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Study On Synthesis Some Thiazoles Derivaties Using Microwave Oven

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***Abstract*—Substituted thiazole derivaties are very well known. This system is widely used in organic chemistry on synthesis new compounds. On the other hand, thiazoles were extensively studied as bioactive compounds. They possess remarkable biological activities, such as antimicrobial, antiviral, anticancer, anti-inflammatory.... In this research, some derivatives of thiazole were synthesized by some chromenes. Structures of obtained products were indentified by modern method such as: IR, ^{1}H-NMR,^{13}C-NMR spectra. Antifungal activities of the obtained compounds have been tested.**

Keywords—component; Synthesis, thiazole, chromene, antifungal, powdery mildew, rose diseases.

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1. INTRODUCTION

Thiazole is a heterocyclic compound that have antimicrobial, antifungal ability quite well such as bacteria:*S. Aureus, S. Paratyophi, E. Coli, V. Cholera and S. Sonnei, Aspergillus niger* and*Candida albicans* [1,2].

Powdery mildew of rose disease often appears in humid weather conditions, heavy rains, high air humidity. This disease usually grows rapidly in the spring. Powdery mildewhas symptoms of grayish-white powder, a non-certain morphology. The fungal disease often attacks on leaves, young shoots and flower buds.Powdery mildewreduces photosynthesis efficiency and plant vitality.If flora is infected severely, it can damage stems, branches, buds and flowers, deformed leaves, dry stem, little buds, non-blooming flowers, stunted trees, affect the growth greatly, development of plants, decrease productivity and quality of flowers. Starting from the fact above, we conducted research synthesis of a number of thiazole derivatives and the first step of testing the treatment of rose's fungal diseases.

2. MATERIALS AND METHODS

2.1. The synthesis method of Thiazole derivatives

The synthesis process of some thiazole derivatives which is carried out from 3 inputs is chromene compounds with different substituent groups – substance(1). Diagram of synthesis is shown in Figure 1.

Dissolvesubstance 1 (0,01mol) completely in acetic acid (25mL) and Potassium carbonate solution (5mL) is saturated. Stir by amagnetic stirrer. Add chloroacetyl chloride (0,12 mol) slowly into the mixture , keep the reaction temperature at 0-5^{0}C. After that, continue stirring for 30 minutes at room temperature. The product which is washed with acetic acid 50% and recrytallized in ethanol solvent obtained 3 corresponding product – substance (2) [3].

Next, poursubstance 2 (0,001 mol) with amine (0,001mol), refluxing using in 2 hours. After the reaction occurs completely, cooling the mixture in an ice tank, crystals are constituted. The product is recrystallized in ethanol[4,5].

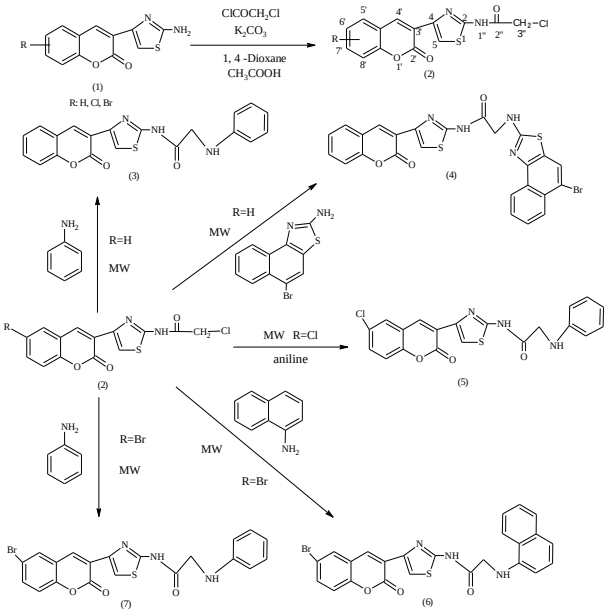

Figure 1: Diagram of synthesis of thiazole derivatives

2.2.Methods of analyzing the structure and product activity

The structure of products is analyzed by modern physicochemical methods: The purity of the products is determined by thin-layer chromatography.The structure of the product is demonstrated by mass spectrometry methods^{1}H-NMR và ^{13}C-NMR. The melting point is measured by the capillary electrophoresis method.^{1}H-NMR spectrum and^{13}C-NMR spectrum are recorded on optical spectrograph AVANCE spectrometer (BRUCKER, German)at a frequency of 500 MHz, DMF-d6 solvent, TMS internal standard. Biological activity was tested in several kinds of *E. Coli, S. Aureus* bacteriaand *C.abicans*fungalby disk diffusion method.

