Iranian Journal of Organic Chemistry Vol. 10, No. 2 (2018) 2343-2351

Synthesis and antimicrobial activity of novel substituted 2-(9-ethyl-9*H*-carbazol-3-yl)-4*H*-chromen-4-one derivatives

Vijay A. Kadnor[a], Gopinath D. Shirole[b], Sharad N. Shelke[b, c]*

[a]*Department of Chemistry, A. C. S. College Satral, Rahuri, Ahmednagar, MH 413711, India.*
[b]*Department of Chemistry, S. S. G. M. College, Kopargaon, Ahmednagar, MH 423601, India.*
[c]*P. G. & Research Center, Department of Chemistry, R. K. M. Mahavidyalay, Ahmednagar, India.*

Received: February 2018; Revised: March 2018; Accepted: April 2018

Abstract: A series of novel carbazole tethered chromone derivatives were synthesized from 3-(9-ethyl-9*H*-carbazol-3-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one. The structures of newly synthesized compounds were confirmed by their IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. The synthesized compounds were evaluated for their *in vitro* antimicrobial activity. Notably, compound **5a** with a broad antimicrobial spectrum was the only compound exhibiting activities against all test bacterial and fungal strains as compared to standard drug ampicillin. Most of the newly synthesized compounds (**4**, **5**, and **6**) have moderate to good antimicrobial activities.

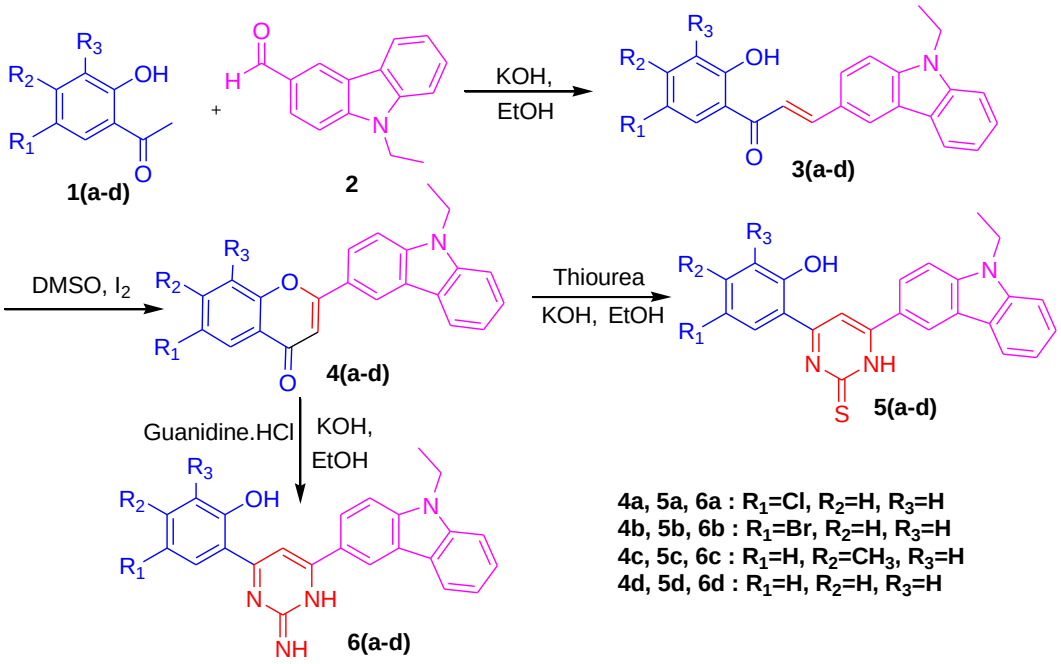
Keywords: Carbazole, Chromone, Thiopyrimidine, Iminopyrimidine, Antimicrobial activity.

