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Synthesis of Some New N-[1-(Benzocoumarin-3`-yl)Ethylidene]Hydrazonothiazolidine, Thiazole and 1, 3, 4-Thidiazole Derivatives

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Abstract: Condensation of 3-acetylbenzo[5,6]coumarin (**1**) with hydrazine-carbodithioate esters and/or thiocarbohydrazide gave the corresponding N-[1-(benzocoumarin-3`-yl)ethylidene]hydrazonecarbodithioate (**2a,b**) and 1,5-bis[1-(benzocoumarin-3`-yl)ethylidene]thiocarbohydrazide (**3**) respectively. Treatment of 2a with ethanolic ammonia solution and/or amines gave the corresponding thiosemicarbazone derivatives (4a-f). The reactions of 4a-f with ethyl bromoacetate/AcONa and ω-bromo derivatives were investigated, where thiazolidinones 5, 6 and thiazoles (**9a,b**) were obtained. Moreover, hydrazonecarbodithioate (**2**) underwent heterocycliczation upon treatment with hydrazonoyl halides (**10**) with Et_3N to give the corresponding 2,3-dihydro-1,3,4-thiadiazoles (**11a-d**) via 1,3-dipolar cycloaddition and/or nuclophilic substiution. The structures of the new derivatives were elucidated by elemental analysis, IR, PMR and mass spectra.

Keywords: Benzocoumarin, 1,3,4-Thiadiazol, Thiazolidinone

1. Introduction

Coumarin nucleus is found in a variety of natural products exhibiting various pharmacological effects. Derivatives of coumarin also form component of important drugs having varied properties. There are excellent monographs and review articles [1-5] describing the structure, synthetic reaction and properties of coumarins. Neumerous reports in the literature describing antimicrobial [6, 7], antiradiation [8, 9], anti-coagulants [10-12] and their biological activities [13, 14].

2. Results and Discussion

3-Acetylbenzo[5,6]coumarin (**1**) was used as our starting material [15]. Thus, treatment of **1** with methyl/ or benzyl hydrazinecarbodithioate [16, 17] in ethanol afforded the corresponding dithioesters (**2a,b**). The structure of **2** was confirmed by elemental analysis and spectral data. The mass spectra of **2a,b** gave a fragment peaks corresponding to ([M^+]-CH_3SH/or $C_6H_5CH_2SH$) instead of molecular ion peak. Condensation of 1 with thiocarbohydrazide in hot dioxane afforded1,5-bis[1-(benzocoumarin-3`-yl)ethylidene]thiocarbohydrazide (**3**), its structure was confirmed by elemental analysis and spectral data. The mass spectrum showed a fragment peak corresponding to ([M^+]-[1-(benzo[5,6]-coumarin-3-yl)ethylidene]hydrazone. Treatment of **2** with ethanolic ammonia solution or amine afforded the corresponding thiosemicarbazone derivatives (**4a**-f, Figure 1).

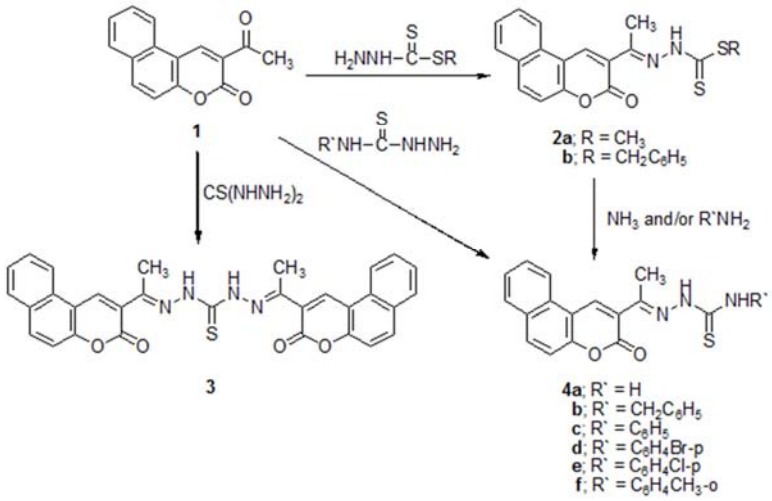

Figure 1. *Condensation of 3-Acetylbenzo[5,6]coumarin with hydrazine derivatives.*