3. RESULTS AND DISCUSSION

3.1. The synthesis result of derivatives (2)

The products (2) are synthesized from chromene derivatives (1) andchloroacethylchloride. The structure of products is determined by modern physicochemical methods:^{1}H-NMR spectrum and^{13}C-NMR spectrum. Specifically:

a) Substance(2a) with R=H:

2-chloro-*N*-[4-(2-oxo-2*H*-chromen-3-yl)-1,3-thiazol-2-yl]acetamide

Reaction efficiency gets 72%. Melting point: 156-158^{o}C. ^{1}H-NMR (DMSO-d_6, δ, ppm): 11.22(2H, s, NH_2); 10,12 (1H, s, H-5);8,1(1H, H-4'); 7.85 (m, 1H, H-5'); 7.59 (m, 1H, H-7');7.45 (d, *J* = 7.5 Hz, 1H, H-8'); 7.42 (m, 1H, H-6'); 4.5 (2H-CH_2).^{13}C-NMR (DMSO-d_6, δ, ppm): 168.4 (C-2"); 162.9 (C-2); 159 (C-2'); 154.3 (C-O); 142 (C-4'); 130.1 (C-7'); 128.4 (C-5); 128 (C-6').

b) Substance(2b)with R=6'-Cl:

2-chloro-*N*-[4-(6-chloro-2-oxo-2*H*-chromen-3-yl)-1,3-thiazol-2-yl]acetamide

Reaction efficiency gets 58%.Melting point: 190-192^{o}C. ^{1}H-NMR (DMSO-d_6, δ, ppm): 12.69(2H, s, NH_2); 7,99 (1H, s, H-5);7,65(1 H, H-4'); 7.75 (m, 1H, H-5'); 7.59 (m, 1H, H-7'); 7.45 (d, *J* = 7.2 Hz, 1H, H-8'); 4.43 (2H-CH_2).^{13}C-NMR (DMSO-d_6, δ, ppm): 165.3 (C-2"); 161,7 (C-2); 159.2 (C-2'); 151.3 (C-O); 134.5 (C-6'). (C-4'); 129.7 (C-7'); 126.4 (C-5').

c) Substance (2c)with R=6'-Br:

N-[4-(6-bromo-2-oxo-2*H*-chromen-3-yl)-1,3-thiazol-2-yl]-2-chloroacetamide

Reaction efficiency gets 57%. Melting point: 190-192^{o}C.^{1}H-NMR (DMSO-d_6, δ, ppm): 12.44(2H, s, NH_2); 8,03 (1H, s, H-5);7.95(1H, H-4'); 7.73 (m, 1H, H-5'); 7.69 (m, 1H, H-7'); 7.55 (d, *J* = 7.1 Hz, 1H, H-8'); 4.53 (2H-CH_2).^{13}C-NMR (DMSO-d_6, δ, ppm): 169 (C-2"); 163,7 (C-2); 159.3 (C-2'); 155,3 (C-O); 134,5 (C-6'). (C-4'); 126.5 (C-7'); 123.1 (C-5').

