RING TRANSFORMATIONS OF 4-ARYL-3-HALOACYLTHIO-3-IOTHIAZOLINE-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 in contrast to those of isoxazoles. 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]-arylthioamidoethioamides. 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 isothiazole (1a) 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 thiazalone (3) [91% yield, brown prisms (from Me2CO), m.p. 209-210°C (decomp.), \( \nu_{\text{max}}(\text{CHCl}_3) \) 1730 and 1700 cm\(^{-1}\) (C=O)]. Its \(^1\)H n.m.r. spectrum [(CD\(_3\))\(_2\)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-ClC₆H₄
   e; n=3, R=H, Ar=Ph

(2) Cl(CHR)ₙCO-NHCS-C(Ar)=S=E

(3) n=1, R=H, Ar=Ph, E=CO₂Me
(4) n=1, R=H, Ar=Ph, E=CO·Ph
(5) n=1, R=Me, Ar=Ph, E=CO₂Me
(7) n=2, R=H, Ar=Ph, E=CO₂Me
(8) n=2, R=H, Ar=Ph, E=CO·Ph
(9) n=2, R=H, Ar=p-ClC₆H₄,
    E=CO₂Me

(6) E=CO₂Me
(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°O C (decomp.), \(\nu_{\text{max.}}\) (nujol) 1770 and 1735 cm\(^{-1}\) (C=O), \(\delta_H\) (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\(_3\)_2]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°O C (decomp.)] and (5) were similarly prepared from la and lb,\(^4\) respectively, among which the latter [66 % yield, m.p. 153-155°O C (decomp.), \(\delta_H\) (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°O C (decomp.), \(\nu_{\text{max.}}\) (CHCl\(_3\)) 1740 and 1670 cm\(^{-1}\) (C=O), \(\delta_H\) (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\(_3\)_2]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°O C (decomp.)] and (9)\(^4\) [70 % yield, m.p. 213-214°O C (decomp.)] were synthesized from 1c and 1d,\(^4\) respectively.

During the course of the reactions of la-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\(_2\)Me) alone, which has defied variously attempted heterocyclisations (e.g. heating in a high-boiling solvent).
REFERENCES AND FOOTNOTES


4 Satisfactory microanalytical results have been obtained for the new compounds (1-4, 5-9) 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.


8 Determined for a crude product which was homogeneous as revealed by t.l.c.


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