These products were obtained directly from condensation of 1 with thiosemicarbazide derivatives (m. p and mixed m. p and identical spectra). The mass spectrum of **4c** showed no molecular ion peak, but the loss of $C_6H_5NH_2$ fragment support the proposed structure. Cyclocondensation of **4a-f** with an equimolar ratio of ethyl bromoacetate afforded the corresponding thiazolidin-4-one derivatives 5a-f respectively. Treatment of **4a** with two moles of ethyl bromoacetate gave N-ethoxycarbonylmethyl-thiazolidin-4-one derivatives (**6**). The structure **6** was further confirmed unequivocally by an independent synthesis from **5a** and ethyl bromoacetate in ethanolic AcONa (Figure 2).

Condensation of **5c** with different aromatic aldehydes gave the corresponding arylidenes **7a-c** (Figure 2). These products **7a-c** could be alternatively prepared by the reaction of **5c** with arylidene malononitriles under Michael reaction conditions (Figure 2). Treatment of **4a** with phenacyl bromide and/or 3-(2-bromoacetyl)benzocoumarin (**8**) gave the corresponding hydrazonothiazole derivatives (**9a,b**) respectively (figure 2).

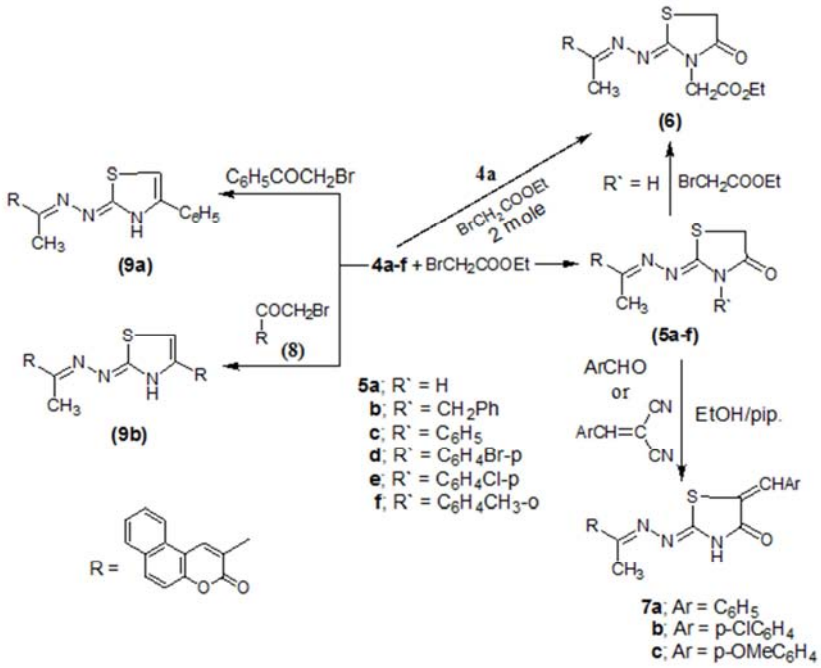

Figure 2. *Synthesis of thiazolidinone and thiazole from cyclocondensation of hydrazone with α-halo carbonyl compounds.*

Interaction of hydrazonecarbodithioate **2a,b** with hydrazonyl halides **10a-d** in ethanol containing triethylamine gave the corresponding 2,3-dihydro-1,3,4-thidiazoles **11a-d**. The formation of **11** can be rationalized via elimination of alkyl mercaptan from the corresponding cycloadduct **B,** which is assumed to be formed from 1,3-dipolar cycloaddition of nitrileimines to the thiocarbonyl double bond. Also, alternatively, the formation of **11** can be explained by a stepwise involving substitution to give a cylic hydrazone **A**, which was readily cyclized to afford the cyclic adduct **B** (Figure 3).

