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Notes

Synthesis of biologically active 4-coumarin-6-yl(amino)-5-coumarin-3-yl-3-phenyl-1,2,4-oxadiazolines

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Reaction of Schiff bases **3** and hydrazones **6** with benzhydroxamoyl chloride respectively afforded the corressponding 4-coumarin-6-yl(amino)-5-coumarin-3-yl-3-phenyl-1,2,4-oxadiazolines **4** and **7**. The structures of all the synthesized compounds have been confirmed on the basis of spectral and analytical data. The above compounds have been screened for their antibacterial activity.

Keywords: Schiff base, hydrazones, oxadiazolines, antibacterial, antifungal, benzhydroxamoyl chloride

Coumarin chemistry has become more and more important over the years, which is documented by thousands of papers and patents on coumarins. This is mainly because of the discovery of their varied biochemical properties[1]. 6-Aminocoumarin itself and its derivatives have been reported to possess wide range of pharmaceutical activities such as antibacterial, antifungal[2], *etc*.

The biological importance of the Schiff bases[3] and the hydrazones[4] of 6-aminocoumarin and oxadiazolines[5] prompted the synthesis of 4-coumarin-6-yl(amino)-5-coumarin-3-yl-3-phenyl-1,2,4-oxadiazolines containing the oxadiazoline ring moiety flanked at 6-position of the coumarin ring which might possess some of the above biological activity.

For this purpose, coumarin-3-aldehydes **1a-d** was reacted with 6-aminocoumarin **2a-d** and coumarin-6-ylhydrazinehydrochloride[4] **5a-d**, respectively to yield the Schiff bases **3a-l** and *N*-(coumarin-6-yl)hydrazono-1-arylmethanes **6a-l**. Compounds **3a-6l** gave positive Beilstein's sodium fusion test for the presence of nitrogen. Compounds **3a-6l** were further subjected to treatment with benzhydroxamoyl chloride to afford 4-coumarin-6-yl(amino)-5-coumarin-3-yl-3-phenyl-1,2,4-oxadiazolines **4** and **7**. The IR spectra of compound **7a-l** showed a broad signal at around 3250 cm^{-1} for >N-H stretching and the ^1H NMR spectra showed a sharp singlet at around δ 9.60 for one proton of –NH- which was D_2O exchangeable. The structures of all the synthesized compounds have been confirmed on the basis of spectral and analytical data.

Antimicrobial activity

All the synthesized compounds **4a-l** and **7a-l** were screened for their antibacterial activity against *S. aureus*, *S. pyogenes*, *S. albus* and *E. coli* according to the standard procedure **(Table I)**. The minimum inhibitory concentration (MIC) was determined using tube dilution method according to the standard procedure[6]. DMF was used as a solvent and blank. Ciproflxacin (MIC: 5 μg/mL) was used as the antibacterial standard. The observation of the data **(Table I)** reveals that the compound **4e** was more effective against *S. aureus* at the concentration of 15 μg/mL compared to the other members of the same

Table I — Antibacterial activity data (MIC μg/mL) of compounds **4a-l** and **7a-l**.

Compd	Antibacterial activity			
	S. aureus	*S. albus*	*S. pyogenes*	*E. coli*
4a	-	200	250	-
4b	200	150	200	100
4c	200	250	150	100
4d	250	150	-	100
4e	15	25	100	100
4f	100	150	100	50
4g	100	100	50	50
4h	50	100	50	25
4i	-	-	-	200
4j	-	-	250	-
4k	250	200	-	-
4l	200	-	-	200
7a	-	-	250	200
7b	150	100	100	50
7c	200	-	-	150
7d	-	150	200	-
7e	100	20	50	100
7f	100	50	50	100
7g	150	50	100	100
7h	50	100	25	50
7i	-	-	200	-
7j	250	200	-	-
7k	150	-	100	200
7l	150	100	200	-
Ciprofloxacin	05	05	05	05

Table II — Spectral and physical characterization data of newly prepared compounds

