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Note

Synthesis and antimicrobial screening of 5-(4,7-dimethyl-2-oxo-2*H*-benzopyran-6-ylazo)-2-methyl-6-morpholin-4-yl-2, 3-dihydro-3*H*-pyrimidin-4-one and 5-(4,7-dimethyl-2-oxo-2*H*-benzopyran-6-ylazo)-2-methyl-6-piperidin-1-yl-2,3-dihydro-3*H*-pyrimidin-4-one

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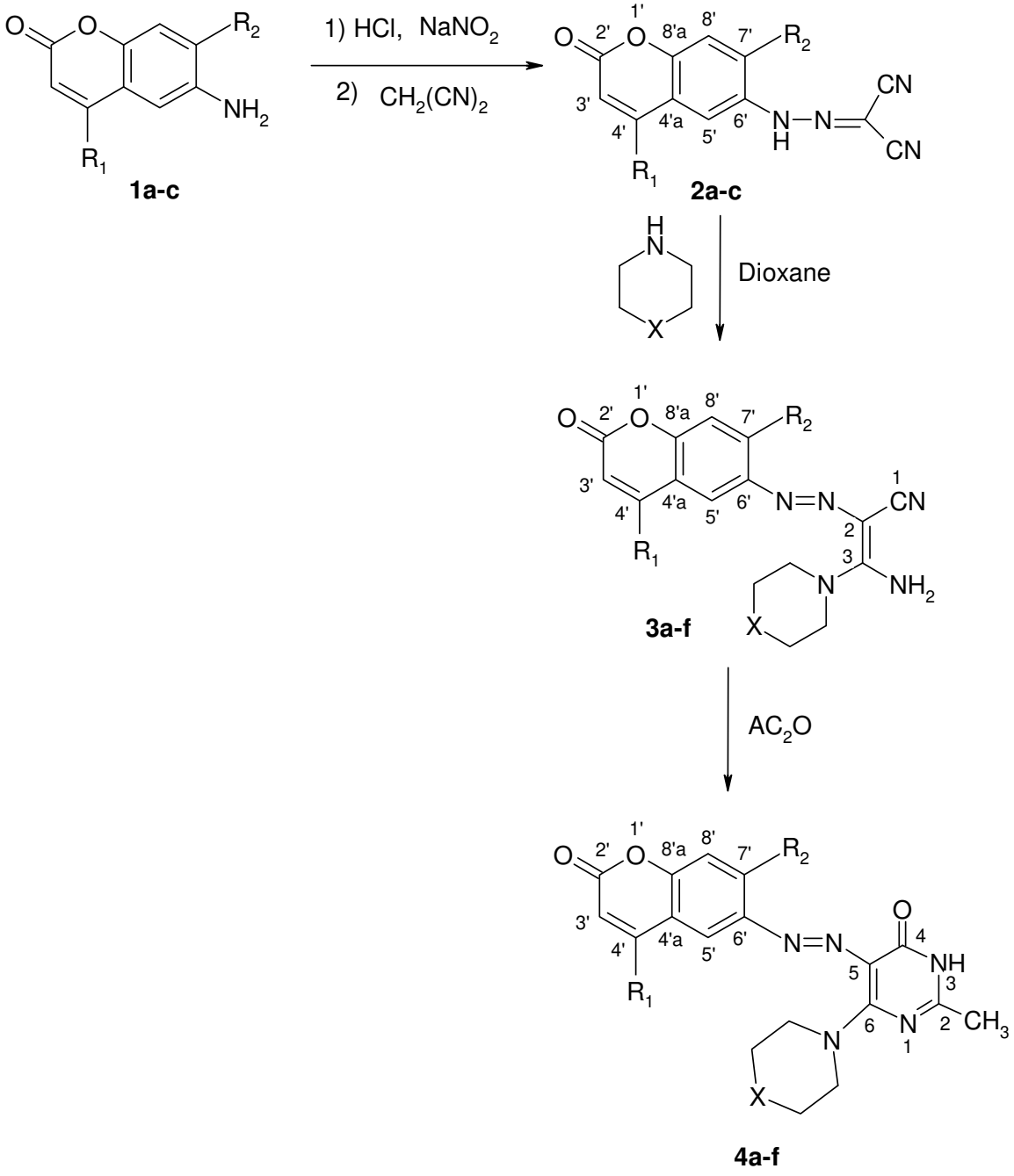
The coupling reaction of the diazonium solution of the 6-aminocoumarins **(1a-c)** with malononitrile affords the corresponding 2-[(4,7-dimethyl-2-oxo-2H-benzopyran-6-yl)-hydrazono]-malononitrile **(2a-c)** which on refluxing with morpholine and piperidine separately yields the corresponding 3-amino-2-(4,7-dimethyl-2-oxo-2H-benzopyran-6-ylazo)-3-morpholin-4-yl-acrylonitrile **(3a-c)** and 3-amino-2-(4,7-dimethyl-2-oxo-2H-benzopyran-6-ylazo)-3-piperidin-1-yl-acrylonitrile **(3d-f)** respectively. The enaminonitrile derivatives (**3a-f)** on heating with acetic anhydride give the corresponding 5-(4,7-dimethyl-2-oxo-2H-benzopyran-6-ylazo)-2-methyl-6-morpholin-4-yl-2,3-dihydro-3H-pyrimidin-4-one and 5-(4,7-dimethyl-2-oxo-2H-benzopyran-6-ylazo)-2-methyl-6-piperidin-1-yl-2,3-dihydro-3H-pyrimidin-4-one (**4a-f)**. The structures of the compounds (**2a-c)**, (**3a-f)** and (**4a-f)** have been established on the basis of spectral and analytical data. All the above compounds have been screened for their antimicrobial activities and are found to possess significant antibacterial activities.

