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Microwave Induced Stereoselective Synthesis of Alkyl *Z*-2-(2-amino-4-oxo-1,3-thiazol-5(4*H*)-yliden)acetates from Thiourea and Dialkyl Acetylenedicarboxylates in Solvent-less Conditions

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Thiourea reacts with dialkyl acetylenedicarboxylates in solvent-less conditions to form 1 : 1 adducts, which undergo a cyclization reaction to produce alkyl *Z*-2-(2-amino-4-oxo-1,3-thiazol-5(4*H*)-yliden)acetates under microwave irradiation and also under thermal conditions in solvent-less system in fairly good yields. Stereochemistry of the ethyl *Z*-2-(2-amino-4-oxo-1,3-thiazol-5(4*H*)-yliden)-acetate was established with using of X-ray single crystal structure analysis. The reaction is completely stereoselective.

Key Words: Microwave irradiation, Thiourea, Acetylenic ester, Michael addition, X-ray single crystal structure analysis, Stereoselectivity, 1,3-thiazol.

INTRODUCTION

Thiazole derivatives have attracted a great deal of interest owing to their antibacterial, antifungal, antiinflammatory and antiviral activities[1]. They are also useful as anti-allergic, anthelmintic agents and as sedative hypnotics[1]. In addition to being used in the pharmaceutical industry[1–3], thiazoles also find a wide application in the dye and photographic industry[1]. Owing to these characteristics and our interest in the synthesis of heterocycles[4, 5], we were prompted to synthesize 2-aminothiazole (1,3-thiazol-2-amino) compounds **(6)** from dialkyl acetylenedicarboxylates **(2)** thiourea **(1)** in solvent-less conditions under microwave irradiation and also under thermal conditions **(Scheme-1).**

RESULTS AND DISCUSSION

The compound **(6)** may result from initial Michael addition reaction of thiourea **1** to the acetylenic ester **2** and concomitant intramolecular proton transfer of the

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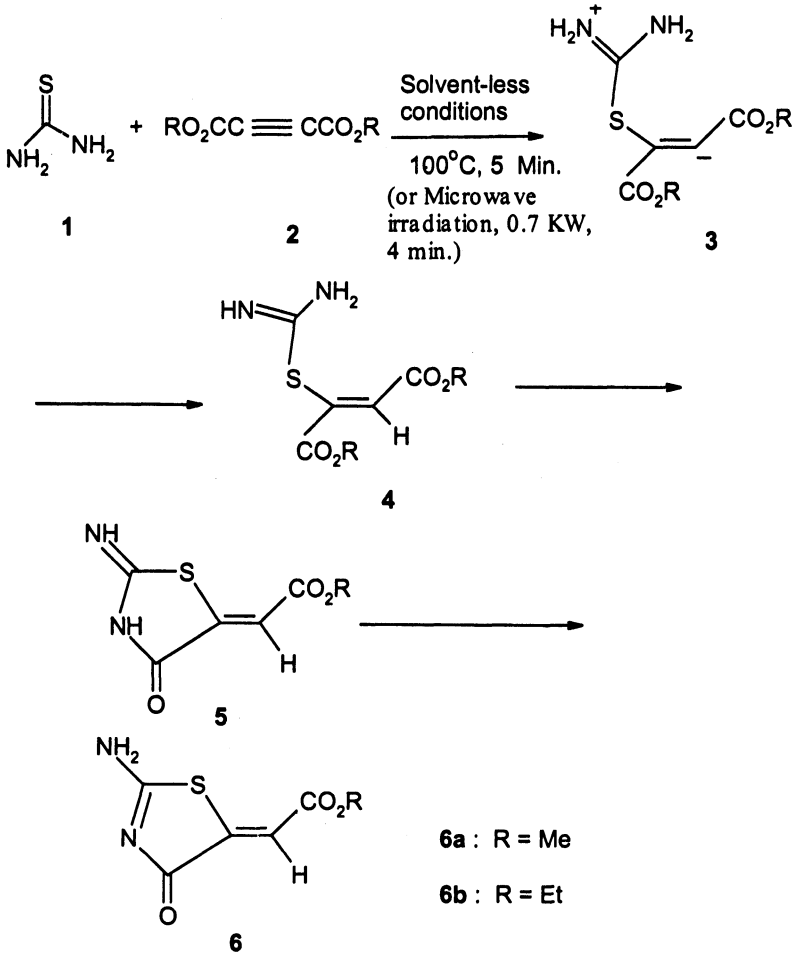
1 : 1 adduct **3,** followed by attack of the imine nitrogen on the carbonyl group of the ester to form intermediate **5 (Scheme-1).** Intramolecular proton transfer of the intermediate **5** leads to formation of the alkyl *Z*-2-(2-amino-4-oxo-1,3-thiazol-5(4*H*)-yliden)acetates **(6),** in fairly good yields. TLC indicated that the reaction was completed in solvent-less conditions at 100°C after 5 min. The reaction was completed in solvent-less conditions under microwave irradiation (0.7 kW) after 4 min. The reaction proceeds smoothly and cleanly under the experimental conditions. The structures of **6a–b** were deduced from their IR, ^{1}H NMR, ^{13}C NMR and MS spectra and elemental analysis. Stereochemistry of the ethyl *Z*-2-(2-amino-4-oxo-1,3-thiazol-5(4*H*)-yliden)acetate **(6b)** was established with using of X-ray single crystal structure analysis (Figs. 1 and 2). The reaction is completely stereoselective.