Compd	Yield (%)	m.p. (°C)	Mol. formula	^{1}H , ^{13}C NMR and MS data
4a	73	171	$C_{26}H_{16}N_2O_5$	^{1}H NMR: δ 5.00 (s, 1H, C_5-H), 6.40 (d, *J* = 7.10 Hz, 1H, C_3'-H), 6.60-7.90 (m, 12Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 80.00 (C_5), 108.00 – 151.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 153.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 436.
4b	75	157	$C_{27}H_{18}N_2O_5$	^{1}H NMR: δ 2.30 (s, 3H, C_7'-CH_3), 5.00 (s, 1H, C_5-H), 6.40 (d, *J* = 7.08 Hz, 1H, C_3'-H), 6.60-7.90 (m, 11Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 80.00 (C_5), 108.00 – 151.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 153.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 450.
4c	68	165	$C_{28}H_{20}N_2O_5$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 2.30 (s, 3H, C_7'-CH_3), 5.00 (s, 1H, C_5-H), 6.40 (s, 1H, C_3'-H), 6.60-7.90 (m, 10Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 21.00 (C_4' -CH_3), 80.00 (C_5), 108.00 – 151.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 153.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 464.
4d	77	179	$C_{28}H_{20}N_2O_6$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 3.70 (s, 3H, C_7'-OCH_3), 5.00 (s, 1H, C_5-H), 6.40 (s, 1H, C_3'-H), 6.60-7.90 (m, 10Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 21.00 (C_4' -CH_3), 56.00 (C_7' -OCH_3), 80.00 (C_5), 108.00 – 151.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 153.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 480.
4e	63	140	$C_{26}H_{15}ClN_2O_5$	^{1}H NMR: δ 5.00 (s, 1H, C_5-H), 6.40 (d, *J* = 7.12 Hz, 1H, C_3' -H), 6.60-7.90 (m, 11Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 80.00 (C_5), 108.00 – 150.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 153.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 471, (M+2) 473.
4f	71	169	$C_{27}H_{17}ClN_2O_5$	^{1}H NMR: δ 2.35 (s, 3H, C_7'-CH_3), 5.00 (s, 1H, C_5-H), 6.40 (d, *J* = 7.08 Hz, 1H, C_3'-H), 6.60-7.90 (m, 10Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 80.00 (C_5), 108.00 – 150.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 153.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 485, (M+2) 487.
4g	67	155	$C_{28}H_{19}ClN_2O_5$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 2.30 (s, 3H, C_7'-CH_3), 5.00 (s, 1H, C_5-H), 6.40 (s, 1H, C_3'-H), 6.60-7.90 (m, 9Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 20.00 (C_4' -CH_3), 80.00 (C_5), 108.00 – 151.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 153.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 499, (M+2) 501.
4h	76	186	$C_{28}H_{19}ClN_2O_6$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 3.70 (s, 3H, C_7'-OCH_3), 5.00 (s, 1H, C_5-H), 6.40 (s, 1H, C_3'-H), 6.60-7.90 (m, 9Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 20.00 (C_4' -CH_3), 56.00 (C_7' -OCH_3), 80.00 (C_5), 107.00 – 150.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 153.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 515, (M+2) 517.
4i	75	167	$C_{26}H_{16}N_2O_6$	^{1}H NMR: δ 4.80 (s, 1H, C_6''-OH), 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.09 Hz, 1H, C_3'-H), 6.60-7.90 (m, 11Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 80.00 (C_5), 108.00 – 152.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 154.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 452.
4j	70	159	$C_{27}H_{18}N_2O_6$	^{1}H NMR: δ 2.30 (s, 3H, C_7'-CH_3), 4.80 (s, 1H, C_6''-OH), 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.11 Hz, 1H, C_3'-H), 6.60-7.90 (m, 10Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 80.00 (C_5), 108.00 – 153.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 155.00 (C_3), 160.00 (C_2' >C=O); MS: *m/z* M^+ 466.
4k	64	174	$C_{28}H_{20}N_2O_6$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 2.30 (s, 3H, C_7'-CH_3), 4.80 (s, 1H, C_6''-OH), 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.10 Hz, 1H, C_3'-H), 6.60-7.90 (m, 9Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 20.00 (C_4' -CH_3), 80.00 (C_5), 108.00 – 153.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 154.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 480.
4l	68	178	$C_{28}H_{20}N_2O_7$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 3.70 (s, 3H, C_7'-OCH_3), 4.80 (s, 1H, C_6''-OH), 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.09 Hz, 1H, C_3'-H), 6.60-7.90 (m, 9Ar-H, C_4'-H, C_4''-H); ^{13}C NMR: δ 20.00 (C_4' -CH_3), 56.00 (C_7' -OCH_3), 80.00 (C_5), 108.00 – 153.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 155.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 496.