Keywords: 6-Aminocoumarin, enaminonitrile, pyrimidine, antimicrobial activity, diazotized.

Compounds incorporating benzopyrone structural units are reported to possess a wide range of biological activities[1]. The 6-substituted coumarin derivatives have been reported to exhibit antibacterial and antifungal activities. Nitrogen mustards synthesized from 6-aminocoumarins exhibit carcinogenic activity[2]. They are also known to possess antiviral[3] activity and especially effective against HIV_1[4]. The schiff bases of 6-aminocoumarins are well-known for their wide range of pharmaceutical like antibacterial, and antifungal[5] activities. The pyrimidine derivatives comprise a diverse and interesting group of drugs[6]. A comprehensive review concerning pyrimidines has been published by Brown[7]. Pyrimidines, in general are extremely important for their biological activities. Such as antiviral agents[8], as selective cholecystokinin subtype 1 (CCK1) receptor antagonists[9], and anti-inflammatory[10,11]. The biological importance of pyrimidine derivatives and the 6-substituted coumarin has prompted to the synthesis coumarinyl azo pyrimidine derivatives, which may have some of the biological activity is of considerable interest.

Result and Discussion

6-Amino coumarin (**1a-c)** was diazotized and coupled with malononitrile to give 2-[(4,7-dimethyl-2-oxo-2*H*-benzopyran-6-yl)-hydrazono]-malononitrile (**2a-c) (Scheme I)**. Structures of **(2a-c)** were confirmed on the basis of spectral and analytical data **Table I**. The IR spectrum of **2a** in KBr showed bands at 3182 cm^{-1} for the N-H stretching, band at 2232 cm^{-1} due to (C≡N) groups, 1743 cm^{-1} for the carbonyl group etc. Its ^1H NMR spectrum in $CDCl_3$ showed the presence of a singlet at δ 2.50 for three protons of methyl group at $C_{4'}$, a singlet at δ 2.52 for three protons of methyl group at $C_{7'}$. A singlet appeared at δ 9.57 for the >NH proton which was D_2O exchangeable. The mass spectrum of **2a** showed molecular ion peak at *m/z* 266 along with other peaks at *m/z* 238, 210, 188, 173, 160, 145, 117 and 91 with base peak at *m/z* 77. 