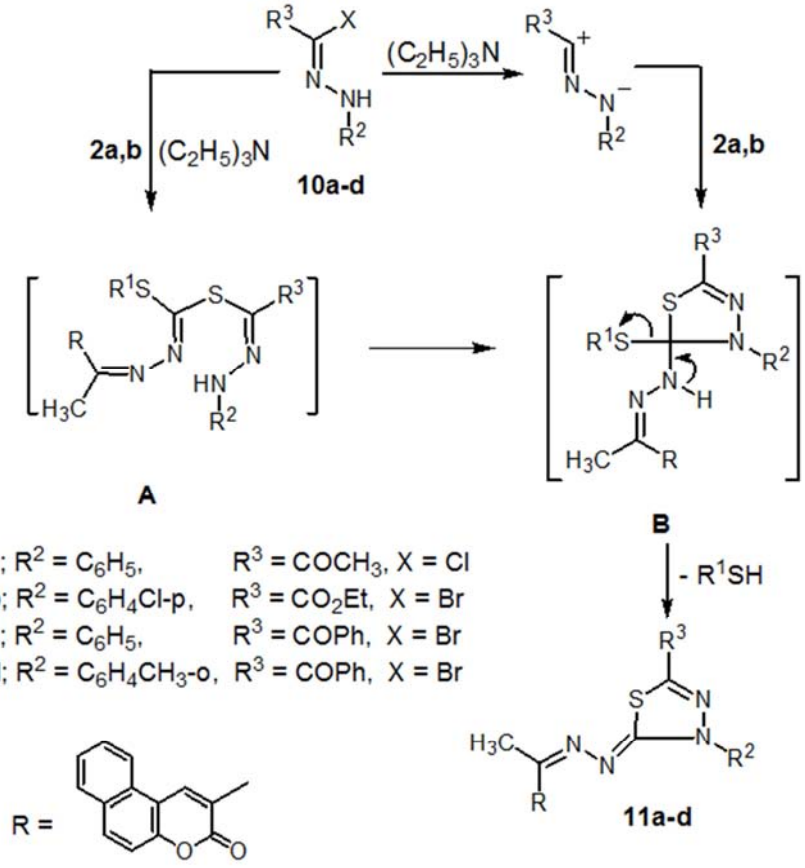

Figure 3. *Reaction of dithioesters with hydrazonyl halides to produce 1, 3, 4-thiadiazole.*

The above structures were established from elemental analysis (table 2,3) and spectral data. Also, the mass spectra fragmentations added further support to the proposed above structures