Contd.

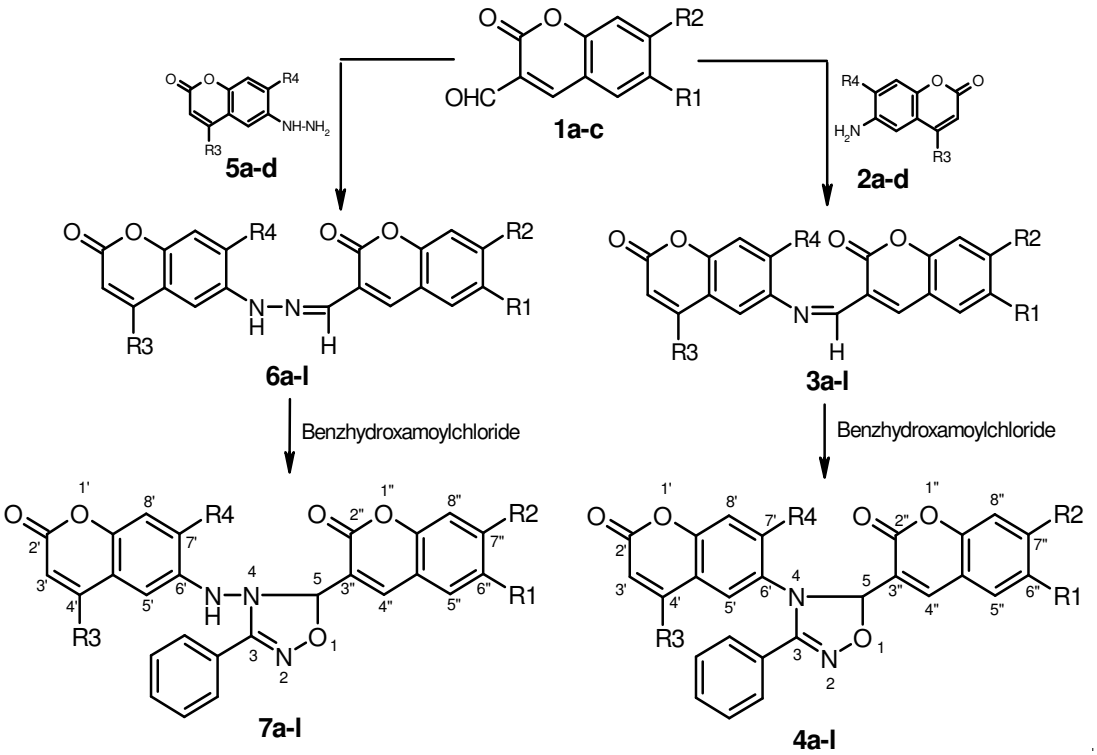
Table II — Spectral and physical characterization data of newly prepared compounds *continued*—*Contd:*

