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3-Acyl-4-hydroxy-2-oxo-2*H*-chromen derivatives **1a-d** were condensed with (7-hydroxy-2-oxo-2*H*-chromen-4-yl)-acetic acid hydrazide **2**, (4-methyl-2-oxo-2*H*-chromen-7-yloxy)-acetic acid hydrazide **3**, and (7-hydrazinocarbonylmethoxy-2-oxo-2*H*-chromen-4-yl)-acetic acid hydrazide **4**, to give corresponding 3-alkyl-1-[2-(7-hydroxy-2-oxo-2*H*-chromeno-4-yl)-acetyl]-1*H*-chromeno[4,3-*c*]pyrazole-4-one **5a-d**, 3-alkyl-1-[2-(4-methyl-2-oxo-2*H*-chromeno-7-yloxy)-acetyl]-1*H*-chromeno[4,3-*c*]pyrazole-4-one **6a-d**, and 1-{4-[(3-alkyl-1*H*-chromeno[4,3-*c*]pyrazole-4-one-1-yl)-carbonylmethyl]-2-oxo-2*H*-chromen-7-yloxy-acetyl}-3-alkyl-1*H*-chromeno[4,3-*c*]pyrazole-4-one **7a-d**.

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Since the coumarin ring forms a part of many heterocyclic compounds of pharmacological interest [1-4], these derivatives are being evaluated for potential biological activity. Different biological activity of the coumarins fused with other heterocycles in 3,4-positions [5-13] prompted the synthesis of coumarino [4,3-*c*]-N_1-substituted pyrazoles. Woulfson and Zhurin [14] reported the synthesis of coumarino [4,3-*c*]-N_1-phenyl-3-methylpyrazoles by cyclizing the phenylhydrazones of 3-acetyl-4-hydroxycoumarins using *p*-toluensulphonic acid. Checchi and co-workers [15] condensed phenylhydrazine with 4-chloro-3-cyano-coumarins and obtained coumarino[4,3-*c*]-N_1-phenyl-3-aminopyrazoles. Moorty and co-workers [16] carried out the intramolecular cyclization of the phenylhydrazones of the respective 4-chloro-3-formylcoumarins using pyridine to which piperidine was added in traces. In this way the coumarino[4,3-*c*]-N_1-phenylpyrazoles were prepared. From 3-acetyl-4-hydroxy-2-oxo-2*H*-chromen, with hydrazine hydrate and phenylhydrazine in ethanol, were obtained 3-(1-hydrazonoethyl)-4-hydroxy-chromen-2-one and 3-methyl-1*H*-chromeno[4,3-*c*]pyrazole-4-one [17]. Klosa [18], under the same conditiones, synthesised only 3-(1-hydrazono-ethyl)-4-hydroxy-chromen-2-one.

While in experiments performed so far, monopyrazole-coumarins were prepared [14-18], we succeeded in synthesis of a new pyrazole and dipyrazole, possesing two and even three coumarin nucleus.

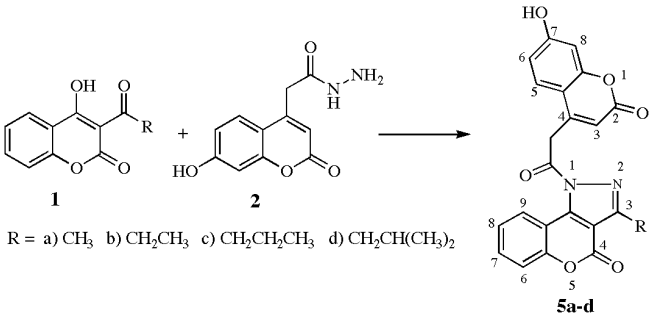
Baker and co-workers [19] reported an unsuccessful attempt in (7-hydroxy-2-oxo-2*H*-chromen-4-yl)-acetic acid hydrazide **2** preparation from the corresponding methyl ester of the carboxylic acid. We succeeded in the preparation of the corresponding hydrazide [20] from (7-hydroxy-2-oxo-2*H*-chromen-4-yl)-acetic acid methyl ester, which was reacted with 100% hydrazine hydrate in methanol. (4-Methyl-2-oxo-2*H*-chromen-7-yloxy)-acetic acid ethyl ester was prepared by the reaction of 7-hydroxy-4-methyl-2-oxo-2*H*-chromen and ethylbromoacetate, which reacted with hydrazine hydrate in ethanol to give **3**. (7-Hydrazinocarbonylmethoxy-2-oxo-2*H*-chromen-4-yl)-acetic acid hydrazide **4** was obtained from (7-hydroxy –2-oxo-2*H*-chromen-4-yl)-acetic acid. Compounds **1a-d** were synthesized from 4-hydroxy-2-oxo-2*H*-chromen [21-23]. Structures of compounds **1a-d** are as previously described [24-28]. Within these structures the α-pyronic form is dominant, while the presence of the γ-pyronic form is insignificant.

