂SO] displays a singlet at δ 4.00 (2H) in addition to signals at δ 3.75 (s, 3H), 3.85



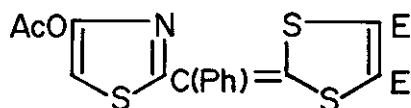
- (1) a; $n=1$, $R=H$, $\text{Ar}=\text{Ph}$
 b; $n=1$, $R=\text{Me}$, $\text{Ar}=\text{Ph}$
 c; $n=2$, $R=H$, $\text{Ar}=\text{Ph}$
 d; $n=2$, $R=H$, $\text{Ar}=\text{p-ClC}_6\text{H}_4$
 e; $n=3$, $R=H$, $\text{Ar}=\text{Ph}$



- (3) $n=1$, $R=H$, $\text{Ar}=\text{Ph}$, $\text{E}=\text{CO}_2\text{Me}$
 (4) $n=1$, $R=H$, $\text{Ar}=\text{Ph}$, $\text{E}=\text{CO}\cdot\text{Ph}$
 (5) $n=1$, $R=\text{Me}$, $\text{Ar}=\text{Ph}$, $\text{E}=\text{CO}_2\text{Me}$
 (7) $n=2$, $R=H$, $\text{Ar}=\text{Ph}$, $\text{E}=\text{CO}_2\text{Me}$
 (8) $n=2$, $R=H$, $\text{Ar}=\text{Ph}$, $\text{E}=\text{CO}\cdot\text{Ph}$
 (9) $n=2$, $R=H$, $\text{Ar}=\text{p-ClC}_6\text{H}_4$,
 $\text{E}=\text{CO}_2\text{Me}$



(2)



(6) $\text{E}=\text{CO}_2\text{Me}$

(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 δ 4.3⁵ and that of 2-phenyl-5(4H)-thiazolone at δ 4.84,⁶ our product must have a 4(5H)-thiazolone structure.

The reaction of 3 with acetic anhydride afforded 93 % yield of an enol acetate (6)⁴ [reddish brown needles (from benzene-ligroin), m.p. 180-181°C (decomp.), ν_{\max} . (nujol) 1770 and 1735 cm^{-1} (C=O), δ_{H} (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 ¹³C n.m.r. spectrum [$(\text{CD}_3)_2\text{SO}$] shows signals of thiazole ring carbons at δ 103.1 (d), 159.9 (s), and 162.3 (s), the first being assigned to the C-5.⁷ From these observations the structure of 3 could be firmly established.

The thiazolones (4)⁴ [80 % yield, m.p. 249-250°C (decomp.)] and (5) were similarly prepared from 1a and 1b,⁴ respectively, among which the latter [66 % yield, m.p. 153-155°C (decomp.), δ_{H} (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)]⁸ was thermally unstable and decomposed into known¹ dimethyl 2-[cyano(phenyl)methylene]-1,3-dithiole-4,5-dicarboxylate during the course of recrystallisation.

The reaction of the isothiazoline (1c)⁴ with DMAD proceeded in a similar way to give 88 % yield of the thiazinone (7)⁴ [yellowish brown needles (from AcOEt), m.p. 203-204°C (decomp.), ν_{\max} . (CHCl_3) 1740 and 1670 cm^{-1} (C=O), δ_{H} (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 ¹³C n.m.r. spectrum [$(\text{CD}_3)_2\text{SO}$] revealed two triplets at δ 28.8 and 25.2 and two singlets at δ 175.0 and 172.5 assignable to the 1,3-thiazinone ring carbons.⁹

Likewise, the thiazinones (8)⁴ [91 % yield, m.p. 219-220°C (decomp.)] and (9)⁴ [70 % yield, m.p. 213-214°C (decomp.)] were synthesized from 1c and 1d,⁴ 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 1e⁴ with DMAD gave the thioamide (2; n=3, R=H, Ar=Ph, E=CO₂Me) alone, which has defied variously attempted heterocyclisations (e.g. heating in a high-boiling solvent).

REFERENCES AND FOOTNOTES

- ¹ T. Nishiwaki, E. Kawamura, N. Abe, and M. Iori, J.C.S. Perkin Trans. I, in the press.
- ² J. Rokach, P. Hamel, Y. Girard, and G. Reader, Tetrahedron Letters, 1979, 1281.
- ³ T. Nishiwaki, Synthesis, 1975, 20.
- ⁴ 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.
- ⁵ S. Gronowitz, B. Mathiasson, R. Dahlbom, B. Holmberg, and K. A. Jensen, Acta Chem. Scand., 1965, 19, 1215.
- ⁶ M. D. Bachi, J.C.S. Perkin Trans. I, 1972, 310.
- ⁷ R. Faure, A. Assaf, É.-J. Vincent, and J.-P. Aune, J. Chim. Phys. Phys.-Chim. Biol., 1978, 75, 727.
- ⁸ Determined for a crude product which was homogeneous as revealed by t.l.c..
- ⁹ Sohar, G. Feher, and L. Toldy, Org. Magn. Reson., 1978, 11, 9.

Received, 9th January, 1981