3.2. The synthesis result of thiazolederivatives

The thiazole products (3), (4), (5), (6), (7) are newly synthesized which base on the foundation of traditional refluxing using method. It has not been found in reference materials yet. The compounds obtained with a quite high efficiency, the structure of products is demonstrated by theresonance spectrum method from ^{1}H-NMR nuclear and^{13}C-NMR. The resonance signals which appear on spectrograms are all suitable for predicting structure. Specifically:

a) Substance(3) with R=H and amin $C_6H_5NH_2$

N-[4-(2-oxo-2*H*-chromen-3-yl)-1,3-thiazol-2-yl]-2-(phenylamino)acetamide

Reaction efficiency gets68%. The melting point: 178-180^{o}C. ^{1}H-NMR (DMSO-d_6, δ, ppm): 9,15 (1H, s, H-5);8.75(1H, H-4'); 7.86 (m, 1H, H-5'); 7.62 (m, 1H, H-7'); 7.45 (d, *J* = 7.2 Hz, 1H, H-8'); 7.23(2H, m, H-3"' và H-5"'); 6.81 (d, *J* =7.1, 2H, H-2"'và H-6"'); 6,65 (1 H, m, H-4"') ;6.25 (1H, s, H-3");.^{13}C-NMR (DMSO-d_6, δ, ppm): 168.7 (C-2"); 162.7 (C-2); 161.5 (C-2'); 155.5 (C-O); 147.5 (C-1"'); 144.5 (C-6'). 130.1 (C-3"' và C-5") 127.3(C-5'); 126.5 (C-7'); 116.7 (C-8'); 112.5 (C-2"' và C-4"); 49,5 (C-3").

b) Substance(4) with R=H and amin $C_{11}H_7BrN_2S$

2-[(5-bromonaphtho[1,2-*d*][1,3]thiazol-2-yl)amino]-*N*-[4-(2-oxo-2*H*-chromen-3-yl)-1,3-thiazol-2-yl]acetamide

Reaction efficiency gets 68%. The melting point: 178-180^{o}C. ^{1}H-NMR (DMSO-d_6, δ, ppm): 8.95 (1H, s, H-5);8.82(1H, s, H-6"); 8.13 (1H,s, H-4"); 8.10 (1H, d, *J*= 7.5 -11"); 7.85(1 H, s, H-8"');7.65 (1H, m, H-6"); 7.60 (1H, m, H-10"'); 7.48 (1H, m, H-9"'); 7.44 (1H, d, *J* = 7.5, H-8'); 6.02 (1 H, s,NH); 4.5 (2H- CH_2). ^{13}C-NMR (DMSO-d_6, δ, ppm): 198,7 (C-2"); 175.2 (C-2"') 161.9 (C-2); 165.1 (C-2'); 155.5 (C-O); 150 (C-4); 147.9 (C-4"'); 147.1 (C-4').

c) Substance(5) with R=Cl and amin $C_6H_5NH_2$

N-[4-(6-chloro-2-oxo-2*H*-chromen-3-yl)-1,3-thiazol-2-yl]-2-(phenylamino)acetamide

Reaction efficiency gets 83%. The melting point: 218-219^{o}C. ^{1}H-NMR (DMSO-d_6, δ, ppm): 8.95 (1H, s, H-5);8.15(1H, H-4'); 8.02 (m, 1H, H-5'); 7.45 (m, 1H, H-7'); 7.30 (d, *J* = 7.2 Hz, 1H, H-8'); 7.09(2H, m, H-3"' và H-5"'); 6,83 (d, *J* = 7.1, 2H, H-2"'và H-6"'); 6.65 (1 H, m, H-4"') ;6. 28 (1H, s, NH);.^{13}C-NMR (DMSO-d_6, δ, ppm): 198.5 (C-1"); 165.2 (C-2); 161.5 (C-2'); 151.5 (C-O);149.5)C-4); 147,5 (C-1"'); 135.1 (C-6'); 129.5 (C-7'); 129.1 (C-3'); 128.5)C-3"' and C5"'); 125.5 (C-5'); 124.5 (C-5); 112.5 (C-2"' và C-4'"); 55.7 (C-CH_2).

d) Substance(6) with R=Br and amin $C_{10}H_9NH$

N-[4-(6-bromo-2-oxo-2*H*-chromen-3-yl)-1,3-thiazol-2-yl]-2-(naphthalen-1-lamino)acetamide

