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Research Article

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Microwave assisted synthesis of 3-(3-phenyl-7*H*[1,2,4]triazole[3,4][1,3,4] thiadiazin-6-yl)-chromen-2-ones

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ABSTRACT

An efficient method for the synthesis of title compounds viz., 3-(3-phenyl-7H-1,2,4]triazole[3,4][1,3,4]thiadiazin-6-yl)-chromen-2-ones ***(3)*** *has been reported by the condensation of 3-(2-bromoacetyl)chromen-2-ones* ***(1)*** *with 4-amino-5-phenyl-4H[1,2,4]triazole-3-thiols* ***(2)****. The reaction has been carried out under conventional as well as under microwave irradiation conditions. The latter procedure has been found to be much more efficient in terms of reaction time and yield. The structures of all the compounds have been established on the basis of their spectral and analytical data.*

Keywords: 3-(2-bromoacetyl)chromen-2-one, 4-Amino-5-phenyl-4H[1,2,4]triazole-3-thiol, ethylene glycol, DMF and MWI.

INTRODUCTION

A survey of literature reveals that several triazole derivatives have a wide range of therapeutical properties [1-5]. They are also known to possess antiasthmatic [6], anti-inflammatory [7], antimicrobial [8], antifungal [9-10], and antibacterial [11] activities. The wide spectrum of biological activities exhibited by various triazole derivatives has made them an important class of chemotherapeutic agents. Further, it has been found that several chromen-2-one derivatives exhibit important biological activities such as anticancer [12] , antibacterial [13] and spasmolytic [14] activities. In view of the above observations and in continuation of our studies in the field of oxygen and nitrogen heterocycles of potential biological interest, the synthesis of certain chromen-2-one derivatives containing triazole moiety have been carried out.

EXPERIMENTAL SECTION

General Conditions: Melting points are uncorrected and were determined in open capillary tubes in sulphuric acid bath. TLC was performed on silica gel-G and spotting was done using iodine or UV light. IR spectra were recorded using Perkin-Elmer 1000 instrument in KBr phase,

^{1}H NMR on VARIAN 400 MHz instrument and Mass spectra on Agilent-LC-MS instrument giving only $M^{\cdot+}$+1and $M^{\cdot+}$-1values.

General procedure for the synthesis of 3 (conventional method): A mixture of **1** (0.5gm, 0.01 mol), **2** (0.5 gm, 0.01 mol) and ethylene glycol (25 mL) was heated at 100 °C for 4 hr. The completion of the reaction was monitored

by TLC. After the complete disappearance of the starting material on TLC, the reaction mixture was cooled to RT and poured in to ice-cold water (50 ml). The separated solid was filtered, thoroughly washed with water and dried to obtain the crude product. The latter was recrystallized from ethanol to yield pure **3**.

3b: IR (KBr): ν 1722 cm^{-1} (strong, sharp, lactone carbonyl due to coumarin ring).; ^{1}H-NMR spectrum (DMSO-d_6/TMS): δ 2.23 (s, 3H –C**H$_3$**-), 4.30 (s, 2H, -C**H$_2$**-S), 7.04-9.08 (complex, m. 9H, **aryl protons**), Mass: m/z 374 ($M^{\cdot+}$+1):. Element. Anal: Found C 67.61%, H 4.08%, N 11.28%; $C_{21}H_{15}N_3O_2S$ requires C 67.54%, H 4.05%, N 11.25%.

3c: IR (KBr): ν 3380-2940 cm^{-1} (broad, medium, bonded OH group) and at 1730 cm^{-1} (strong, sharp lactone C=O, due to coumarin ring).; ^{1}H-NMR spectrum (DMSO-d_6/TMS): δ 4.30 (s, 2H, -C**H$_2$**-S), 7.02-9.10 (complex, m, 9H, **aryl protons**) 11.9 (s, 1H, D_2O exch., –O**H**), Mass: m/z 376 ($M^{\cdot+}$+1). Element. Anal: Found. C 64.05%, H 3.51%, N 11.28%; $C_{20}H_{13}N_3O_3S$ requires C 63.99%, H 3.49%, N 11.19%.

3d: IR (KBr): ν 3410-2980 cm^{-1} (broad, medium OH group), and at 1741 cm^{-1} (strong, sharp lactone C=O, due to coumarin ring).; ^{1}H-NMR spectrum (DMSO-d_6/TMS): δ 2.30 (s, 3H, Ar- **CH$_3$**), 4.29 (s, 2H, -C**H$_2$**-S),7.02-9.10 (complex, m, 8H, **aryl protons**), 11.42 (s, 1H, D_2O exch., –O**H**), Mass: m/z 390 ($M^{\cdot+}$+1). Element. Anal: Found C 64.80%, H 3.91%, N 10.81%; $C_{21}H_{15}N_3O_3S$ requires C 64.77%, H 3.88%, N 10.79%.