Scheme-1

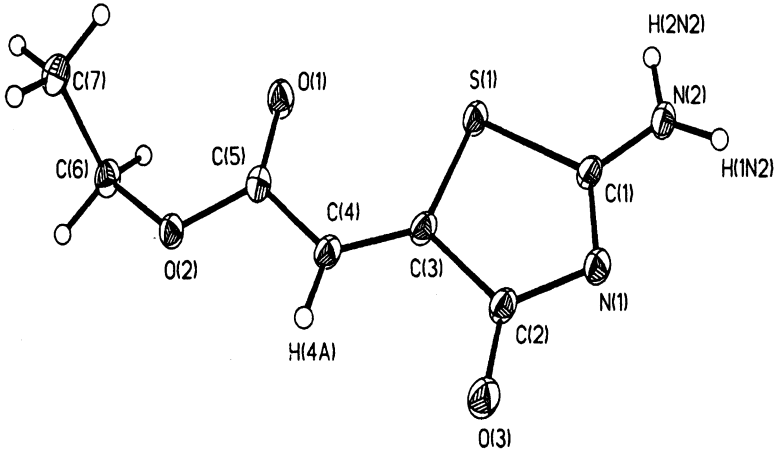


Fig. 1. Molecular structure of **6b**

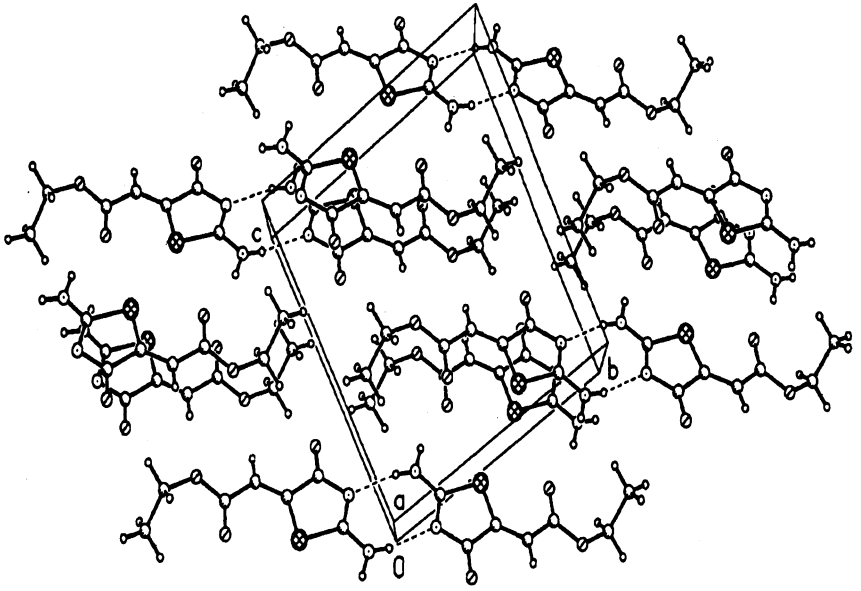


Fig. 2. Unit cell crystal structure of **6b**

EXPERIMENTAL

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were recorded on a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with Bruker DRX-500 Avance spectrometer at 500 and 125 MHz, respectively. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV.

General procedure for the preparation of alkyl *Z*-2-(2-amino-4-oxo-1,3-thiazol-5(4*H*)-yliden)acetates (6a–b): Thiourea **1** (1 mmol) and acetylenic ester **2** (1 mmol) were ground at 100°C in 5 min (or under microwave irradiation,

0.7 kW, 4 min). The mixture was then washed with cold acetone (3 mL) and white powders of **6** were collected by filtration.

Selected data for methyl *Z*-2-(2-amino-4-oxo-1,3-thiazol-5(4*H*)-yliden)-acetate (6a): White crystals, m.p. 232.0–233.0°C (dec.), yield 63.7%. IR (KBr) (ν_{max}, cm^{-1}): 3315; 1710; 1679. ^1H NMR (DMSO-d_6) δ_H: 3.83 (3H, s, CH_3); 6.62 (1H, s, =CH); 9.31 (1H, s, NH); 9.5–9.7 (1H, br s, NH). ^{13}C NMR (DMSO-d_6) δ_C: 50.82 (CH_3), 113.45 (=CH); 147.06 (=CS); 164.95 (C=N); 176.29 and 177.24 (2C=O). MS (m/z, %): 187 (MH^+, 29); 186 (M^+, 67); 144 (100); 116 (95); 85 (100); 57 (100). Analysis: Calcd. for $C_6H_6N_2O_3S$ (186.19): C, 38.71; H, 3.25; N, 15.05%; Found: C, 38.7; H, 3.2; N, 15.1%.

Selected data for ethyl *Z*-2-(2-amino-4-oxo-1,3-thiazol-5(4*H*)-yliden)-acetate (6b): White crystals, m.p. 239.0–240.0°C (dec.), yield 57.8%. IR (KBr) (ν_{max}, cm^{-1}): 3347; 3219; 1715; 1675; 1642. ^1H NMR (DMSO-d_6) δ_H: 1.24 (3H, t, $^3J_{HH}$ = 7.1 Hz, CH_3); 4.21 (2H, q, $^3J_{HH}$ = 7.1 Hz, OCH_2); 6.60 (1H, s, =CH); 9.4–9.7 (2H, br s, NH_2). ^{13}C NMR (DMSO-d_6) δ_C: 14.52 (CH_3), 61.82 (OCH_2), 115.55 (=CH); 148.53 (=CS); 166.30 (C=N); 177.99 and 179.09 (2 C=O). MS (m/z, %): 201 (MH^+, 25); 200 (M^+, 61); 172 (10); 158 (100); 130 (90); 128 (8); 86 (10); 85 (96); 58 (7); 57 (98). Analysis: Calcd. for $C_7H_8N_2O_3S$ (200.22): C, 41.99; H, 4.03; N, 13.99%; Found: C, 41.8; H, 4.1; N, 14.2%.

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