3-Amino-2-(4,7-dimethyl-2-oxo-2*H*-benzo-pyran-6-ylazo)-3-morpholin-4-yl-acrylonitrile (**3a-c)** and 3-amino-2-(4,7-dimethyl-2-oxo-2H-benzopyran-6-ylazo)-3-piperidin-1-yl-acrylonitrile (**3d-f)** were obtained by refluxing (**2a-c)** with morpholine and piperidine separately in dioxane solvent. The IR spectra of the compounds **3a** exhibited absorption bands in the region of 3435-3290 cm^{-1} due to $-NH_2$ group, appearance of bands at 2187 cm^{-1} due to (C≡N) group, 1717 cm^{-1} for the carbonyl group etc. Its ^1H NMR spectrum in $CDCl_3$ showed a sharp singlet at δ 2.40 and 2.65 for the three protons each of the two methyl groups of $C_{4'}$ and $C_{7'}$ respectively, multiplet appeared at δ 3.78 for the four protons of the two methylene groups of $-CH_2-N-CH_2-$ of the morpholine ring; another multiplet was observed at δ 3.89 for the four protons of the two



1a-c **2a-c** **3a-f** **4a-f**

1a, 2a. $R_1 = CH_3$, $R_2 = CH_3$ **3a, 4a.** $R_1 = CH_3$, $R_2 = CH_3$, X = O.
1b, 2b. $R_1 = H$, $R_2 = CH_3$ **3b, 4b.** $R_1 = H$, $R_2 = CH_3$, X = O.
1c, 2c. $R_1 = H$, $R_2 = H$ **3c, 4c.** $R_1 = H$, $R_2 = H$, X = O.
3d, 4d. $R_1 = CH_3$, $R_2 = CH_3$, $X = CH_2$
3e, 4e. $R_1 = H$, $R_2 = CH_3$, $X = CH_2$.
3f, 4f. $R_1 = H$, $R_2 = H$, $X = CH_2$.

Scheme I

Table I — Characterization data of compounds **2a-c, 3a-f** and **4a-f**

Compd	Mol. Formula (Mol. Wt.)	m.p.°C	Yield (%)	{Required(%) (Found.)}		
				C	H	N
2a	$C_{14}H_{10}N_4O_2$ (266.26)	212-15	81	63.15% (63.05)	3.79% (3.73)	21.04% (20.84)
2b	$C_{13}H_8N_4O_2$ (252.23)	178-80	78	61.90% (61.79)	3.20% (3.39)	22.21% (22.10)
2c	$C_{12}H_6N_4O_2$ (238.21)	165-67	83	60.51% (60.32)	2.54% (2.64)	23.52% (23.65)
3a	$C_{18}H_{19}N_5O_3$ (353.38)	201-05	74	61.18% (61.37)	5.42% (5.24)	19.82% (19.66)
3b	$C_{17}H_{17}N_5O_3$ (339.36)	162-64	69	60.17% (60.37)	5.05% (5.25)	20.64% (20.42)
3c	$C_{16}H_{15}N_5O_3$ (325.33)	154-56	72	59.07% (59.37)	4.65% (4.84)	21.53% (21.33)
3d	$C_{19}H_{21}N_5O_2$ (351.41)	178-81	67	64.94% (64.78)	6.02% (5.89)	19.93% (19.74)
3e	$C_{18}H_{19}N_5O_2$ (337.38)	137-40	66	64.08% (64.22)	5.68% (5.56)	20.76% (20.69)
3f	$C_{17}H_{17}N_5O_2$ (323.36)	133-36	72	63.15% (63.05)	5.30% (5.15)	21.66% (21.44)
4a	$C_{20}H_{21}N_5O_4$ (395.42)	178-80	60	60.75% (60.88)	5.35% (5.20)	17.71% (17.56)
4b	$C_{19}H_{19}N_5O_4$ (381.41)	171-73	61	59.84% (59.96)	5.02% (5.24)	18.36% (18.59)
4c	$C_{18}H_{17}N_5O_4$ (367.37)	165-167	64	58.85% (58.60)	4.66% (4.44)	19.06% (19.02)
4d	$C_{21}H_{23}N_5O_3$ (393.45)	180-82	65	64.11% (64.26)	5.89% (5.77)	17.80% (17.63)
4e	$C_{20}H_{21}N_5O_3$ (379.42)	174-76	59	63.31% (63.62)	5.58% (5.44)	18.46% (18.54)
4f	$C_{19}H_{19}N_5O_3$ (365.39)	165-66	54	62.46% (62.32)	5.24% (5.39)	19.17% (19.02)