3e: IR (KBr): ν 1738 cm^{-1} (strong, sharp, lactone carbonyl group, due to coumarin ring).; ^{1}HNMR spectrum (DMSO-d_6/TMS): δ 2.30 (s, 3H, Ar-OC**H$_3$**), 4.21 (s, 2H, -C**H$_2$**-S),7.04-9.21 (complex, m, 9H, **aryl protons**), Mass: m/z 390 ($M^{\cdot+}$+1):. Element. Anal: Found C 64.82%, H 3.93%, N 10.82%; $C_{21}H_{15}N_3O_4S$ requires C 64.77%, H 3.88%, N 10.79%.

3f: IR (KBr): ν 1720 cm^{-1} (strong, sharp lactone carbonyl group, due to coumarin ring),; ^{1}HNMR spectrum (DMSO-d_6/TMS): δ 2.30 (s, 3H, Ar-**CH$_3$**), 2.56 (s, 3H, Ar-OC**H$_3$**), 4.23 (s, 2H, -C**H$_2$**-S),7.04-9.10 (complex, m. 8H, **aryl protons**). Mass: m/z 404 ($M^{\cdot+}$+1):. Element. Anal:Found C 65.52%, H 4.28%, N 10.47%; $C_{22}H_{17}N_3O_4S$ requires C 65.49%, H 4.25%, N 10.42%.

3g: IR (KBr): ν 1738 cm^{-1} (strong, sharp lactone CO group, due to coumarin ring).; ^{1}H-NMR spectrum (DMSO-d_6/TMS): δ 4.18 (s, 2H, -C**H$_2$**-S),7.10-9.08 (complex, m. 8H, **aryl protons**), Mass: m/z 428 ($M^{\cdot+}$+1):. Element. Anal: Found C 56.11%, H 2.63%, N 9.88%; $C_{20}H_{17}Cl_2N_3O_3S$ requires C 56.09%, H 2.59%, N 9.81%.

3h: IR (KBr): ν 1740 cm-1 (strong, sharp lactone CO group, due to coumarin ring).; ^{1}H-NMR spectrum (DMSO-d_6/TMS): δ 2.30 (s, 3H, Ar-**CH$_3$**), 4.10 (s, 2H, -C**H$_2$**-S-), 7.04-9.12 (complex,

m, 7H, **aryl protons**) 3255-3021 cm^{-1} (OH), 1714 (C=O). Mass: m/z 443 ($M^{\cdot+}$+1):. Element. Anal: Found. C 57.04%, H 2.99%, N 9.55%; $C_{21}H_{13}Cl_2N_3O_3S$ requires C 57.02%, H 2.96%, N 9.50%.

General procedure for the preparation of 3 under Microwave Irradiation method: A mixture of **1** (0.01 mol) and **2** (0.01 mol) in dry DMF (10 mL) was taken in a 50 ml Erlenmeyer Flask and subjected to microwave irradiation in domestic microwave oven at 450W level for a period of 10-15 minutes. The completion of reaction was monitored by TLC. The reaction mixture was cooled to RT and poured into ice-cold water (50 ml). The separated solid was filtered, washed with water and dried to obtain crude **3**. It was recrystallized from ethanol to obtain pure **3**.

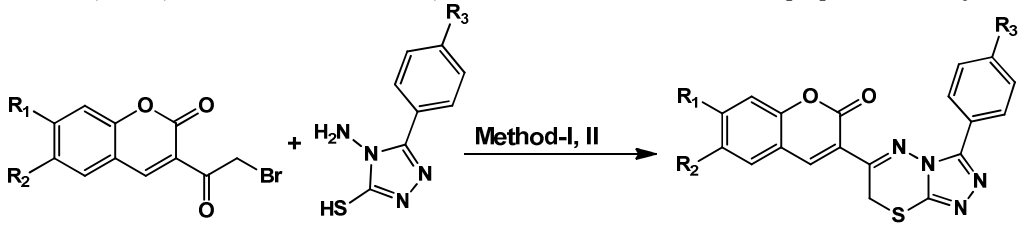
Physical data of compounds **3a-h** is already given above. For Melting Points and yields, please refer to the Table-1.

