Synthesis of Some New 2-Substituted Thiazolid-4-ones

Mansour I. Younes^a, Maher F. El-Zohry^b, and Saoud A. Metwally^{b,*}

- ^a Chemistry Department, Faculty of Science, Assiut University, Qena, Egypt
- ^b Chemistry Department, Faculty of Science, Assiut University, Assiut, Egypt

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2-Substituted Thiazolid-4-ones, Synthesis

2-Substituted thiazolid-4-ones were prepared by interaction of thioglycolic acid with certain acyl derivatives in presence of ammonium carbonate and dry benzene. The reaction mechanism is discussed.

Introduction

Thiazolid-4-ones are biologically active compounds and in particular exhibit a wide variety of pharmacological properties, including anticonvulsant, antipyretic, analgesic and antibacterial effects [1-5]. The majority of thiazolid-4-one known are 2,3-disubstituted derivatives and were synthesised by the addition of a variety of thiols to Schiff's bases or by the interaction of monochloroacetic acid with thiocarbamides prepared from the reaction of arylthiocyanates and aralkylamines [6, 7]. In the present study we started the preparation of thiazolid-4-one derivatives which are fully substituted in the 2-position. This will enables us to get other substituent in the 3-position using other simple reaction routes.

Results and Discussion

The biological importance of thiazolid-4-one derivatives prompted us to prepare some new 2-substituted thiazolid-4-one derivatives by phenyl, and 3methyl-2-pyrazolin-5-onyl groups. Thus acetophenone (1a), benzophenone (1b), 2-acetylpyridine (1c), 1-acetyl-3-methyl-2-pyrazolin-5-one (1d) and 4-acetyl-1-phenyl-3-methyl-2-pyrazolin-5-one (1e) were reacted with thioglycolic acid in dry benzene in presence of ammonium carbonate to give the corresponding 2-substituted thiazolid-4-one derivatives (3a-d) (Scheme 1). The addition product (2) could not be isolated. Using 4-acetyl-1-phenyl-3-methyl-2-



pyrazolin-5-one (1e) as acyl derivative no thiazolid-4-one derivative was isolated. This may be explained on the basis of the strong enolisation of 1e to 4.



The identities of the formed 2-substituted thiazolid-4-one derivatives were established by elemental analysis, IR, and mass spectra.

Experimental

Melting points are uncorrected. Analytical data were carried out at Technische Hochschule Darmstadt, West Germany. Mass spectra were obtained using an AE1 MS 12 mass spectrometer operating at 70 eV and the direct insertion technique was used with a probe temperature range between 150-200 °C. The IR spectra were obtained on a pye Unicam SP-1000 Spectrometer.

^{*} Reprint requests to Prof. Dr. S. A. Metwally.

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1-Acetyl-3-methyl-2-pyrazolin-5-one (1d) and 4acetyl-1-phenyl-3-methyl-2-pyrazolin-5-one (1e) were prepared according to literature procedures [9] and they showed analytical and spectral data in agreement with their structures.

Synthesis of 2-substituted thiazolid-4-ones (general procedure)

A solution of the acetyl or benzoyl derivative (0.1 mole), thioglycolic acid (0.1 mole) and ammonium carbonate (0.12 mole) in dry benzene was refluxed on water bath and the liberated water was removed using a water separator. The reaction mixture is removed. At the end of the reflux time, the product was precipitated. The reaction mixture was cooled to room temperature and the product was collected by filteration then recrystallized from the proper solvent.

2-Methyl-2-phenylthiazolid-4-one (3a)

A mixture of acetophenone (1a) (11.9 ml, 0.1 mole), thiogycolic acid (9.2 g, 0.1 mole) and ammonium carbonate (11.5 g, 0.12 mole) in 100 ml dry benzene was allowed to react according to the general procedure to give 10.2 g (52.8%) of **3a**, crystallized from benzene/petroleum ether (40-60 °C) mixture 1:3, m.p. 145 °C.

$C_{10}H_{11}NOS$ (193)

Calcd C 55.67 H 5.15 N 14.13, Found C 55.46 H 5.09 N 14.51.

MS: m/e = 193 (M⁺); IR (KBr): ν 3290 (NH), 1675 (C=O) cm⁻¹.

2,2-Diphenylthiazolid-4-one (**3b**)

The reaction of benzophenone (18.2 g, 0.1 mole), thioglycolic acid (9.2 g, 0.1 mole) and ammonium carbonate (11.5 g, 0.12 mole) according to the previous general procedure gave 14.5 g (56.68%) of **3b**,

crystallized from benzene/petroleum ether 40-60 °C mixture 1:3, m.p. 185–187 °C.

$$\begin{array}{c} C_{15}H_{13}NOS \ (255) \\ Calcd \ C \ 70.58 \ H \ 5.09 \ N \ 5.49, \\ Found \ C \ 70.33 \ H \ 5.12 \ N \ 5.47. \end{array}$$

MS: m/e = 255 (M⁺); IR (KBr): ν 3330 (NH), 1670 (C=O) cm⁻¹.

2-Methyl-2-(2-pyridyl)thiazolid-4-one (3c)

2-Acetylpyridine (11.2 ml, 0.1 mole), thioglycolic acid (9.2 g, 0.1 mole) and ammonium carbonate (11.5 g, 0.12 mole) were reacted according to the general procedure to give 10.8 g (55.6%) of **3c**, crystallized from benzene/petroleum ether 40-60 °C mixture 1:1, m.p. > 300 °C.

$$\begin{array}{c} C_{9}H_{10}N_{2}OS \ (194) \\ Calcd C \ 55.67 \ H \ 5.15 \ N \ 14.43, \\ Found C \ 55.46 \ H \ 5.09 \ N \ 14.51. \end{array}$$

MS: $m/e = 194 (M^+)$; IR (KBr): ν 3295 (NH), 1685 (C=O) cm⁻¹.

2-Methyl-2-(1-3-methyl-2-pyrazolin-5-onyl)thiazolid-4-one (**3d**)

A solution of 1-acetyl-3-methyl-2-pyrazolin-5-one (14 g, 0.1 mole), thioglycolic acid (7.1 ml, 0.1 mole) and ammonium carbonate (11.5 g, 0.12 mole) were reacted in dry benzene (150 ml) according to the general procedure to give 12.4 g of **3d** (58.2%) crystallized from ethanol, m.p. > 300 °C.

 $\begin{array}{c} C_8 H_{II} N_3 O_2 S \ (213) \\ \text{Calcd} \ \ \text{C} \ 45.07 \quad \text{H} \ 5.16 \quad \text{N} \ 19.71, \\ \text{Found} \ \ \text{C} \ 45.17 \quad \text{H} \ 5.12 \quad \text{N} \ 19.81. \end{array}$

MS: $m/e = 213 (M^+)$; IR (KBr): ν 3295 (NH), 1710 (C=O) cm⁻¹.

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