methylene groups of -CH_2-O-CH_2- of the morpholine ring, a broad singlet at δ 5.62 integrating for two protons of –NH_2 group which is D_2O exchangeable. The ^{13}C NMR spectrum showed signals at δ 17.93 for the methyl carbon at $C_{4'}$, 18.71 for the carbon of the methyl group at $C_{7'}$, 49.32 for the methylene carbons of -CH_2-N-CH_2- of the morpholine ring, 66.53 for the methylene carbons of –CH_2-O-CH_2- of the morpholine ring, 162.84 for the carbonyl of coumarin. The mass spectrum of **3a** showed molecular ion peak at *m/z* 353 along with other peaks at *m/z* 284, 266, 210, 188, 174, 160, 146, 145, 115, 91 and 65 with base peak at *m/z* 160. The enaminonitrile derivative **(3a-f)** was reacted with acetic anhydride to give the corresponding 5-(4,7-dimethyl-2-oxo-2*H*-benzopyran-6-ylazo)-2-methyl-6-morpholin-4-yl-2,3-dihydro-3*H*-pyrimidin-4-one and 5-(4,7-dimethyl-2-oxo-2*H*-benzopyran-6-ylazo)-2-methyl-6-piperidin-1-yl-2,3-dihydro-3*H*-pyrimidin-4-one (**4a-f, Scheme I)**. The IR spectra of the compounds **4a** exhibited absorption band in the region of 3295 cm^{-1} due to –NH group, 1710 for the carbonyl group of coumarin and 1683 for the carbonyl group of pyrimidine, the disappearance of bands at 2187 cm^{-1} of (C≡N) group also proved the product formation. Its ^1H NMR spectrum in $CDCl_3$ showed a sharp singlet at δ 2.20, 2.39 and 2.49 for the three protons each of the three methyl groups at $C_{4'}$, $C_{7'}$ and C_2 respectively, multiplet appeared at δ 3.76 for the four protons of the two methylene groups of -CH_2-N-CH_2- of the morpholine ring; another multiplet was observed at δ 3.93 for the four protons of the two methylene groups of -CH_2-O-CH_2- of the morpholine ring, a singlet at δ 8.85 integrating for >NH which is D_2O exchangeable. The mass spectrum of **4a** showed molecular ion peak at *m/z* 395 along with other peaks at *m/z* 377, 362, 326, 284, 239, 214, 188, 173, 160 and 117 with base peak at *m/z* 188.

Antimicrobial activity

All the synthesized compounds (**2a-c),** (**3a-f)** and (**4a-f)** were screened for their antibacterial activity

against *S. aureus*, *S. typhi* and *E. coli* (**Table II**) by the drug diffusion method[12]. The zone of inhibition was measured in mm and was compared with standard drug. DMSO was used as a blank and Streptomycin was used as antibacterial standard. All the compounds were tested at 100 μg/mL and 250 μg/mL concentration.

From the antimicrobial screening of the compounds (**2a-c),** (**3a-f)** and (**4a-f)** it could observe that the introduction of morpholine and pyrimidine to an azo compound shows the comparable biological activity.