Compd	Yield (%)	m.p. (°C)	Mol. formula	^{1}H , ^{13}C NMR & MS data
7a	83	126	$C_{26}H_{17}N_3O_5$	^{1}H NMR: δ 5.00 (s, 1H, C_5-H), 6.40 (d, *J* = 7.08 Hz, 1H, C_3'-H), 6.60-7.90 (m, 12Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 80.00 (C_5), 108.00 – 150.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 451.
7b	78	141	$C_{27}H_{19}N_3O_5$	^{1}H NMR: δ 2.30 (s, 3H, C_7'-CH_3), 5.00 (s, 1H, C_5-H), 6.40 (d, *J* = 7.11 Hz, 1H, C_3'-H), 6.60-7.90 (m, 11Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 80.00 (C_5), 108.00 – 150.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 465.
7c	81	173	$C_{28}H_{21}N_3O_5$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 2.30 (s, 3H, C_7'-CH_3), 5.90 (s, 1H, C_5-H), 6.40 (s, 1H, C_3'-H), 6.60-7.90 (m, 10Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 20.00 (C_4' -CH_3), 80.00 (C_5), 108.00 – 152.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 479.
7d	80	169	$C_{28}H_{21}N_3O_6$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 3.70 (s, 3H, C_7'-OCH_3), 5.10 (s, 1H, C_5-H), 6.40 (s, 1H, C_3'-H), 6.60-7.90 (m, 10Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 20.00 (C_4' -CH_3), 56.00 (C_7' -OCH_3), 80.00 (C_5), 108.00 – 153.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 495.
7e	84	144	$C_{26}H_{16}ClN_3O_5$	^{1}H NMR: δ 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.09 Hz, 1H, C_3'-H), 6.60-7.90 (m, 11Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 80.00 (C_5), 108.00 – 150.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 486, (M+2) 488.
7f	77	158	$C_{27}H_{18}ClN_3O_5$	^{1}H NMR: δ 2.30 (s, 3H, C_7'-CH_3), 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.10 Hz, 1H, C_3'-H), 6.60-7.90 (m, 10Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 80.00 (C_5), 108.00 – 151.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 500, (M+2) 502.
7g	74	166	$C_{28}H_{20}ClN_3O_5$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 2.30 (s, 3H, C_7'-CH_3), 5.10 (s, 1H, C_5-H), 6.40 (s, 1H, C_3'-H), 6.60-7.90 (m, 9Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 15.00 (C_7' -CH_3), 20.00 (C_4' -CH_3), 80.00 (C_5), 108.00 – 152.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 514, (M+2) 516.
7h	76	168	$C_{28}H_{20}ClN_3O_6$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 3.70 (s, 3H, C_7'-OCH_3), 5.10 (s, 1H, C_5-H), 6.40 (s, 1H, C_3'-H), 6.60-7.90 (m, 9Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 20.00 (C_4' -CH_3), 56.00 (C_7' -OCH_3), 80.00 (C_5), 108.00 – 153.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M^+ 530, (M+2) 532.
7i	75	139	$C_{26}H_{17}N_3O_6$	^{1}H NMR: δ 4.80 (s, 1H, C_6''-OH), 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.09 Hz, 1H, C3′-H), 6.60-7.90 (m, 11Ar-H, C4′-H, C4″-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 80.00 (C_5), 108.00 – 155.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M+ 467.
7j	69	162	$C_{27}H_{19}N_3O_6$	^{1}H NMR: δ 2.30 (s, 3H, C7′-CH_3), 4.80 (s, 1H, C_6''-OH), 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.10 Hz, 1H, C_3'-H), 6.60-7.90 (m, 10Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 15.00 (C7′ -CH_3), 80.00 (C_5), 108.00 – 156.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C2″ >C=O); MS: *m/z* M+ 481.
7k	78	168	$C_{28}H_{21}N_3O_6$	^{1}H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 2.30 (s, 3H, C_7'-CH_3), 4.80 (s, 1H, C_6''-OH), 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.08 Hz, 1H, C_3'-H), 6.60-7.90 (m, 9Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 15.00 (C7′ -CH_3), 20.00 (C_4' -CH_3), 80.00 (C_5), 108.00 – 155.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M+ 495.
7l	73	163	$C_{28}H_{21}N_3O_7$	1H NMR: δ 1.70 (s, 3H, C_4'-CH_3), 3.70 (s, 3H, C_7'-OCH_3), 4.80 (s, 1H, C_6''-OH), 5.10 (s, 1H, C_5-H), 6.40 (d, *J* = 7.11 Hz, 1H, C_3'-H), 6.60-7.90 (m, 9Ar-H, C_4'-H, C_4''-H), 9.50 (s, 1H, >NH, D_2O exchangeable); ^{13}C NMR: δ 20.00 (C_4' -CH_3), 56.00 (C_7' -OCH_3), 80.00 (C_5), 108.00 – 155.00 (18Ar-C + C_3', C_4', C_3'', C_4''), 158.00 (C_3), 160.00 (C_2' >C=O), 162.00 (C_2'' >C=O); MS: *m/z* M+ 511.