Introduction

Chromones are oxygen based heterocyclic compounds display a broad spectrum of biological properties such as anticancer [1], antimicrobial [2], antiviral [3] and anti-tobacco mosaic virus [4] activities. They are suitable molecules because their chemical reactivity towards nucleophiles provides a useful route for the preparation of a variety of heterocyclic systems [5, 6]. The use of chromone compounds to synthesize heterocyclic systems via ring opening and ring closure sequences with suitable nucleophiles is well known [7-9]. Chromones possessing heterocyclic substituents at 2 and 3 position possess coronary dilatory [10], muscle relaxant property [11] and antimicrobial activities [12]. Recently an efficient route for the synthesis of derivatives of tetrahydrochromeno [2,3-b] carbazoles has been developed [13], also 3-hydroxy carbazole chromones have been synthesized and displayed an effective antimicrobial activity [14]. On the other hand, carbazole derivatives are an important class of heterocyclic compounds have been created considerable attention to these structures due to their capability to accommodate the substituents around the carbazole frame [15], biological activities and potential application as pharmacological agents [16, 17]. Pyrimidine and thiopyrimidine are one of an important class of heterocyclic compounds for new drug development that fascinated much attention due to their extensive spectrum of biological potential. [18-20], a recent study has shown carbazole pyrimidine derivatives display a new class of anticancer agents [21]. Therefore, the carbazole is shown to be a useful starting material for physiologically or pharmacologically important products. Bioactivity associated with carbazole moiety in association with chromone and pyrimidine nucleus and our contribution in this field [22-25], we report the series of new substituted 2-(9-ethyl-9*H*-carbazol-3-yl)-4*H*-chromen-4-one derivatives (Scheme **1**) and reported their *in*

*Corresponding author. Tel: +(91) 8888199853/ 9403634885; Fax: (+91) 241-2430679 E-mail: snshelke@yahoo.co.in

vitro antimicrobial activities against several test microorganisms.

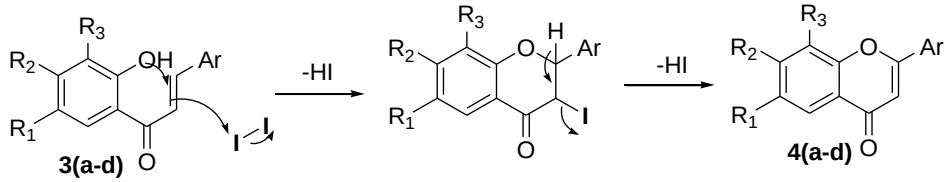


Scheme 1: Synthesis of 2-(9-ethyl-9*H*-carbazol-3-yl)-4*H*-chromen-4-one derivatives

