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Malononitrile (I) reacted with thioglycolic acid to yield the thiazolin-4-one derivatives II or III depending on the molar ratio of the reactants. Compound II reacted with benzaldehyde in refluxing pyridine to yield the arylidene derivative IV. On the other hand, the benzylidene bis derivative VIII was obtained when II was reacted with benzaldehyde in refluxing ethanol. The structure of IV was established *via* its synthesis from the reaction of benzylidenemalononitrile (VI) and thioglycolic acid in refluxing acetic acid. Similar to II, compound III condensed with benzaldehyde to yield the benzylidene derivative IX.

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Malononitrile (I) is a compound of exceptional reactivity. It is used extensively as a reactant or reaction intermediate since the methylene group and either one or both cyano groups can take part in condensation reactions to give a variety of products or heterocyclic compounds (1). In conjunction with our program aiming to explore the synthetic potential of compound I and its derivatives (2-7), we report here on the reaction of I and its derivatives with thioglycolic acid.

When I was treated with equimolecular amount of thioglycolic acid in refluxing pyridine or acetic acid a product of molecular formula $C_5H_4N_2OS$ was formed in almost quantitative yield. The ir spectrum of the product revealed absorption bands at 1730 cm^{-1} (CO), 2200 cm^{-1} (conjugated CN) and at 3000 cm^{-1} (CH_2). The 1H nmr of this product showed two singlets of equal integrals at δ 4.35 and 5.05 ppm which were assigned for two different methylene (CH_2) groups. Based on these data, structure II was suggested for this product. The formation of II from the reaction of I and thioglycolic acid may be assumed to proceed *via* addition of the mercapto group in the reagent to the cyano group in I followed by elimination of water (*cf.* Chart I).

The formation of thiazol-4-one derivatives from the reaction of nitriles with thioglycolic acid has been previously reported (8,9). However, careful inspection of the reported procedure revealed that the reaction in this case proceeds, most likely, *via* initial formation of imidoyl chloride (8). Moreover, compound II could not be obtained *via* reaction of I and thioglycolic acid utilising this procedure.

When compound I was treated with thioglycolic acid in the molar ratio of 1:2 in refluxing pyridine a resinified product was formed. However, when I was treated with thioglycolic acid in the same molar ratio in refluxing acetic acid solution the bis-thiazol-4-one derivative III was

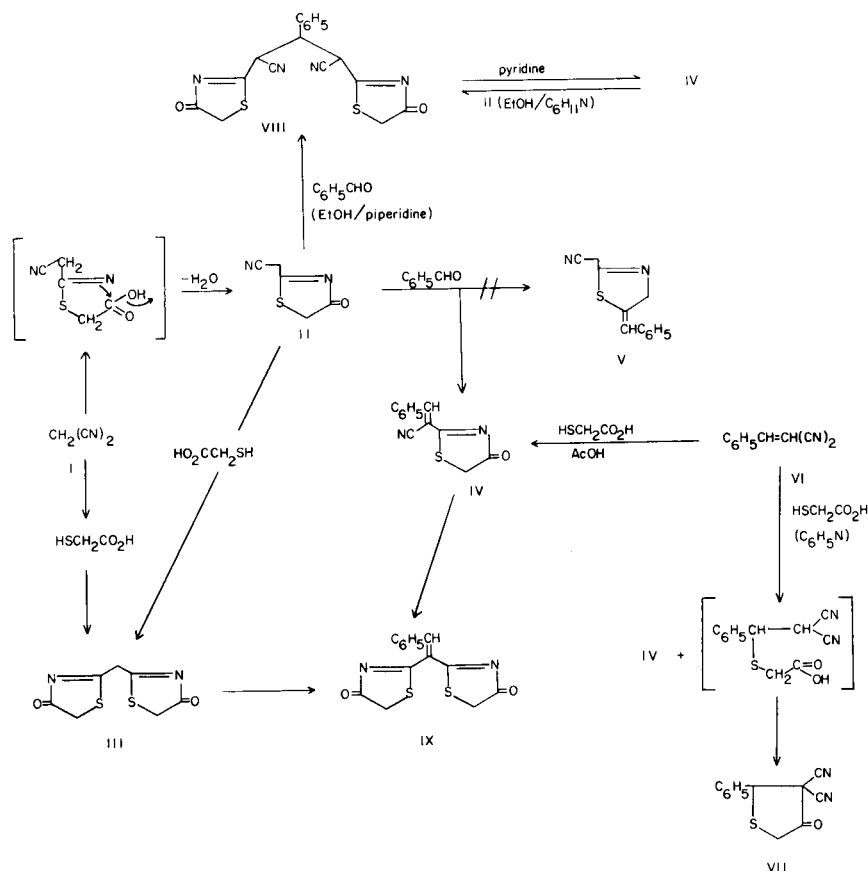
formed in excellent yield. Compound III could be also obtained from the reaction of II with thioglycolic acid in refluxing pyridine.