Refluxing an equimolar amounts of 3-acyl-4-hydroxy-2-oxo-2*H*-chromen **1** and **2** in ethanol led to a new series of compounds **5a-d**. (Scheme I). The same reaction when carried out by **3** and **4** leads to the fomation of **6a-d** and **7a-d** (Schemes II and III).

Screening Data.

Derivatives of coumarins **5a-d, 6a-d** and **7a-d** described here were examined for their antimicrobial activity. The best results were obtained in the case of 1-[2-(7-hydroxy-2-oxo-2*H*-chromen-4-yl)-acetyl-3-methyl-1*H*-chromeno[4,3-*c*]-pyrazole-4-one **5a**, 3-ethyl-1-[2-(7-hydroxy-2-oxo-2*H*-chromen-4-yl)-acetyl-1*H*-chromeno[4,3-*c*]pyrazole-4-one **5b**, 1-[2-(7-hydroxy-2-oxo-2*H*-chromen-4-yl)-acetyl-3-propyl-1*H*-chromeno[4,3-*c*]pyrazole-4-one **5c** and 1-[2-(7-hydroxy-2-oxo-2*H*-chromen-4-yl)-acetyl-3-izobuthyl-1*H*-chromeno[4,3-*c*]pyrazole-4-one **5d**. These compounds were found to possess high antimicrobial activity against *Staphyloccocus pneumoniae* and were slightly less active

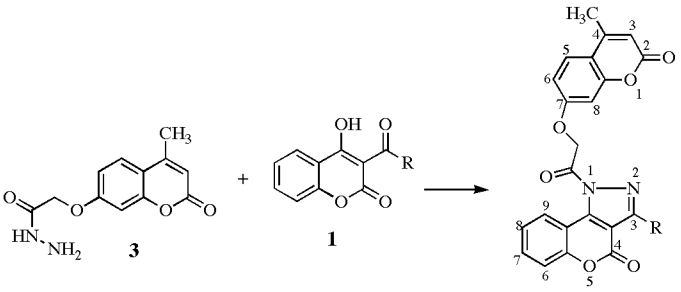
Scheme I



R = a) CH_3 b) CH_2CH_3 c) $CH_2CH_2CH_3$ d) $CH_2CH(CH_3)_2$

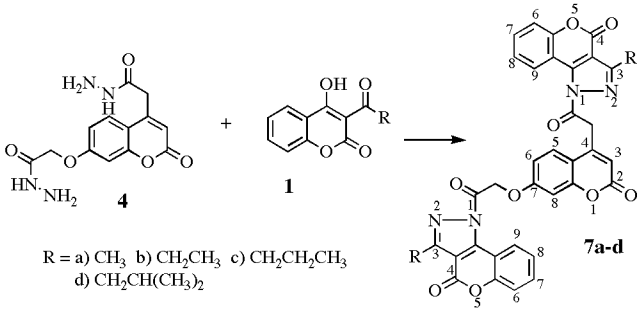
against *Bacillus subtilis, Bacillus cereus and Salmonela panama*. In case of 3-alkyl-1-[2-(4-methyl-2-oxo-2*H*-chromeno[4,3-*c*]pyrazole-4-one **6a-d** and 1-{4-[(3-alkyl-1*H*-chromeno[4,3-*c*]pyrazole-4-one-1-yl)-carbonylmethyl]-2-oxo-2*H*-chromen-7-yloxy-acetyl}-3-alkyl-1*H*-chromeno-[4,3-*c*]pyrazole-4-one **7a-d**, we have found them to have very weak activity against all the tested microorganisms.