Reaction efficiency gets 72%. The melting point: 214-215^{o}C. ^{1}H-NMR (DMSO-d_6, δ, ppm): 8.85 (1H, s, H-5);8.13(1H, H-4'); 8.05 (m, 1H, H-5'); 7.79 (1H, m, H-4"') 7.75 (1H, m, H-7"'); 7.65 (m, 1H, H-7'); 7.56 (1 H, d, *J*= 7.2, H-2"'); 7.55 (1H,m, H-6"'); 7.45 (1 H, m H-3"'); 7.25 (d, *J* = 7.2 Hz, 1H, H-8'); 7.12 (1H, m H-8"'); 7,09(2H, m, H-3"' và H-5"'); 6.50 (1 H,s, NH); 4,50 (2H-CH_2).^{13}C-NMR (DMSO-d_6, δ, ppm): 196.5 (C-1"); 164.5 (C-2); 162.5 (C-2'); 155.5 (C-O);149.4 (C-4); 146,1 (C-4'); 145.9 (C-1"'); 135,1 (C-5'); 129.5 (C-3'); 129,1 (C-3"'); 125.5 (C-4"'); 123.5 (C-6"'); 123.1 (C-7"'); 124.1 (C-5); 117.5 (C-8'); 56.5 (C-CH_2).

e) Substance(7) with R=Br and amin $C_6H_5NH_2$

N-[4-(6-bromo-2-oxo-2*H*-chromen-3-yl)-1,3-thiazol-2-yl]-2-(phenylamino)acetamide

Reaction efficiency gets 68%. The melting point: 178-180^{o}C. ^{1}H-NMR (DMSO-d_6, δ, ppm): 9.15 (1H, s, H-5);8.55(1H, H-4'); 7.92 (m, 1H, H-5'); 7.55 (m, 1H, H-7'); 7.30 (d, *J* = 7.5 Hz, 1H, H-8'); 6.95(2H, m, H-3"' và H-5"'); 6,73 (d, *J* = 7.1, 2H, H-2"'và H-6"'); 6.55 (1 H, m, H-4"') ;6. 25 (1H, s, NH);.^{13}C-NMR (DMSO-d_6, δ, ppm): 199.5 (C-1"); 175.2 (C-2); 169.5 (C-2'); 155.5 (C-O);149.5)C-4); 145,1 (C-1"'); 140.5 (C-6'); 130.5 (C-7') ; 128.5 (C-3'); 125.5)C-3"' và C5"'); 123.1 (C-5'); 122.5 (C-5); 112.0 (C-2"' và C-4'"); 54.7 (C-CH_2).

3.3. Survey of antimicrobial, antifungal ability of thiazole derivatives

The antimicrobial, antifungal ability of thiazole derivatives is tested on*E.coli, S.aureus bacteria*and *C.abicans fungal*, the result is shown in table 1.

Table 1: The result of testing the biological activity of thiazole derivatives

Diameter (mm)

Thiazole derivatives	*E.coli*		*S.aureus*		*C.abicans*	
	100µg/ml	200µg/ml	100µg/ml	200µg/ml	100µg/ml	200µg/ml
(3)	-	10	-	16	10	28
(4)	-	12	-	18	13	24
(5)	-	17	14	23	18	33
(6)	-	22	21	30	29	38
(7)	-	18	19	26	25	36

The thiazole derivatives (3), (4), (5), (6), (7) are tested antimicrobial, antifungal activity on objects as*E. Coli, S. Aureus* and*C.abicans* by the disk diffusion method (Table 1). With concentration 100µg/ml, the derivatives do not have activity with E. coli, with S. aureus and C. Abicans have the activated derivatives (5), (6), (7) . Almost thiazole derivatives have antibacterial, antifungal activity at concentration 200µg/ml. In particular, the best expression is thederivative (6) with a diameter that influences up to 38mm.

4. CONCLUSION

Synthesize 5 thiazole derivatives from chromene compounds. The product structure is determined by modern physicochemical methods: ^{1}H-NMR and^{13}C-NMR. Testing the antibacterial, antifungal ability on *E. coli, S. aureus and C. abicans*. The result shows that the obtained products all have antibacterial, antifungal ability at testing concentration 200µg/ml. In particular, showing the best activity is the product (6).

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