series, **7e** was more active against *S. albus* at the concentration of 20 µg/mL. Compound **7h** was active against *S. pyogenes* at the concentration of 25 µg/mL and compound **4h** was more effective against *E. coli* at the concentration of 25 µg/mL. All other compounds of the same series exhibited significant to moderate antibacterial activity.

Experimental Section

Melting points were determined by open capillary method and are uncorrected. Homogenity of the compounds was monitered by TLC. IR spectra were recorded on Perkin Elmer IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AM 400 (400 MHz) instrument using TMS as an internal standard and DMSO-d_6 as a solvent. Chemical shifts are given in δ (ppm) and coupling constants (*J*) in Hertz (Hz). Splitting patterns are designated as follows: s- singlet, br s- broad singlet, d- doublet, t- triplet and q- quartet, qt- quintet, m- multiplet. Mass spectra were recorded on Schimadzu GC-MS. Elemental analysis (C, H, N) was performed on Perkin Elmer 240 analyzer and all analysis results are within ±0.4% of the theoretical value unless otherwise specified. All products were purified by recrystallisation from ethanol. Physicochemical and spectral data for the synthesized compounds are given in **Table II**. The synthetic route is presented in **Scheme I**.



1a-7a: R1= R2= R3= R4= -H

1b-7b: R1= -H, R2= -Cl, R3= -H, R4= -CH_3

1c-7c: R1= -OH, R2= -H, R3= -CH_3, R4= -CH_3

2d-7d: R3= -CH_3, R4= -OCH_3

3e, 4e, 6e, 7e: R1= -H, R2= -Cl, R3= R4= -H

3f, 4f, 6f, 7f: R1= -H, R2= -Cl, R3= -H, R4= -CH_3

3g, 4g, 6g, 7g: R1= -H, R2= -Cl, R3= -CH_3, R4= -CH_3

3h, 4h, 6h, 7h: R1= -H, R2= -Cl, R3= -CH_3, R4= -OCH_3

3i, 4i, 6i, 7i: R1= -OH, R2= -H, R3= R4= -H

3j, 4j, 6j, 7j: R1= -OH, R2= -H, R3= -H, R4= -CH_3

3k, 4k, 6k, 7k; R1= -OH, R2= -H, R3= -CH_3, R4= -CH_3

3l, 4l, 6l, 7l: R1= -OH, R2= -H, R3= -CH_3, R4= -OCH_3

Scheme I

4-Coumarin-6-yl(amino)-5-coumarin-3-yl-3-phenyl-1,2,4-oxadia-zolines, 4a-l and 7a-l (Table II)

To a solution of compound **3a-l** and **6a-l** (0.01 mole) in dry chloroform (50 mL) separately, cooled in ice bath, a solution of benzhydroxamoyl chloride (0.01 mole) in chloroform was added. Triethylamine (0.01 mole) in chloroform (20 mL) was added to the reaction mixture at 0°C over a period of 15 min with continuous stirring. After the addition was complete the stirring was continued for further 4 hr at 0°C. The chloroform layer was washed with water (2×25 mL) to free it from triethylamine hydrochloride and dried (anhyd. Na_2SO_4). The solvent was distilled off and the crude product triturated with light petrol (40-60°C) repeatedly. The residue on shaking with methanol became an amorphous substance that was purified by recrystallization from ethanol to yield the product.

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