Scheme II



R = a) CH_3 b) CH_2CH_3 c) $CH_2CH_2CH_3$ d) $CH_2CH(CH_3)_2$

Scheme III



R = a) CH_3 b) CH_2CH_3 c) $CH_2CH_2CH_3$
d) $CH_2CH(CH_3)_2$

300 spectrometer (300 MHz) with tetramethylsilane as internal standard. The IR spectra (ν/cm^{-1}) were recorded as potassium bromide pellets on a Magna FT-IR 760 Nicolet spectrometer.

Starting from 4-hydroxy-2-oxo-2*H*-chromen using a known procedure, we have prepared 3-acyl-4-hydroxy-2-oxo-2*H*-chromen **1a-d** [21-23]. We have also used known procedures for the preparation of (7-hydroxy-2-oxo-2H-chromen-4-yl)-acetic acid hydrazide **2**.

Table I

Physical and Analytical Data for Compounds **5a-d, 6a-d** and **7a-d**

Compound	R	Yield (%)	Mp (°C)	Formula (MW)	Analysis C	Calcd./ H	Found (%) N
5a	$-CH_3$	82	262	$C_{22}H_{14}N_2O_6$	65.67	3.51	6.96
			(402.6)	65.43	3.80	6.80	
5b	$-CH_2CH_3$	76	265	$C_{23}H_{16}N_2O_6$	66.34	3.87	6.73
			(416.1)	66.31	4.06	6.57	
5c	$-CH_2CH_2CH_3$	70	271	$C_{24}H_{18}N_2O_6$	66.97	4.22	6.51
			(430.4)	66.94	4.36	6.24	
5d	$-CH_2CH(CH_3)_2$	63	279	$C_{25}H_{20}N_2O_6$	67.54	4.54	6.30
			(444.4)	67.47	4.48	6.41	
6a	$-CH_3$	78	249	$C_{23}H_{16}N_2O_6$	66.34	3.87	6.73
			(416.4)	66.31	4.10	6.62	
6b	$-CH_2CH_3$	68	253	$C_{24}H_{18}N_2O_6$	66.97	4.22	6.51
			(430.4)	66.73	4.48	6.44	
6c	$-CH_2CH_2CH_3$	72	259	$C_{25}H_{20}N_2O_6$	67.54	4.54	6.30
			(444.4)	67.30	4.51	6.22	
6d	$-CH_2CH(CH_3)_2$	58	265	$C_{26}H_{22}N_2O_6$	68.11	4.84	6.11
			(458.4)	68.20	4.74	5.98	
7a	$-CH_3$	80	246	$C_{35}H_{22}N_4O_9$	65.42	3.45	8.72
			(642.57)	65.57	3.40	8.92	
7b	$-CH_2CH_3$	82	248	$C_{37}H_{26}N_4O_9$	66.27	3.91	8.35
			(670.62)	66.20	4.15	8.42	
7c	$-CH_2CH_2CH_3$	75	255	$C_{39}H_{30}N_4O_9$	67.04	4.33	8.02
			(698.68)	67.06	4.23	8.04	
7d	$-CH_2CH(CH_3)_2$	48	268	$C_{41}H_{34}N_4O_9$	67.76	4.72	7.71
			(726.73)	67.87	4.84	7.80	

EXPERIMENTAL

General Information.

Melting points were determined on a Fisher-Johns apparatus and are uncorrected. Microanalyses for C, H and N were performed on a Perkin-Elmer Analyzer 2400. The ^{1}H NMR spectra (δ values; DMSO-d_6 solutions) were recorded on a Varian Gemini

(4-Methyl-2-oxo-2*H*-chromen-7-yloxy)-acetic acid hydrazide (**3**).

