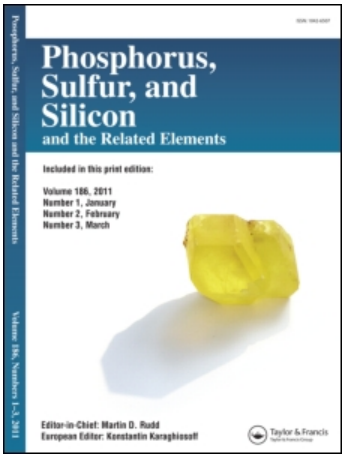

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REGIOSELECTIVE S→N ALLYLIC TRANSPOSITION OF 3-ALLYLTHIO 1,2,4-TRIAZINONE WITHOUT SOLVENT, AND CATALYST UNDER MICROWAVE IRRADIATION

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The facile and regioselective cyclization of 3-allylsulfanyl-6-methyl-2H-[1,2,4-]triazin-5-one ***2*** to 3,6-dimethyl-2,3-dihydro-thiazolo [3,2-.b.][1,2,4] triazin-7-one ***3***has been performed by the catalytic action of H_2SO_4. Compound ***2*** underwent [3,3] sigmatropic shift under microwave irradiation to afford 4N allyl derivative ***5*** in fairly good yield. Treatment of ***5*** with conc, sulphuric acid afforded the corresponding 2-methyl thiazolo[2,3-c] triazinone ***7***.

Keywords: Claisen rearrangement; microwave irradiation; regioselective cyclization

INTRODUCTION

Palladium catalyzed and thermal S→N allylic rearrangment of allylthio pyrimidinone and allylthio 1,2,4-triazinone have been studied owing to their synthetic utility[1-3]. Although Pd-catalysts enjoy widespread application in organic synthesis[4] the price of them, sometimes is chemist's concern.

When temperatures in the order of 200°C or above are required for thermal reaction the choice of solvents is limited. Although such temperatures can be achieved through heating of low boiling solvents under pressure in conventional autoclaves[5], careful control and tedious batch work is

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required as well as time consuming heating up. Safety, economic and environmental consideration also[6,7] dictate the need for decreased usage of organic solvents and catalysts in organic laboratories and in industrial processes.

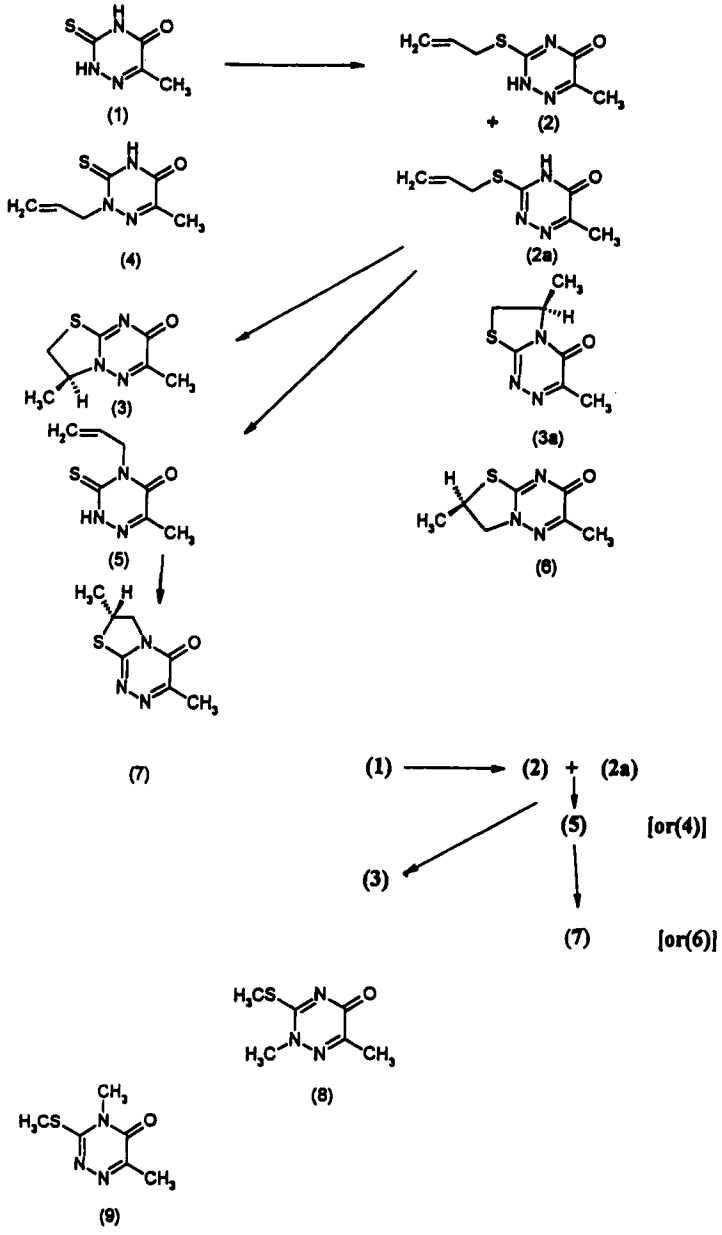
Microwave irradiation in organic synthesis is presenly widely used[8,11]. Dry media techniques by microwave heating have attracted much attention[12–14] since there is no need to use either sealed tube or closed and transparent teflon vessels. Recently Claisen type sigmatropic shifts of allyl phenyl ether[15] and propargyl naphthyl ethers[16] by microwave assisted reaction have been reported.