Experimental Section

General: Melting points were taken in open capillaries and are uncorrected. Purity of the compounds was checked on TLC. IR spectra (ν_{max} in cm^{-1}) were recorded on a Perkin Elmer FTIR; NMR (^1H and ^{13}C) on 300 MHz JEOL NMR AL300 using TMS as standard and $CDCl_3$ as a solvent; and mass spectra on a Shimadzu GC-MS QP-2010.

2-[(4,7-Dimethyl-2-oxo-2*H*-benzopyran-6-yl)-hydrazono]-malononitrile (2a-c). General Procedure.

A solution 6-amino coumarin (**1a-c)** (0.01 mole) in conc. HCl (5 mL) and water (5 mL) was cooled to 0-5°C with stirring. Sodium nitrite (0.70 g, 0.01mole) in water (5 mL) was gradually added to the solution over a 15 min period at 0-5°C with stirring. The reaction mixture was stirred for further 30 min at 0-5°C, the solution was filtered to obtain a clear diazonium salt solution. The cold diazonium solution was added then drop wise to a well cooled and stirred mixture of the malononitrile (0.01 mole) and sodium acetate (2.0 g dissolved in 10 mL of 50% ethanol). The stirring was continued for further 2 hr after the addition at the same temperature. The product formed was filtered, washed with water, dried and recrystallized from ethanol to give (**2a-c)**.

Table II — Antibacterial activity of compounds **2a-c, 3a-f** and **4a-f**

Compd	Zone of inhibition in mm					
	S. aureus		*S. typhi*		E. coli	
	100 μg	250 μg	100 μg	250 μg	100 μg	250 μg
2a	10	11	14	15	14	15
2b	8	10	12	13	12	14
2c	7	9	8	10	9	11
3a	14	15	14	16	15	16
3b	12	13	14	15	14	15
3c	9	11	11	13	12	13
3d	13	14	15	16	16	17
3e	13	15	12	14	13	15
3f	11	12	13	14	12	14
4a	14	15	15	17	16	17
4b	12	13	13	14	13	15
4c	9	11	12	13	12	13
4d	15	16	14	15	15	16
4e	12	14	13	14	14	15
4f	11	13	12	14	12	13

Disc size: 6.35mm
Duration: 24 hr.
Standard: Streptomycin
resistant (11mm/less)
Sensitive (15 mm/more)
Control: DMSO
Intermediate (12-14 mm)

3-Amino-2-(4,7-dimethyl-2-oxo-2*H*-benzopyran-6-ylazo)-3-morpholin-4-yl-acrylonitrile and 3-amino-2-(4,7-dimethyl-2-oxo-2*H*-benzopyran-6-ylazo)-3-piperidin-1-yl-acrylonitrile (3a-f). General Procedure.

A solution of (**2a-c)** (0.01 mole) and morpholine or piperidine (2 mL) in dioxane (20 mL) was refluxed for 6 hr (TLC monitoring). After the completion of reaction, the excess of dioxane was recovered by distillation. The residue obtained was treated with cold water, the solid obtained was filtered, washed with excess of water, dried and recrystallized from ethanol to give (**3a-f)**.

5-(4,7-Dimethyl-2-oxo-2*H*-benzopyran-6-ylazo)-2-methyl-6-morpholin-4-yl-2,3-dihydro-3*H*-pyrimidin-4-one and 5-(4,7-dimethyl-2-oxo-2*H*-benzopyran-6-ylazo)-2-methyl-6-piperidin-1-yl-2,3-dihydro-3*H*-pyrimidin-4-one (4a-f). General Procedure.

Compound **(3a-f)** (0.01 mole) was refluxed in 5 mL acetic anhydride for 3 hr. After cooling, the reaction mixture was poured into ice-water. The solid obtained was filtered, washed with water, dried and recrystallized from ethanol to give **(4a-f).**

Spectral data:

2a: IR (KBr): 3182 (-NH), 2232 (-CN), 1743 (>C=O), 1625, 1541, 1461 cm^{-1}. ^1H NMR: δ 2.50 (s, 3H, $C_{4'}$-CH_3), 2.52 (s, 3H, $C_{7'}$-CH_3), 6.36 (s, 1H, $C_{3'}$-H), 7.25 (s, 1H, $C_{8'}$-H), 7.71 (s, 1H, $C_{5'}$-H), 9.57 (s, 1H, >NH, D_2O exchangeable). Mass: *m/z* (%) M^+ 266(31) 238(6), 210(5), 188(31), 173(25), 160(46), 145(31), 117(61), 91(100), 77(67).