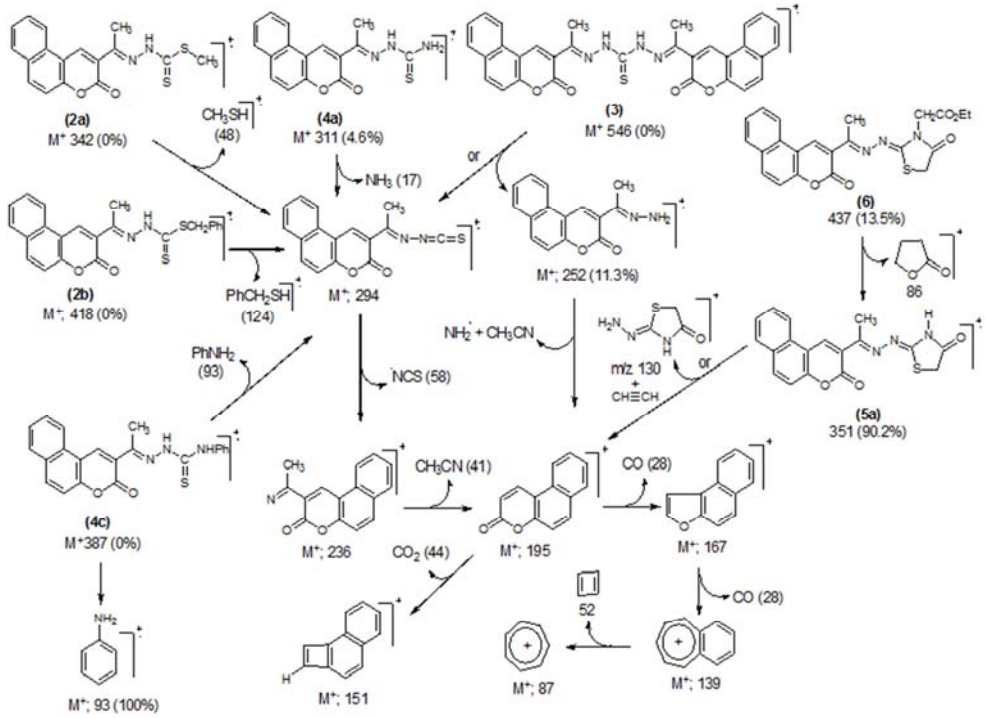

Figure 4. *The proposed pathway fragmentation for the EI spectra of substituted benzocoumarin-3`-yl derivatives* ***2a, b, 3, 4a, c, 5a*** *and* ***6.***

The most important peaks observed in the mass spectra of the substituted benzocoumarin-3`-yl derivatives **2a, b, 3, 4a, 4c, 5a** and **6** are listed in (table 1) and are arranged in columns according to the presumed composition. In the EI spectra the molecular ion of compounds **2a,b, 3, 4c** are not detected but the corresponding detected fragment ion was formed by elimination of the methylmercaptan, benzylmercaptan, aniline and 3-acetylbenzocoumarin hydrazone as neutral fragment, respectively. Also, the molecular ion was detected at low intensity for compounds **4a** and **6**, these peaks undergoes further fragmentation to the main fragment ion (m/z 294) by the elimination of NH_3 in case of compound 4a and to the base peak (m/z 351) by the elimination of γ-butyrolactone ($C_4H_6O_2$) for compound **6**. The mass spectrum of compound 5a is characterized by molecular ion at high abundance. The main fragment at m/z (294) undergoes fragmentation by successive elimination of NCS, acetonitrile, CO, CO_2), and cyclobutadiene. The elimination of thiazolidinonehydrazone fragment cation at m/z (130) as very intense peak exhibit benzocoumarin cation fragment m/z (195) which underwent further fragmentation.

Table 1. *Significant peaks in the EI (70 eV) spectra of compounds 2a,b, 3, 4a,c, 5a and 6.*

Compd.	M^+	m/z (intensity %)									
2a	342		294	236	195	167	151	139	87		
	(0)		(30.8)	(15.8)	(8.1)	(2.1)	(3.3)	(100)	(7.5)		
2b	418		294	236	195	167	151	139	87		
	(0)		(23.2)	(13.2)	(3.9)	(1.3)	(2)	(61.6)	(4.9)		
3	546		294	236	195	167	151	139	87	252	
	(0)		(54)	(26.1)	(13.6)	(5.6)	(6.5)	(100)	(9.7)	(11.3)	
4a	311		294	236	195	167	151	139	87		
	(4.6)		(19.4)	(19.8)	(17.7)	(5.6)	(8.1)	(100)	(11.9)		
4c	387		294	236	195	167	151	139	87	93	
	(0)		(16.9)	(19.3)	(13.7)	(5.6)	(7.9)	(90)	(12)	(100)	
5a	351				195	167	151	139	87	166	130
	(90.2)				(47.7)	(5.5)	(90.2)	(92.8)	(23)	(17.5)	(100)
6	437	351 (100)			195	167	151	139	87	166	130
	(13.9)				(36.8)	(16.7)	(14)	(73.3)	(21.4)	(16.7)	(86.8)

3. Experimental

All melting points are uncorrected. IR spectra (KBr) were recorded on a FTIR 5300 spectrometer (ν, cm^{-1}). The ^1H NMR spectra were recorded in DMSO-d_6 at 300 MHz on a Varian Gemini NMR spectrometer (δ, ppm) using TMS as an internal standard. Mass spectra were obtained on GC Ms-QP 1000 EX mass spectrometer at 70 ev. Elemental analyses were carried out by the Microanalytical Research Center, Faculty of Science, Cairo University.