In honor of professor Abbas Shafiee[17] who worked for many years with dedication in the field of synthetic heterocyclic chemistry we wish to report the regioselective cyclization of ***2*** to ***3*** and the regioselective S→N allylic rearrangment of ***2*** to ***5*** induced by microwave irradiation. This rearrangment gave us an opportunity to synthesis 2-substituted thiazolo [2,3-c] [1,2,4] triazin -4-one ***7***.

RESULTS AND DISCUSSION

3-sulfanyl 6-Methyl-4H-[-1,2,4-triazine]-5-one ***1*** was caused to react with allyl bromide in the presence of potassium hydroxide to afford 3-allylsulfanyl-6-methyl-2H-[1,2,4-triazin]-5-one ***2***. This compound exist as a mixture of tautomers ***2*** and ***2a***. Spectroscopic analysis of 3-allylsulfanyl -2H-[-1,2,4-triazin]-5-ones indicates that the compound of type ***2*** is the main tautomer[18] and alkylation of this type occurs at the N-2 nitrogen[19] (Scheme).

Many efforts have been devoted to prepare a variety of heterocyclic systems by using acid-mediated. cyclization intramolecular functionalization of olefines as the ring forming step[20]. In spite of the interest in the rapid synthesis of a variety of heterocyclic systems under microwave irradiation in domestic microwave ovens[21] a literature survey revealed that little attention has been focused towards intramolecular cyclization of olefines. Nitrogen bridgehead heterocycles have shown antibacterial, antifungal and antiviral activity. Keeping in view the importance of MORE(Microwave Induced Organic Reaction Enhancement), chemistry and biological importance of nitrogen bridghead heterocycles it was thought worthwhile to



SCHEME

develop a method for the rapid synthesis of thiazolotriazine of type ***3*** or ***3a*** using microwaves.

In the classical approach, cyclization of ***2*** to ***3*** required 50 min in conc sulphuric acid. When ***2*** was placed under microwave irradiation for 5 min without any solvent, a mixture was obtained which was directly subjected to column chromatography to afford a crystalline compound as a major product (58%). Mass spectrum of this compound indicated the same parent peak as its precursor. In its ^{1}HNMR the olefinic protons remained, there was no doublet for methyl on the thiazole ring, however the chemical shift for allylic methylene was considerably different from that of the starting material ***2***. ^{1}HNMR of compound ***2*** showed allylic methylene at δ 3.8 as a doublet whereas the allylic methylene in the product appeared at δ 4.6. This result clearly indicates that instead of cyclization, a [3,3] sigmatropic shift has occurred to yield either ***4***or ***5***. However we could not discriminate between these two isomers using spectroscopic methods. In order to circumvent this problem, we decided to cyclize either ***4*** or ***5*** to the corresponding thiazolotriazine. As part of our ongoing studies on heterocyclization we have recently demonstrated the use of acid catalysis[22]. When either ***4*** or ***5*** was heated in sulphuric acid a single (tlc) compound was isolated. Mass spectrum of this compound showed a parent peak at the same m/z as its precursor. In the ^{1}HNMR of this compound no olefinic protons were present and a doublet which integerated for three protons appeared for a methyl group on the thiazole ring. These observation indicated the formation of a fused five membered ring (***6*** or ***7***).

It has been reported that 3,4-disubstituted triazinone ***9*** shows the absorption maxima uniformly at the longer wavelengths compared with those of 2,3- diubstituted ***8***[5,23,24]. The cyclized product (***6*** or ***7***) showed a similar absorption, shapes and maxima as ***9***. This means microwave irradiation has implemented the [3,3] sigmatropic shift of the 3-allylthio compound ***2*** regioselectively to N-4 of the 1,2,4-triazinone nucleus to afford ***5***.