2b: IR (KBr): 3184 (-NH), 2221 (-CN), 1737 (>C=O), 1625, 1544, 1477, 1261, 1127 cm^{-1}. ^1H

NMR: δ 2.51 (s, 3H, $C_{7'}$-CH_3), 6.46 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.23 (s, 1H, $C_{8'}$-H), 7.64 (s, 1H, $C_{5'}$-H), 7.69 (d, 1H, *J* = 9Hz, $C_{4'}$-H), 9.52 (s, 1H, >NH, D_2O exchangeable).

2c: IR (KBr): 3193 (-NH), 2224 (-CN), 1715 (>C=O), 1620, 1549, 1469, 1145 cm^{-1}. ^1H NMR: δ 6.52 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.33-7.74 (m, 4H, coumarine moiety), 9.50 (s, 1H, >NH, D_2O exchangeable).

3a: IR (KBr): 3435, 3290 (-NH_2), 2187 (-CN), 1717 (>C=O), 1615, 1548, 1492, 1110 cm^{-1}. ^1H NMR: δ 2.40 (s, 3H, $C_{4'}$-CH_3), 2.65 (s, 3H, $C_{7'}$-CH_3), 3.78 (m, 4H, -CH_2-N-CH_2), 3.89 (m, 4H, -CH_2-O-CH_2), 6.23 (s, 1H, $C_{3'}$-H), 7.18 (s, 1H, $C_{8'}$-H), 7.41 (s, 1H, $C_{5'}$-H), 5.62 (br, 2H, >NH_2, D_2O exchangeable). ^{13}C NMR: δ 17.93 ($C_{4'}$-CH_3), 18.71 ($C_{7'}$-CH_3), 49.32 (-CH_2-N-CH_2-, morpholine ring), 66.53 (-CH_2-O-CH_2-, morpholine ring), 110.64, 111.32, 111.60, 113.96, 117.24, 118.10, 118.39, 138.57 ($C_{4'}$), 151.18 ($C_{8a'}$), 154.43 (C_2), 160.54 (C_3), 162.84 ($C_{2'}$ >C=O). Mass: *m/z* (%) M^+ 353(29) 284(8), 266(6), 210(9), 188(43), 174(6), 160(100), 146(35), 145(42), 115(53), 91(78), 65(80).

3b: IR (KBr): 3421, 3288 (-NH_2), 2180 (-CN), 1724 (>C=O), 1625, 1531, 1488, 1103 cm^{-1}. ^1H NMR: δ 2.66 (s, 3H, $C_{7'}$-CH_3), 3.77 (m, 4H, -CH_2-N-CH_2), 3.89 (m, 4H, -CH_2-O-CH_2), 6.37 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.18 (s, 1H, $C_{8'}$-H), 7.33 (s, 1H, $C_{5'}$-H), 7.66 (d, 1H, *J* = 9Hz, $C_{4'}$-H), 5.60 (br, 2H, >NH_2, D_2O exchangeable).

3c: IR (KBr): 3427, 3284 (-NH_2), 2177 (-CN), 1710 (>C=O), 1618, 1541, 1478, 1115 cm^{-1}. ^1H NMR: δ 3.77 (m, 4H, -CH_2-N-CH_2), 3.88 (m, 4H, -CH_2-O-CH_2), 6.40 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.26-7.68 (m, 4H, coumarine moiety), 5.59 (br, 2H, >NH_2, D_2O exchangeable).