3.1. N`-[1-(benzo[5`,6`]coumarin-3`-yl)ethylidene] hydrazinearbodithioate derivatives 2a,b

A mixture of 3-acetylbenzo[5,6]coumarin (0.01 mol) and alkyl hydrazine carbodithioate (0.012 mol) in ethanol (50 ml) was refluxed for one hour. The separated solid on heating was filtered off and recrystallized from the proper solvent to give (**2a,b**), (Table 2).

3.2. Reaction of 3-acetylbenzo[5,6]oumarin with thiocarbohydrazide

A solution of 3-acetyl[5,6]benzocoumarin (0.01 mol) in dioxane (30 ml) and thiocarbohydrazide (0.01 mol) was refluxed for 1h.

A solution of 3-acetyl[5,6]benzocoumarin (0.01 mol) in dioxane (30 ml) and thiocarbohydrazide (0.01 mol) was refluxed for 1h, the obtained product on heating was collected and recrystallized from DMF to give 1,5-bis[1-(benzocoumarin-3`-yl)ethylidene]thiocarbohydrazide (**3**), (Table 2).

3.3. N`-[1-(benzocoumarin-3`-yl)ethylidene]thiosemicarbazone derivatives 4a-e

3.3.1. Method A

A mixture of **2a** or **2b** (0.01 mol) and primary amine (0.012 mol) in ethanol (50 ml) was refluxed for **5h**. The separated solid on heating was filtered off and recrystallized from the proper solvent to give (**4a-e**).

3.3.2. Method B

A solution of 3-acetylbenzo[5,6]coumarin (0.01mol) in dioxane (30ml) and aryl or alkylthiosemicarbazides [18, 19] (0.01mol) was refluxed for 2h. After cooling, the solid product which formed was collected and recrystallized from the proper solvent to give **4a-e**, m.p. and mixed m.p. determined with authentic sample gave no depression (Table 2).