Consequently cyclization of ***5*** could only afford ***7***. However two points are noteworthy to be mentioned. First, column chromatography of the reaction of ***2*** under microwave irradiation gave as by-producte small amounts of ***4*** and deallylated product ***1*** and secondly, in fact ***7*** exists as a diastereomeric mixture. The diastereomers were not separated.

EXPERIMENTAL

Melting points (uncorrected) were obtained on a Büchi 530, ^{1}HNMR spectra were recorded on a Brucker Ac 80 spectrometer in solvents and with internal standard. IR spectra were recorded on a Perkin Elmer model 883 using KBr disc, Mass spectra were obtained on a Varian CH-7. UV spectra were recorded on a Lambda Perkin Elmer. Microwave irradiation was carried out in a National oven Model 6755 at power of P/W 900.

3-Allylsulfanyl-6-methyl-2H-[1,2,4] triazin-5-one 2

Compound *1* (0.5g; 3.49 mmol) was dissolved in potassium hydroxide (0.26g) in BuOH (20 ml). To this solution, allyl bromide (0.47g, 0.33 ml, 3.87 mmol) was added dropwise at ambient temperature. After that the reaction mixture was stirred at the same temperature for 2h, the solvent was removed in vacuo and the residue was dissolved in $CHCl_3$ and then washed with H_2O. The organic extract was dried over Na_2SO_4 and concentrated to give a crystalline product. yield (0.46g, 71%), m.p 180–182., ^{1}HNMR, $\delta(CDCl_3)$ 2.3(s, 3H, Me), 3.85(d, J=6Hz, 2H, CH_2), 5.2–5.4 (m, 2H, CH_2), 5.6–6.2 (m, 1H, =CH). IR(KBr disc) M^-.S, M^+, m/z 183.

3,6-dimethyl-2,3-Dihydro-thiazolo [3,2-b][1,2,4] triazin –7-one 3

Compound *2* (0.2g, 1.09 mmol) was dissolved in conc H_2SO_4 (5 ml). The reaction mixture was kept at 50°C for 50 min and then poured onto crushed ice. This solution was neutralized with addition of NaOH (10%) till pH-8. The organic materials were extracted with $CHCl_3$. It was dried over Na_2SO_4 and evaporated to dryness to afford. the title compound. yield (0.16g, 80%), mp. 148–150°C, ^{1}HNMR, $\delta(CDCl_3)$, 1.55(d, J=6.0Hz, 3H, Me), 2.49(s, 3H, Me) 3–3.7(m, 2H, diastereotopic CH_2, 4.5–4.8(m, 1H, CH) IR(KBr disc), 3423, 2929, 1650, 1486, 1373, 1229, 1135, 777Cm^{-1}, M.S, m/z, M^+, 183.UV (EtOH) λmax 248nm.

3-sulfanyl 6-methyl-4-allyl-2H-[1,2,4-triazine]-5-one 5

Compound *2*(0.4; 2.18mmol) contained in an Erlenmreyer (50 ml) was placed in a microwave oven (National) and irradiated for 5–6 min with

power of P/W 900. The reaction mixture was allowed to cool to room temperature. The crude was directly subjected to column chromatography using pet ether/ EtOAc, 9:1 as eluent to obtain the title compound. yield (0.25g, 58%), mp, 99–100°C. ^{1}HNMR δ(d_6-DMSO), 2.2(s, 3H, Me), 4.6(d, 6Hz, 2H, CH_2), 5–5.2 (m, 2H, CH_2) 5.4–5.9 (m, 1H, CH), IR(KBr disc) 3257, 3102, 1680, 1512, 1222, 750Cm^{-1}, M.S, M/z, M^+, 183.

3,7-Dimethyl-6,7-dihydro-thiazolo [2,3-c] [1,2,4]triazin-4-one 7

Compound *5* (0.1g, 0.5.4 mmol) was dissolved in conc sulphuric acid (3 ml). This reaction mixture was kept at 50°C for 50 min and then poured onto crushed ice. The solution was neutralized till pH8 by addition of aq NaOH. The organic material was extracted with ethyl acetate, the extract dried over Na_2SO_4 and evaporated to dryness to afford the title compound, yield (0.07 g, 70%) mp 104–106°C, ^{1}HNMR, δ ($CDCl_3$), 1.5(d, J=6, 3H, Me) 2.4(s, 3H, Me), 4.4(m, 2H, diastereotopic CH_2), 4.5–4.8 (m, 1H, CH), IR ν(KBr disc), 3426, 3112, 1657, 1478, 1244, 1054, 877Cm^{-1}, M.S, m/z, M^+. 183. UV(EtOH), λmax, 290nm.

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