A mixture of (4-methyl-2-oxo-2*H*-chromen-7-yloxy)-acetic acid ethyl ester (2.6 g, 0.01 mol) and 100% hydrazine hydrate (1 ml, 0.02 mol) in absolute ethanol (30 ml) was refluxed for 1.5 to 2.0 hours. The white precipitate which was formed during the reaction was collected by filtration, washed with water and crystallized

Table II

IR Data of Compounds **5a-d, 6a-d** and **7a-d**

Compounds	IR (cm^{-1})					
	ν OH	ν CH_2	ν CH_3	ν C=O	ν C=C	ν C=N
5a	3422	3128	3008	1708	1651	1611
	w	w	s	s	s	sh
5b	3448	3175	3012	1709	1692	1610
	w	w	sh	s	s	sh
5c	3420	3181	3163	1711	1641	1608
	w	w	sh	s	s	sh
5d	3432	3160	3142	1706	1654	1612
	w	w	sh	s	s	sh
6a	-	3170	3120	1712	1665	1605
		w	sh	s	s	sh
6b	-	3165	3134	1712	1690	1600
		w	sh	s	s	sh
6c	-	3147	3020	1705	1695	1610
		w	sh	s	s	sh
6d	-	3160	3080	1710	1694	1600
		w	sh	s	s	sh
7a	-	3142	3004	1718	1700	1612
		w	sh	s	s	sh
7b	-	3120	2980	1715	1695	1600
		w	sh	s	s	sh
7c	-	3130	2995	1712	1700	1600
		w	sh	s	s	sh
7d	-	3140	3000	1710	1705	1610
		w	sh	s	s	sh

from ethanol, m.p. 201-202 °C, yield 2.3 g (92.6%); IR (potassium bromide):ν 3269; 3100 (NH), (NH_2), 1713; 1683 (C=O), 1617(C=C, arom.); ^{1}H NMR (DMSO-d_6): δ 9.34 (s, 1H, NH), 7.64 (d, 1H, H-5), 6.81(d, 1H, H-6), 6.78(s, 1H, H-8), 6.24 (s, 1H, H-3), 5.32 (s,2H, CH_2), 3.24 (d, 2H, NH_2), 2.40 (s, 3H, CH_3).

*Anal.*Calcd. for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29. Found: C, 58.12; H, 4.82; N, 10.98.

(7-Hydrazinocarbonylmethoxy-2-oxo-2*H*-chromen-4-yl)-acetic Acid Hydrazide (**4**).

In a solution containing methanol (120 ml) and 100% hydrazine hydrate (12 ml)was dissolved (7-ethoxycarbonyl-methoxy-2-oxo-2*H*-chromen-4-yl)-acetic acid methyl ester (3.2 g, 0.01 mol) and the mixture was left to stand over night at 5 °C. The product was separated, was collected by suction filtration, washed with methanol, and recristallized from dil. acetic acid.

M.p. >300°C, yield 2.14 g, (70%); IR (potassium bromide):ν 3325; 3263 (NH),(NH_2),1707;1690 (C=O), 1623 (C=C,arom.). ^{1}H NMR (DMSO-d_6): δ 9.41 (s, 1H, NH), 9.34 (s, 1H, NH), 7.76 (d, 1H, H-5), 7.04 (d, 1H, H-6), 7.02 (s, 1H, H-8), 6.34 (s, 1H, H-3), 4.69 (s, 2H, CH_2), 4.34 (s, 2H, NH_2), 4.08 (s, 2H,CH_2), 3.38 (s, 2H,NH_2).

Anal. Calcd. For $C_{13}H_{14}N_4O_5$: C, 50.98; H, 4.61; N, 18.29. Found: C, 51.02; H, 4.38; N, 18.15.

General Procedure for Condensation and Cyclization of 3-Acyl-4-hydroxy-2-oxo-2*H*-chromen with Hydrazide **2,3** and Dihydrazide **4**.

A mixture of 3-acyl- 4-hydroxy-2-oxo-2*H*-chromen **1a-d** (0.01 mole) and the corresponding hydrazide **2,3** (0.01 mole) in absolute ethanol (50 ml) was refluxed for 2 hours or at the end of the reaction (monitored by TLC). The reaction mixture was

Table III.