Compound II readily condenses with benzaldehyde in refluxing acetic acid to yield a benzylidene derivative which can be formulated as IV or the isomeric V. (*cf.* Chart 1). Structure IV could be established for the reaction product by its synthesis *via* the reaction of benzylidenemalononitrile (VI) and thioglycolic acid in refluxing acetic acid. Attempts to synthesize IV by reaction of VI and thioglycolic acid in refluxing pyridine afforded in addition to IV another product of m.p. 265° . The analytical data of this product revealed a molecular formula of $C_{12}H_8N_2SO$. The ir spectrum of the product revealed absorptions at 1730, 2200, 2220, 3000 and 3400 cm^{-1} which are attributable for C=O two CN groups, CH_2 and enolic OH stretching absorptions. Based on these data structure VII was suggested for this product. The formation of thiophene derivatives *via* reaction of VI and thioglycolic acid is similar to our recently reported thiophene synthesis *via* reaction of α -cyanochalcones with thioglycolic acid under the same experimental conditions (10).

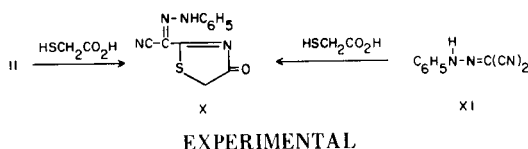
The formation of VII from the reaction of VI and thioglycolic acid may be assumed to proceed *via* a Micheal type addition of the reagent to the activated double bond in VI to yield an intermediate Micheal type adduct which then cyclises into the final isolable product as shown in Chart 1.

In contrast to the behaviour of II toward the action of benzaldehyde in refluxing pyridine, it reacted with the same reagent in ethanol in the presence of piperidine to yield the benzylidene bis derivative VIII. Compound VIII could be readily converted into IV on reflux in pyridine. On the other hand, the benzylidene derivative IV could be converted into the benzylidene bis derivative VIII on

Chart I



treatment with II in refluxing ethanol in the presence of piperidine. Similar to compound II, compound III also condensed with benzaldehyde to yield the benzylidene derivative IX. The structure of compound IX was established by its synthesis from VI and thioglycolic acid in refluxing pyridine. Whereas, compound II readily coupled with benzenediazonium chloride to yield the corresponding arylazo derivative, compound III did not couple with aryldiazonium salts under a variety of experimental conditions. Structure X could be established for the coupling product of II with benzene diazonium chloride *via* its synthesis from phenylhydrazonomesoxalonnitrile (XI) and thioglycolic acid.



EXPERIMENTAL

All melting points are uncorrected. Ir spectra were obtained on a Pye-Unicam SP 1100 spectrophotometer. ^1H nmr spectra were obtained in DMSO on a Variant A-60 using TMS as the

internal indicator and chemical shifts are expressed as δ ppm. 2-Cyanomethyl-2-thiazolin-4-one (II).

Method A.

A solution of I (0.01 mole) in glacial acetic acid (20 ml.) was treated with thioglycolic acid (0.01 mole). The reaction mixture was refluxed for two hours, allowed to cool and poured onto water. The solid product, so formed, was collected by filtration and crystallised from ethanol. Compound II formed buff crystals, m.p. 185-186°, yield 85%; ir: 1730 cm^{-1} (CO), 2230 cm^{-1} (CN), 3000 cm^{-1} (CH₂); ^1H 4.15 (s, 2H, CH₂) and 5.01 (s, 2H, CH₂).

Anal. Calcd. for C₅H₄N₂OS: C, 42.9; H, 2.9; N, 20.0; S, 22.9. Found: C, 42.8; H, 3.1; N, 20.2; S, 22.5.

Method B.

A solution of equimolecular amounts of each of I and thioglycolic acid (0.01 mole each) in pyridine (20 ml.) was refluxed for one hour. The solvent was then removed *in vacuo*. The remaining product was triturated with water and the resulting solid product was collected by filtration and identified (m.p. and mixed m.p. and by ir) as II, yield 90%.

Methylene-bis(4-oxo-2-thiazolin-2-yl) (III).

Method A.

A solution of I (0.01 mole) in pyridine (10 ml.) was treated with thioglycolic acid (0.02 mole). The reaction mixture was

refluxed for thirty minutes then evaporated *in vacuo*. The remaining product was triturated with water and the resulting solid product was collected by filtration and crystallised from a dioxane-water mixture. Compound III formed buff crystals, m.p. 225°, yield 90%; ir: 1725 cm⁻¹ (CO) and 2980, 3000, 3030 cm⁻¹ (CH₂ group).

Anal. Calcd. for C₇H₆N₂O₂S₂: C, 39.3; H, 2.8; N, 13.0; S, 29.9. Found: C, 39.0; H, 2.8; N, 12.5; S, 30.1.