RESULTS AND DISCUSSION

Reaction of 3-(2-bromoacetyl)-chromen-2-one [15] (**1a** i.e., **1**, R_1=R_2=H), with 3-aryl-4-amino-5-mercapto-1,2,4-triazole [16] (**2a,** i.e., R_3=H), in ethylene glycol under heating at 100 °C for 4 hrs, gave a product which has been characterized as 3-(3-phenyl-6H-7-thia-2,3,4-triazainden-5-yl)-chromen-2-one (**3a,** i.e., 3, R_1=R_2=R_3=H**),** on the basis of its spectral data. Thus, its IR spectrum in KBr, showed a strong peak at 1722 cm^{-1} due to lactone C=O group, the second absorption at around 1680 cm^{-1} was absent, showing the disappearance of keto carbonyl group

(C=O), which was promptly seen in the IR of starting compound **1a** (i.e., 1, R_1=R_2=H). Its ^{1}H-NMR spectrum in DMSO-d_6/TMS showed signals at δ 4.20 (s, 2H, -S-**CH_2**), and at 6.99-8.89 (complex, m, 10H, **aryl protons**). Its mass spectrum when recorded in the CI method showed a molecular ion peak at m/z (i.e., $M^{\cdot+}$+1) at 360 (base peak) corresponding to a molecular mass of 359.

The above reaction of **1a** (i.e., **1**, R_1=R_2=H) with **2a** (i.e., 2, R_3=H) was found to be a general one and was extended to other derivatives namely, **3b,** (i.e., **3,** R_1=R_2=H,R_3=CH_3), **3c** (i.e., **3,** R_1=OH,R_2=R_3=H), **3d**, (i.e., **3,** R_1=OH,R_2=H,R_3=CH_3), **3e**, (i.e., **3,** R_1=OCH_3, R_2=R_3=H), **3f**, (i.e., **3,** R_1=OCH_3,R_2=H,R_3=CH_3),**3g**,(i.e., **3,**R_1=R_2=Cl,R_3=H), **3h**, (i.e., **3,** R_1=R_2=Cl,R_3=CH_3). All these derivatives have been prepared similarly.

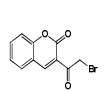
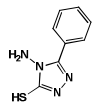
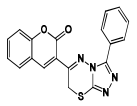
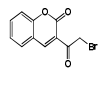
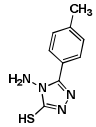
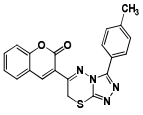
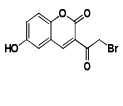
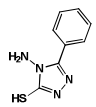
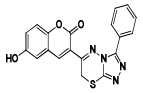
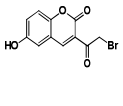
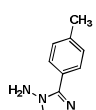
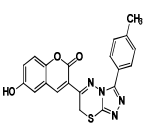
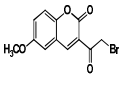
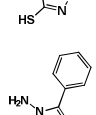
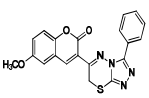
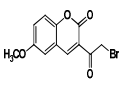
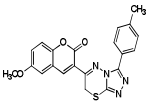


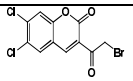
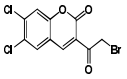
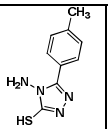
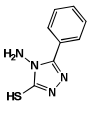
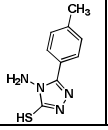
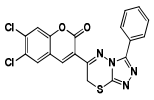
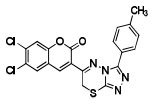
1 **2** **3**

Method-I : ethyleneglycol / 100 ^{0}C / 4-6 h
Method-II: DMF / MWI / 10-15 min.

3a (i.e., 3, R_1=R_2=H) could also be prepared in an alternative method using microwave irradiation method. Thus, **1a** (i.e., **1, R_1=R_2=H**) on treating with **2** in N, N-dimethylformamide (DMF) under micro-wave condition for 10 min, gave a product identical with **3a** (i.e., **3**, R_1=R_2=H) in all respects (m.p., m.m.p., and co-tlc analysis). (**Scheme-I**). Similarly, **3b-3h** compounds have been prepared using MWI of reactants **1a-1h** and **2a-2h** in DMF respectively.

Table-1: Physical data of compounds (3a-h)

S. No.	Starting material		Product	M.P (^{0}C)	Method-I (conventonal)		Method-II (MWI)	
	1	2	3		Time (Hrs)	Yield (%)	Time (mins)	Yield (%)
a				212	4	80	10	88
b				217	4 ½	77	12	82
c						71	15	83
d				248	5	73	15	80
e				231	5 ½	74	13	79
f				221	4 ½	69	15	80
g				247	6	76	11	82
h						70	10	84

	 	  	 	236 241	4 4 ½			

The results of these two methods (i.e., conventional, microwave method are summarized in Table-1. A comparison between these two methods shown that in the microwave technique the reaction time is drastically reduced and the yields are comparable.

CONCLUSION

In conclusion, we simple and efficient methods have been developed for preparation of title compound **5** in conventional as well as MWI conditions. The MWI system gave good results in terms of reaction time and product yields.

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