^{1}H NMR Data for Compounds **5a-d, 6a-d and 7a-d**

Compound	H-3 H-3′	H-5 H-5′	H-6 H-6′	H-7 H-7′	H-8 H-8′	R R′	-CH_2- -CH_2-	CH_3
5a	-	7.96(d)	7.66(d)	7.64(d)	7.29(d)	2.50(s)	-	-
	6.74(s)	7.32(d)	6.82(d)	10.62(s)	6.75(d)	-	3.94(s)	-
5b	-	7.95(d)	7.67(q)	7.63(d)	7.29(d)	3.15(q), 1.12(t)	-	-
	6.30(s)	7.31(d)	6.78(q)	10.63(s)	6.76(d)	-	3.95(s)	-
5c	-	7.96(d)	7.65(d)	7.64(d)	7.26(d)	3.07(t), 1.51(q), 0.94(t)	-	-
	6.29(s)	7.31(d)	6.81(d)	10.55(s)	6.75(d)	-	3.94(s)	-
5d	-	7.97d(d)	7.66(d)	7.64(d)	7.31(d)	3.9(d); 0.89(d); 0.87(d)	-	-
	6.26(s)	7.34(d)	6.80(d)	10.58(s)	6.72(d)	-	3.93(s)	-
6a	-	7.98(d)	7.72(d)	-	7.17(s)	2.65(s)	4.94(s)	-
	6.24(s)	7.32(d)	7.29(d)	7.63(d)	7.05(d)	-	-	2.40(s)
6b	-	7.98(d)	7.74(d)	-	7.30(s)	3.11(q); 1.12(t)	4.96(s)	-
	6.24(s)	7.32(d)	7.28(d)	7.70(d)	7.00d)	-	-	2.40(s)
6c	-	7.96(d)	7.72(d)	-	7.29(s)	2.65(t); 2.50(q); 1.40(t)	4.94(s)	-
	6.24(s)	7.32(d)	7.29(d)	7.66(d)	7.06(d)	-	-	2.40(s)
6d	-	7.94(d)	7.74(d)	-	7.26(s)	3.8(d), 0.92(d); 0.89(d)	4.94(s)	-
	6.26(s)	7.31(d)	7.30(d)	7.78(d)	7.00(d)	-	-	2.40(s)
7a	-	8.25(d)	7.84(d)	-	7.22(s)	2.29(s)	4.96(s)	-
	6.40(s)	8.04(d)	7.68-	7.40-	7.09(d)	2.50(s)	4.02(s)	
		7.96(d)	7.78(m)	7.60(m)	7.17(d)			
7b	-	8.02(d)	7.84(d)	-	7.28(s)	2.67(t); 1.16(t)	4.97(s)	-
	6.38(s)	7.98(d)	7.64-	7.38-	7.08(d)	-	4.08(s)	
		7.93(d)	7.80(m)	7.63(m)	7.16(d)			
7c	-	8.05(d)	7.84(d)	-	7.28(s)	2.60(t); 2.42(q); 1.40(t)	4.97(s)	-
	6.37(s)	7.98(d)	7.64-	7.35-	7.08(d)	-	4.02(s)	
		7.94(d)	7.81(m)	7.60(m)	7.12(d)			
7d	-	7.99(d)	7.87(d)	-	7.25(s)	3.52(s); 1.15(d); 1.07(d)	5.11(s)	-
	6.39	7.96(d)	7.62-	7.32-	7.00(d)		4.00(s)	
		7.90(d)	7.75(m)	7.57(m)	7.14(d)			

cooled and solid was collected by filtration and recrystallized from ethanol.

In a similar manner to that described for the preparation of compounds **5a-d** and **6a-d**. By the action of 3-acyl-4-hydroxy-2-oxo-2*H*-chromen **1a-d** (0.02 mole) and dihydrazide **4** (0.01 mole) in absolute ethanol (75 ml), compounds **7a-d** were obtained. Data for yields, melting points, molecular formula and analyses are given in Table I. IR and ^{1}H NMR data are given in Table II and Table III.

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