Table 2. *Characteristics data for prepared compounds.*

Compd. No.	M. P. (°C) Recryst. Solvent	Yield (%) (Colour)	Mol. Formula (M. wt)	Required (found) C	H	N
2a	214-216 EtOH/Dioxane	87 Pale yellow	$C_{17}H_{14}N_2O_2S_2$ (342.44)	59.63 59.51	4.12 4.10	8.18 8.12
2b	210-212 EtOH/Benzene	90 Red	$C_{23}H_{18}N_2O_2S_2$ (418.53)	66.00 66.02	4.33 4.20	6.89 6.82
3	215-216 DMF	82 Pale yellow	$C_{31}H_{22}N_4O_4S$ (546.60)	68.12 68.16	4.06 4.11	10.25 10.40
4a	216-218 Acetic acid	79 Yellow	$C_{16}H_{13}N_3O_2S$ (311.36)	61.72 61.74	4.21 4.12	13.50 13.47
4b	191-192 AcOH	80 Yellow	$C_{23}H_{19}N_3O_2S$ (401.48)	68.81 68.71	4.77 4.64	10.47 10.23
4c	211-213 AcOH	77 Yellow	$C_{22}H_{17}N_3O_2S$ (387.45)	68.20 68.01	4.42 4.33	10.85 10.82
4d	213-214 EtOH/Benzene	79 Orange	$C_{22}H_{16}BrN_3O_2S$ (466.35)	56.66 56.71	3.46 3.44	9.01 9.12
4e	193-195 AcOH	71 Yellow	$C_{22}H_{16}ClN_3O_2S$ (421.90)	62.63 62.43	3.82 3.72	9.96 9.91
4f	191-193 AcOH	74 Yellow	$C_{23}H_{19}N_3O_2S$ (401.48)	68.81 68.62	4.77 3.63	10.47 10.32
5a	271-273 Acetic acid	75 Pale yellow	$C_{18}H_{13}N_3O_3S$ (351.38)	61.53 61.43	3.73 3.67	11.96 11.92
5b	235-237 AcOH	83 Yellow	$C_{25}H_{19}N_3O_3S$ (441.50)	68.01 68.18	4.34 4.28	9.52 9.43
5c	289-290 DMF	78 Yellow	$C_{24}H_{17}N_3O_3S$ (427.48)	67.43 67.33	4.01 3.98	9.83 9.87
5d	306-308 DMF	75 Pale Yellow	$C_{24}H_{16}BrN_3O_3S$ (506.37)	56.93 56.92	3.18 3.02	8.30 8.24
5e	273-275 AcOH	80 Pale Yellow	$C_{24}H_{16}ClN_3O_3S$ (461.92)	62.40 62.34	3.49 3.44	9.10 9.21
5f	220-221 AcOH	77 Pale Yellow	$C_{25}H_{19}N_3O_3S$ (441.50)	68.01 68.12	4.34 4.29	9.52 9.41
6	238-240 Benzene	63 Yellow	$C_{22}H_{19}N_3O_5S$ (437.47)	60.40 60.35	4.38 4.36	9.61 9.57
7a	325-327 DMF	65 Yellow	$C_{31}H_{21}N_3O_3S$ (515.58)	72.22 72.12	4.11 4.06	8.15 8.04
7b	328-330 DMF	70 Yellow	$C_{32}H_{23}N_3O_4S$ (545.61)	70.44 70.32	4.25 4.31	7.70 7.65
7c	320-322 DMF	68 Yellow	$C_{24}H_{16}ClN_3O_3S$ (547.81)	67.69 67.52	3.67 3.71	7.64 7.53
9a	268-270 DMF	80 Yellow	$C_{24}H_{17}N_3O_2S$ (411.48)	70.05 70.12	4.16 4.20	10.21 10.22
9b	258-260 DMF	62 Red	$C_{31}H_{19}N_3O_4S$ (529.59)	70.31 70.25	3.62 3.57	7.93 7.85
11a	278-280 EtOH/Benzene	80 Yellow	$C_{25}H_{18}N_4O_3S$ (454.50)	66.07 66.05	3.99 3.83	12.33 12.24
11b	246-248 EtOH/Benzene	68 Yellow	$C_{26}H_{19}ClN_4O_4S$ (518.97)	60.17 60.11	3.69 3.63	10.80 10.73
11c	248-250 EtOH/DMF	75 Yellow	$C_{30}H_{20}N_4O_3S$ (516.57)	69.75 69.64	3.90 3.86	10.85 10.81
11d	280.282 Dioxane	77 Pale yellow	$C_{31}H_{22}N_4O_3S$ (530.60)	70.19 70.11	4.18 4.08	10.56 10.48
9b	258-260 DMF	62 Red	$C_{31}H_{19}N_3O_4S$ (529.59)	70.31 70.25	3.62 3.57	7.93 7.85
11a	278-280 EtOH/Benzene	80 Yellow	$C_{25}H_{18}N_4O_3S$ (454.50)	66.07 66.05	3.99 3.83	12.33 12.24
11b	246-248 EtOH/Benzene	68 Yellow	$C_{26}H_{19}ClN_4O_4S$ (518.97)	60.17 60.11	3.69 3.63	10.80 10.73
11c	248-250 EtOH/DMF	75 Yellow	$C_{30}H_{20}N_4O_3S$ (516.57)	69.75 69.64	3.90 3.86	10.85 10.81
11d	280.282 Dioxane	77 Pale yellow	$C_{31}H_{22}N_4O_3S$ (530.60)	70.19 70.11	4.18 4.08	10.56 10.48

3.4. 3-Substituted-2-({1-benzocoumarin-3`-yl]ethylidene}-hydrazono)thiazolidin-4-one 5a-e

A mixture of (**4a-e**) (0.01 mol), ethyl bromoacetate (0.01 mol) and fused sodium acetate (0.02 mol) in ethanol (40 ml) was refluxed for 2h. The obtained product was filtered off, washed with water (50 ml) and recrystallized from the proper solvent to give (**5a-e**), (Table 2).