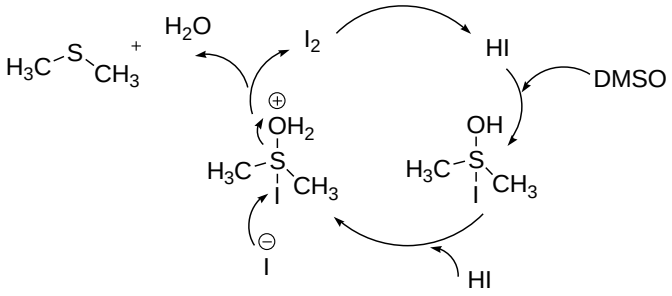
Results and discussion

Chemistry

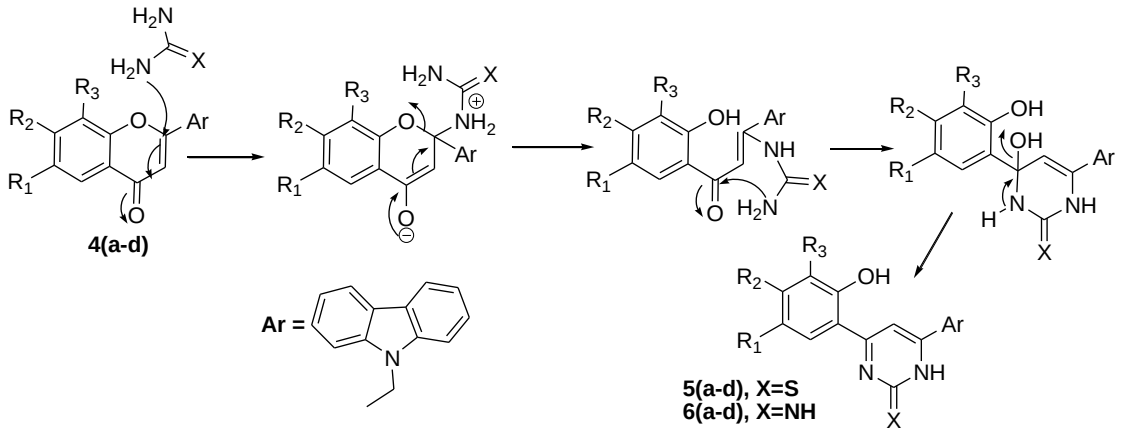
The structures of carbazole derivatives were confirmed on the basis of IR, ^{1}H NMR, ^{13}C NMR and mass technique. The IR spectra of **4(a-d)** exhibited in all cases C=O stretch vibrations in the range 1643-1625 cm^{-1}. The ^{1}H NMR spectra of were similar except for the aromatic protons. The chromone protons C_3 of **4(a-d)** has merged with aromatic part as multiplet in the range of δ 7.20-7.26ppm. The ^{13}C NMR spectra displayed aromatic carbon signals in the region δ 109.49-156.42 ppm. The IR spectra of **5(a-d)** and **6(a-d)** reveal OH and NH stretching bands appeared in the region of 3395-3378 and 3072-3050 cm^{-1}, respectively. In addition to this IR spectra of **5(a-d)** shows the thioketone band in the region 1270-1190 cm^{-1}. The ^{1}H NMR spectra of representative **5a** displayed singlet at δ 6.87 and 9.10 ppm due to thiopyrimidine ring and NH proton respectively, whereas **6a** showed three singlets at δ 5.36, 8.62 and 8.92 ppm because of iminopyrimidine ring and NH protons. The ^{13}C NMR spectra of **5(a-d)** and **6(a-d)** showed aromatic carbon signals in the region δ109.10-154.68 ppm**.** The mass spectra of **4, 5** and **6** displayed, in all cases, peaks corresponding to molecular ions which confirmed their molecular weights.



Scheme 2: Plausible mechanism for the synthesis of compounds **4**



Scheme 3: DMSO mediated regeneration of I_2



Scheme 4: Plausible mechanism for the synthesis of compounds **5** and **6**

Biology:

Antimicrobial activity of newly synthesized compounds **4**, **5** and **6** was evaluated against two gram negative (*Escherichia coli*, *Pseudomonas putide*), two gram positive (*Bacillus subtilis*, *Streptococcus lactis*) bacterial strains, and three (*Aspergillus niger*, *Penicillium sp*,*Candida albicans*,) fungal strains by the agar diffusion method using ampicillin as standard drug. The inhibition zone diameter (mm) and activity index (AI) of all synthesized compounds are enclosed in Table **1.** Graphical representations Figure **1** and **2**, inhibition zone diameter (mm) against a compound number (**4**, **5** and **6**), exhibiting moderate to a promising activity against tested bacterial and fungal strains. It was found that compounds **4(a-d)**, **4b** and **4d** exhibited strong activities (0.86 AI) against gram positive bacteria *Streptococcus lactis* comparable to that of the positive control, also **4a** and **4c** could inhibit the growth of most tested bacterial strains. As for antifungal activities compound **4b** and **4d** inhibit the growth of *Penicillium sp* and *Candida albicans*, fungal strain with (0.92 AI) activity index. Compounds **5(a-d),5a** with a 6 chlorothiopyrimidine derivative attached to the carbazole backbone gave nearly equipotent (0.90-1.00 AI) antibacterial broader bioactive spectrum against gram negative *Pseudomonas putide* and gram positive *Bacillus subtilis* and *Streptococcus lactis* as compared with standard drugs, compounds **5a** and **5c** could inhibit growth of *Penicillium sp* fungal strain to that of the positive control. Compounds **6b** and **6c** exhibited a broad spectrum against *Streptococcus lactis* bacterial strain with (0.81 AI), while compounds **6a**, **6b** and **6d** showed promising antifungal activities against three tested fungal strains. From structure-activity relationship (SAR) studies, it was indicated that the incorporation of chromone, thiopyrimidine and iminopyrimidine to carbazole moiety caused enhanced activities against most tested microorganisms. The results also suggested that the antimicrobial activities of the carbazole derivatives were distinctly influenced by the aromatic substituents. Compounds with electron withdrawing substituent (Cl and Br) in the aromatic ring were more active against all test microbes than compounds with electron donating ones.