Method B.

A solution of II (0.01 mole) in pyridine (10 ml.) was treated with thioglycolic acid (0.01 mole). The reaction mixture was refluxed for one hour then evaporated *in vacuo*. The remaining product was triturated with water and the resulting solid product was collected by filtration and crystallised from dioxane and identified (m.p. and mixed m.p.) as III, yield 85%.

2-(4-Oxo-2-thiazolin-2-yl)cinnamionitrile (IV).

Method A.

A solution of II (0.01 mole) in glacial acetic acid (10 ml.) was treated with acetic anhydride (5 ml.), anhydrous sodium acetate (3 g.) then with benzaldehyde (0.01 mole). The reaction mixture was refluxed for two hours, cooled, then poured onto water. The solid product, separated on standing, was collected by filtration and crystallised from ethanol. Compound IV formed brown crystals, m.p. 200° dec.; yield 50%; ir: 1730 cm⁻¹ (CO) and 2220 cm⁻¹ (conjugated CN).

Anal. Calcd. for C₁₂H₈N₂OS: C, 63.2; H, 3.5; N, 12.3; S, 14.0. Found: C, 63.1; H, 3.9; N, 12.0; S, 13.5.

Method B.

A suspension of VI (0.01 mole) in acetic acid (30 ml.) was treated with thioglycolic acid (0.01 mole). The reaction mixture was refluxed for five hours then evaporated *in vacuo*. The remaining product was triturated with water and the resulting solid product was collected by filtration, crystallised and identified (m.p. and mixed m.p.) as IV.

Method C.

A solution of equimolecular amounts of VI and thioglycolic acid (0.01 mole each) in pyridine (10 ml.) was refluxed for one hour, then allowed to cool. The solid product, so formed, was collected by filtration and crystallised from dioxane to yield 3,3-dicyano-2-phenyl-4-oxotetrahydrothiophene. Compound VII formed yellow crystals, m.p. 265°; 1730 cm⁻¹ (CO), 2200 and 2220 cm⁻¹ (two CN groups).

Anal. Calcd. for C₁₂H₈ON₂S: C, 63.2; H, 3.5; N, 12.2; S, 14.0. Found: C, 62.9; H, 4.0; N, 11.9; S, 14.0.

Evaporation of the filtrate afforded, after trituration with water, a solid product which was identified (m.p. and mixed m.p.) as IV, yield 35%.

2,2'-Bis-(4-oxo-2-thiazolin-2-yl)-3-phenylpentanedinitrile (VIII).

A solution of II (0.02 mole) in ethanol (30 ml.) was treated with piperidine (0.1 ml.) then with benzaldehyde (0.01 mole). The reaction mixture was refluxed for two hours then evaporated *in vacuo*.

The remaining product was triturated with petroleum ether and the resulting solid product was collected by filtration and crystallised from ethanol. Compound VIII formed red crystals, m.p. 130°; ir: 1730 cm⁻¹ (CO); 2210 cm⁻¹ (CN) and 3000, 3020 cm⁻¹ (CH₂ groups).

Anal. Calcd. for C₁₇H₁₂O₂N₄S₂: C, 55.4; H, 3.4; N, 15.1. Found: C, 55.0; H, 3.5; N, 15.5.

Compound VIII could be also obtained *via* reaction of equimolecular amounts of II and IV using reaction conditions similar to those described above.

1,1-Bis-(4-oxo-2-thiazolin-2-yl)styrene (IX).

A suspension of III (0.01 mole) in acetic acid (10 ml.) and acetic anhydride (3.0 ml.) was treated with anhydrous sodium acetate (2.0 g.) then with benzaldehyde (0.01 mole). The reaction mixture was refluxed for two hours then cooled and poured on ice cold water. The solid product, which separated on standing, was collected by filtration and crystallised from dioxane-water. Compound IX formed brown crystals, m.p. 240° dec.; yield 50%.

Anal. Calcd. for C₁₄H₁₀N₂O₂S₂: S, 20.8. Found: S, 20.7.

Coupling of II with Benzenediazonium Chloride.

A solution of II (0.01 mole) in ethanol (20 ml.) was treated with sodium acetate (2.0 g.) and then with a solution of benzenediazonium chloride (prepared from 0.01 mole of aniline and the appropriate quantities of hydrochloric acid and sodium nitrile). The solid product, which separated on standing, was collected by filtration and crystallised from dioxane-water. Compound X formed dark brown crystals, m.p. 240°, yield 70%; ir: 1730 cm⁻¹ (C=O) and 2225 cm⁻¹ (CN).

Anal. Calcd. for C₁₁H₈ON₄S: C, 54.1; H, 3.3; S, 13.1. Found: C, 54.6; H, 3.5; S, 12.7.

Compound X could be also obtained *via* refluxing equimolecular amounts of XI and thioglycolic acid in acetic acid and working up the reaction mixture.

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