3d: IR (KBr): 3437, 3301 (-NH_2), 2184 (-CN), 1714 (>C=O), 1615, 1537, 1478, 1116 cm^{-1}. ^1H NMR: δ 2.39 (s, 3H, $C_{4'}$-CH_3), 2.63 (s, 3H, $C_{7'}$-CH_3), 3.71 (m, 4H, -CH_2-N-CH_2), 1.79-1.65 (m, 6H, piperydinyl moiety), 6.22 (s, 1H, $C_{3'}$-H), 7.17 (s, 1H, $C_{8'}$-H), 7.41 (s, 1H, $C_{5'}$-H), 5.69 (br, 2H, >NH_2, D_2O exchangeable).

3e: IR (KBr): 3424, 3309 (-NH_2), 2183(-CN), 1723 (>C=O), 1619, 1555, 1493, 1365, 1219, 1144 cm^{-1}. ^1H NMR: δ 2.65 (s, 3H, $C_{7'}$-CH_3), 3.71 (m, 4H, -CH_2-N-CH_2), 1.78-1.65 (m, 6H, piperydinyl moiety), 6.35 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.15 (s, 1H, $C_{8'}$-H), 7.27 (s, 1H, $C_{5'}$-H), 7.66 (d, 1H, *J* = 9Hz, $C_{4'}$-H), 5.68 (br, 2H, >NH_2, D_2O exchangeable). Mass: *m/z* (%) M^+ 337(6) 301(15), 270(9), 252(16), 175(45), 160(26), 146(29), 131(17), 112(59), 84(100), 69(32).

3f: IR (KBr): 3430, 3291 (-NH_2), 2187 (-CN), 1737 (>C=O), 1625, 1554, 1499, 1129 cm^{-1}. ^1H NMR: δ 3.71 (m, 4H, -CH_2-N-CH_2), 1.78-1.64 (m, 6H, piperydinyl moiety), 6.40 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.26-7.66 (m, 4H, coumarine moiety), 5.67 (br, 2H, >NH_2, D_2O exchangeable).

4a: IR (KBr): 3295 (-NH) 1710 (>C=O), 1683 (>C=O), 1623, 1519, 1445, 1383, 1195 cm^{-1}. ^1H NMR: δ 2.20 (s, 3H, $C_{4'}$-CH_3), 2.39 (s, 3H, $C_{7'}$-CH_3), 2.49 (s, 3H, C_2-CH_3), 3.76 (m, 4H, -CH_2-N-CH_2), 3.93 (m, 4H, -CH_2-O-CH_2), 6.33 (s, 1H, $C_{3'}$-H), 7.20 (s, 1H, $C_{8'}$-H), 7.43 (s, 1H, $C_{5'}$-H), 8.85 (s, 1H, >NH, D_2O exchangeable). Mass: *m/z* (%) M^+ 395 (10), 377 (14), 362 (19), 326 (39), 284 (68), 239 (32), 214 (19), 188 (100), 173 (66), 160 (82), 117(53).

4b: IR (KBr): 3288 (-NH), 1716 (>C=O), 1686 (>C=O), 1626, 1525, 1449, 1377, 1180 cm^{-1}. ^1H NMR: δ 2.38 (s, 3H, $C_{7'}$-CH_3), 2.51(s, 3H, C_2-CH_3), 3.77 (m, 4H, -CH_2-N-CH_2), 3.90 (m, 4H, -CH_2-O-CH_2), 6.43 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.26 (s, 1H, $C_{8'}$-H), 7.36 (s, 1H, $C_{5'}$-H), 7.64 (d, 1H, *J* = 9Hz, $C_{4'}$-H), 8.85 (s, 1H, >NH, D_2O exchangeable).

4c: IR (KBr): 3296 (-NH), 1700 (>C=O), 1676 (>C=O), 1619, 1512, 1440, 1373, 1169 cm^{-1}. ^1H NMR: δ 2.52 (s, 3H, C_2-CH_3), 3.78 (m, 4H, -CH_2-N-CH_2), 3.90 (m, 4H, -CH_2-O-CH_2), 6.49 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.34-7.74 (m, 4H, coumarine moiety), 8.85 (s, 1H, >NH, D_2O exchangeable).

