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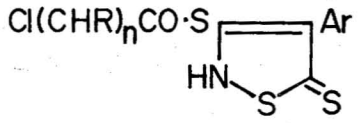
Abstract- The reactions of 4-aryl-3-haloacylthio-3-isothiazoline-5-thiones with reactive acetylenes (e.g. dimethyl acetylenedicarboxylate and dibenzoylacetylene) afford 2-[1,3-dithiol-2-ylidene(aryl)methyl]-4(5H)-thiazolones and 5,6-dihydro-2-[1,3-dithiol-2-ylidene(aryl)methyl]-4H-1,3-thiazin-4-ones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

RING transformations of isothiazoles have received only scattered attention[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(alkoxycarbonyl)-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 Me_2CO), m.p. 209-210°C (decomp.), $\nu_{max.}$ ($CHCl_3$) 1730 and 1700 cm^{-1} (C=O)]. Its ^1H n.m.r. spectrum [$(CD_3)_2SO$] displays a singlet at δ 4.00 (2H) in addition to signals at δ 3.75 (s, 3H), 3.85



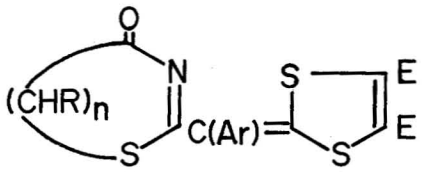
(1) a; n=1, R=H, Ar=Ph

b; n=1, R=Me, Ar=Ph

c; n=2, R=H, Ar=Ph

d; n=2, R=H, Ar=p-ClC_6H_4

e; n=3, R=H, Ar=Ph



(3) n=1, R=H, Ar=Ph, E=CO_2Me

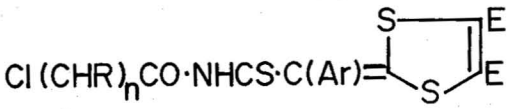
(4) n=1, R=H, Ar=Ph, E=CO·Ph

(5) n=1, R=Me, Ar=Ph, E=CO_2Me

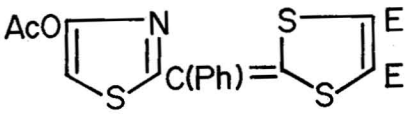
(7) n=2, R=H, Ar=Ph, E=CO_2Me

(8) n=2, R=H, Ar=Ph, E=CO·Ph

(9) n=2, R=H, Ar=p-ClC_6H_4, E=CO_2Me



(2)



(6) E=CO_2Me

(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 4.3[5] 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.), $\nu_{max.}$ (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 ^{13}C n.m.r. spectrum [$(CD_3)_2SO$] 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, J 7 Hz, 3H), 3.82 (s, 3H), 3.92 (s, 3H), 4.08 (q, J 7 Hz, 1H), and 7.27-7.60 (m, 5H)][8] was thermally unstable and decomposed into known[1] 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.), $\nu_{max.}$ ($CHCl_3$) 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 ^{13}C n.m.r. spectrum [$(CD_3)_2SO$] 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 1e[4] with DMAD gave the thioamide (2; n=3, R=H, Ar=Ph, E=CO_2Me) 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, E.-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] Sohár, G. Fehér, and L. Toldy, Org. Magn. Reson., 1978, 11, 9.

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