Table 3. *Spectral data of synthesized compounds.*

Compd. No.	IR (v, cm^{-1})	^{1}HNMR (δ, ppm) (DMSO-d_6)
2a	3194 (NH), 1710 (C=O) and 1323 (C=S).	2.45 (s, 3H, CH_3-C=N), 2.70 (s, 3H, SCH_3), 7.47-8.35 (6H, m, Ar-H), 9.01 (s, 1H, benzo-coumarin H-4) and 10.05 ppm (s, 1H, NH).
2b	3246 (NH), 1707 (C=O) and 1265 (C=S).	
3	3247 (NH) and 1708 (C=O).	
4a	3405, 3246, 3154 (NH,NH_2), 1719 (C=O).	
4c	3147 (NH), 1727 (C=O) and 1343 (C=S).	2.42 (s, 3H, CH_3-C=N), 7.18-8.17 (m, 11H, Ar-H), 9.16 (s, 1H, benzocoumarin H-4) and 10.27 & 10.87 ppm (2s, 2H, 2NH exchangeable with D_2O).
4e	3196 (NH), 1711 (C=O) and 1340 (C=S).	
5a	3163 (NH), 1712 (C=O).	
5c	1722 (C=O), 1600 (C=N).	2.18 (s, 3H, CH_3-C=N), 3.14 (s, 2H, CH_2CO), 7.43-8.49 (m, 11H, Ar-H) and 8.93 ppm (s, 1H, benzocoumarin H-4).
6	1709 (C=O), 1627 (C=N).	1.33 (t, 3H, CH_2-CH_3), 2.48 (s, 3H, CH_3-C=N), 3.88 (s, 2H, >N-CH_2), 4.27 (2H, q, CH_2-CH_3), 4.59 (s, 2H, CH_2CO), 7.45-8.32 (m, 6H, Ar-H) and 8.95 ppm (s, 1H, benzocoumarin H-4).
9a	3166 (NH) and 1727 (C=O).	
9b	3148 (NH) and 1716 (C=O).	
11a	1726 (C=O; δ lactone) and 1684 (C=O; CH_3CO).	2.57 (s, 3H, CH_3-C=N), 2.65 (s, 3H, $COCH_3$), 7.36-8.32 (m, 11H, Ar-H) and 8.97 ppm (s, 1H, benzocoumarin H-4).
11b	1724 (C=O).	1.43 (t, 3H, CH_2-CH_3), 2.57 (s, 3H, CH_3-C=N), 4.47 (q, 2H, CH_2-CH_3), 7.45-8.10 (m, 10H, Ar-H) and 8.93 ppm (s, 1H, benzocoumarin H-4).
11c	1724 (C=O).	

3.5. 4-Oxo-2-{[1-(benzocoumarin-3`-yl)-ethylidene]-hydrazono} thiazolidin-3-yl) acetic acid ethyl ester (6)

3.5.1. Method A

A mixture of (**5a**; 0.01 mol), fused sodium acetate (0.02 mol) and ethyl bromoacetate (0.01 mol) in ethanol (30 ml) was refluxed for 3h, after cooling the solid which formed was collected and recrystallized from benzene to give (**6**) (63%) as yellow crystals, m. p. 238-240°C.

3.5.2. Method B

A mixture of (**5a**; 0.01 mol), ethyl bromoacetate (0.02 mol) and fused sodium acetate (0.02 mol) in ethanol (50 ml) was refluxed for 3h, after cooling, the obtained product was collected and recrystallized from benzene to give (**6**) in yield (74%), m. p. and mixed m. p. with product from procedure (A) gave no depression.

3.6. 3,5-Disubstituted-2-{[benzocoumarin-3`-yl]ethyl-idene]hydrazono}thiazolidin-4-one 7a-c

A mixture of (**5a**; 0.01 mol), the appropriate aromatic aldehydes and / or arylidenemalononitrile (0.0.1 mol) in dioxane (30 ml) and few drops of piperidine was refluxed for 3h, the solid product was collected by filtration and recrystallized from DMF to give **7a-c**, (Table 2).

3.7. 4-Substituted-2-({1-Benzocoumarin-3`-yl]Ethylidene}-Hydrazono)Thiazole 9a,b

A mixture of (**4a**; 0.01 mol) and phenacyl bromide or bromoacetyl-benzocoumarin[20] (0.01 mol) in ethanol (50 ml) was refluxed for 2hrs, the solid product which formed on heating was collected by filtration and recrystallized from the appreciate solvent to give **9a,b**, (Table 2).