4d: IR (KBr): 3305 (-NH), 1724 (>C=O), 1673 (>C=O), 1616, 1509, 1425, 1392, 11990 cm^{-1}. ^1H NMR: δ 2.19 (s, 3H, $C_{4'}$-CH_3), 2.39 (s, 3H, $C_{7'}$-CH_3), 2.49 (s, 3H, C_2-CH_3), 3.69 (m, 4H, -CH_2-N-CH_2), 1.76-1.62(m, 6H, piperydinyl moiety), 6.31(s, 1H, $C_{3'}$-H), 7.19 (s, 1H, $C_{8'}$-H), 7.40 (s, 1H, $C_{5'}$-H), 8.88 (s, 1H, >NH, D_2O exchangeable).

4e: IR (KBr): 3314 (-NH), 1720 (>C=O), 1669 (>C=O), 1629, 1534, 1442, 1391, 1175 cm^{-1}. ^1H NMR: δ 2.38 (s, 3H, $C_{7'}$-CH_3), 2.51 (s, 3H, C_2-CH_3), 3.68 (m, 4H, -CH_2-N-CH_2), 1.76-1.62 (m, 6H, piperydinyl moiety), 6.43 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.25 (s, 1H, $C_{8'}$-H), 7.36 (s, 1H, $C_{5'}$-H), 7.64 (d, 1H, *J* = 9Hz, $C_{4'}$-H), 8.89 (s, 1H, >NH, D_2O exchangeable).

4f: IR (KBr): 3310 (-NH), 1718 (>C=O), 1688 (>C=O), 1629, 1512, 1461, 1378, 1188 cm^{-1}. ^1H NMR: δ 2.53 (s, 3H, C_2-CH_3), 3.67 (m, 4H, -CH_2-N-CH_2), 1.76-1.62 (m, 6H, piperydinyl moiety), 6.49 (d, 1H, *J* = 9Hz, $C_{3'}$-H), 7.33-7.73 (m, 4H, coumarine

moiety), 8.90 (s, 1H, >NH, D_2O exchangeable).

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References

1 Ghosh C.K, *J Indian Chem Soc*, 67, **1990**, 5.
2 Schuda P F, *Top Org Chem*, 91, **1980**, 75.
3 Kun E & Aurelian L, *US Pat* 412 783, **1991**; *Chem Abstr*, 115, **1991**, 92071t.
4 Kun E (*Octamer Inc USA*) *PCT Int App*, WO9851, 307.
5 Mulwad V V & Shirodkar J M, *Indian J Heterocyclic Chem*, 11, **2002**, 199.
6 Chabner B A, Wilson W & Supko J, Pharmacology & Toxicity of Antineoplstic Drugs in *Williams Hematology* edited by E Beutler, M A Lichtman, B S Coller, T J Kipps & U Seligsoh, 6th Edn, (McGraw-Hill, New York) **2001**, pp. 185.
7 Brown D J, Pyrimidines and their Benzo derivatives in *Comprehensive Heterocyclic Chemistry, The Stucture, Reactions, Synthesis & Uses of Heterocyclic Compounds*, edited by A R Katritzky & C W Rees (Prgamon Press, Oxford) **1984**, pp. 57.
8 Nasr M N & Gineinah M M*, Arch. Pharm*. 335. **2002**, 289.
9 Bartolome-Nebreda J M, Garcia-Lopez M T & Gonzalez-Muniz R, *J Med Chem,*24, **2001**, 4196.
10 Santagati A, Granata G, Santagati M, Cutuli V, Mangano M G & Caruso A, *Arznei-Forsch* 52, **2002**, 448.
11 Unangst C P, Conner D T, Kostlan C R & Shrum G P, *J Heterocycl Chem*, 32, **1995,** 1197
12 Frankle S, Reitman S & Sonnenwirth A C; Gradwol's *Clinical Laboratory Method and Diagnosis*, 7th Edn, Vol 2, (C V Mosby Co, Germany), **1970**, 1406.