3.8. Reaction of 2a,b with Hydrazonoyl Halides

A mixture of (**2a,b**; 0.01 mol) and the appropriate hydrazonoyl halide **10a-d** (0.01 mol) in ethanol (50 ml) triethylamine (0.5 ml) was added [21-23]. The reaction mixture was refluxed for 3h. The resulting product was collected by filtration and recrystallized from the proper solvent to give **11a-d**, (Table 2).

4. Conclusions

In this study, N-[1-(benzocoumarin-3`-yl)ethylidene]-hydrazineecarbodithioate (**2**) it is very good starting material for the synthesis of 1,3,4-thiadiazole,thiazolidinone and thiazole derivatives which containing coumrin moiety which posses biological activity. However further studies are needed to complete these study for the biological activity.

References

[1] S. Wawzonek, *Heterocyclic Compounds,2*, 173, (1975).

[2] F. M. Dean, *Naturally occurring oxygen ring compounds*, (Butter Worths, London) *176*, 1963.

[3] R. Livingstone, Rod's *Chemistry of carbon compounds*, Vol. *4*, 2nd Edn (Elsevier, Amsterdam) 1996.

[4] A. R. Kartritzky, C. W. Rees; *Comprehensive heterocyclic chemistry* vol. *3* (Bergaman Press, Oxford) (1984).

[5] J. Starnoton, *comprehensive organic chemistry* Vol. *4*, edited by DHR Barton, W D Ollis (Pergaman Press, Oxford 629, (1979).

[6] M. D. Freiendmann, P. L. Stoller, T. H. Porter, and K. J. Folkevs; *J. Med. Chem., 16,* 1314 (1973).

[7] A. S. Hamam, and H. S. El-Kasher, *Egyptian Pharmaceutical Congress Cairo*, 7-10 Dec. (1975).

[8] R. D. Westl, M. H. Lin, Cooly (Jr) R. A. Zuviester M. L., and M. M. Grenan, *J. Med. Chem., 16,* 328 (1973).

[9] P. S. Furmer, C. C. Heung, and M. K. Luie*, J. Med. Chem., 16*, 411 (1973).

[10] M. S. Y. Khan and P. Sharma, *Indian. J. Chem., 32B*, 374 (1993).

[11] D. I. Brahmbhatt, G. B. Radji, S. U. Pandya, and U. R. Pandya; Indian *J. Chem., 38B*, 212 (1999).

[12] M. S. Y. Khan and P. Sharma, *Indian J. Chem*., *34B*, 237 (1995).

[13] H. Sun, W. Hua and L. Chen, *Bull. Soc. Chem. Belg*., *106*, 47 (1997).

[14] H. Sun, W. Hua and L. Chen,*Chem. J. Chin. Univ*., *18*, 730 (1997).

[15] G. S. S. Murthi, M. Basak, *J. Indian Chem. Soc*. *70* (2), 170 (1993).

[16] D. L. Klayman, J. F. Bartosevichm, T. S. Griffin, C. J. Mason and J. P. Scovill; *J. Med. Chem., 22,* 855 (1979).

[17] J. Korosi, *Ger. Offen*. *1*, 934, 89929 Jan (1979), C. A. *72*, 100334s (1970).

[18] U. Verabhadra and V. Rajeswar, *J. Indian Chem. Soc., 67* (1), 81 (1990).

[19] V. Yakazakov and I. Ya Potovski, Inv. *Yashikucheb. Zavedii Khim. Ikhim. Technol*. *4*, 238 (1961) C. A., *55*, 23415 (1961).

[20] P. Czerny and H. Hartmann, J. Prakt. Chem., 325, 551 (1983).

[21] N. F. Weiss and A. O. Abdelhamide*, J. Heterocycl. Chem*.,*17*, 1713 (1980).

[22] M. Nagakura, T. Ota, N. Shimadzu, K. Kawamura, Y. Eto; and Y. Wada, *J. of Med. Chem., 22,* 48 (1979).

[23] A. S. Shawali and A. O. Abdelhamide, Bull. Soc. Japan, 49, 321 (1976).