Table 1: Antimicrobial activities of compounds **4**, **5** and **6**

Compds	[a]Inhibition zone diameter, mm, (activity index)[b]						
	Gram -ve bacteria		Gram +ve bacteria		Fungi		
	Escherichia coli	*Pseudomonas putide*	*Bacillus subtilis*	*Streptococcus lactis*	*Aspergillus niger*	*Penicillium Sp*	*Candida albicans*
4a	12 (0.50)	16 (0.80)	15 (0.78)	14 (0.63)	14 (0.58)	09 (0.64)	12(0.85)
4b	14 (0.58)	15 (0.75)	16 (0.84)	19 (0.86)	17 (0.70)	11(0.78)	13 (0.92)
4c	11 (0.45)	13 (0.65)	15 (0.78)	17 (0.77)	16 (0.66)	11(0.78)	11(0.78)
4d	16 (0.66)	15 (0.75)	15 (0.78)	19 (0.86)	17 (0.70)	13 (0.92)	10(0.71)
5a	18 (0.75)	19 (0.95)	19 (1.00)	20 (0.90)	18 (0.75)	12(0.85)	10(0.71)
5b	14 (0.58)	13 (0.65)	16 (0.84)	19 (0.86)	12 (0.50)	11(0.78)	08 (0.57)
5c	11 (0.45)	14 (0.70)	12 (0.63)	16 (0.72)	11(0.45)	12(0.85)	09 (0.64)
5d	12 (0.50)	14 (0.70)	13 (0.68)	14 (0.63)	12 (0.50)	10 (0.71)	10 (0.71)
6a	13 (0.54)	12 (0.60)	13 (0.68)	15 (0.68)	16 (0.66)	11(0.78)	12 (0.85)
6b	14 (0.58)	14 (0.70)	17 (0.89)	18 (0.81)	15(0.62)	12 (0.85)	11 (0.78)
6c	14 (0.58)	13 (0.65)	16 (0.84)	18 (0.81)	14 (0.58)	11 (0.78)	11 (0.78)
6d	12 (0.50)	11 (0.55)	13 (0.68)	12 (0.54)	14 (0.58)	12 (0.85)	09 (0.64)
Ampicillin	24	20	19	22	24	14	14
Control (1%DMSO)	No activity	No activity	No activity	No activity	No activity	No activity	No activity

[a]Inhibition zone diameters were measured for stock solutions with a concentration of 100µg/mL.
[b]Activity index (AI) =Inhibition zone of test compounds (mm) /inhibition zone of standard (mm).

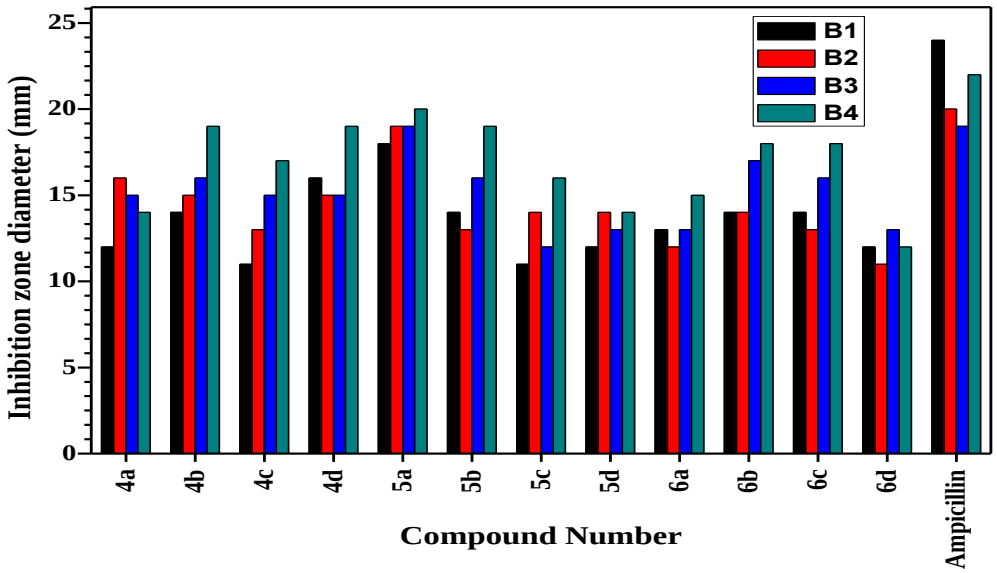


Figure 1: Antibacterial activities of compounds **4**, **5** and **6**.

B1=*Escherichia coli*, **B2**= *Pseudomonas putide*, **B3**= *Bacillus subtilis*, **B4**= *Streptococcus lactis*

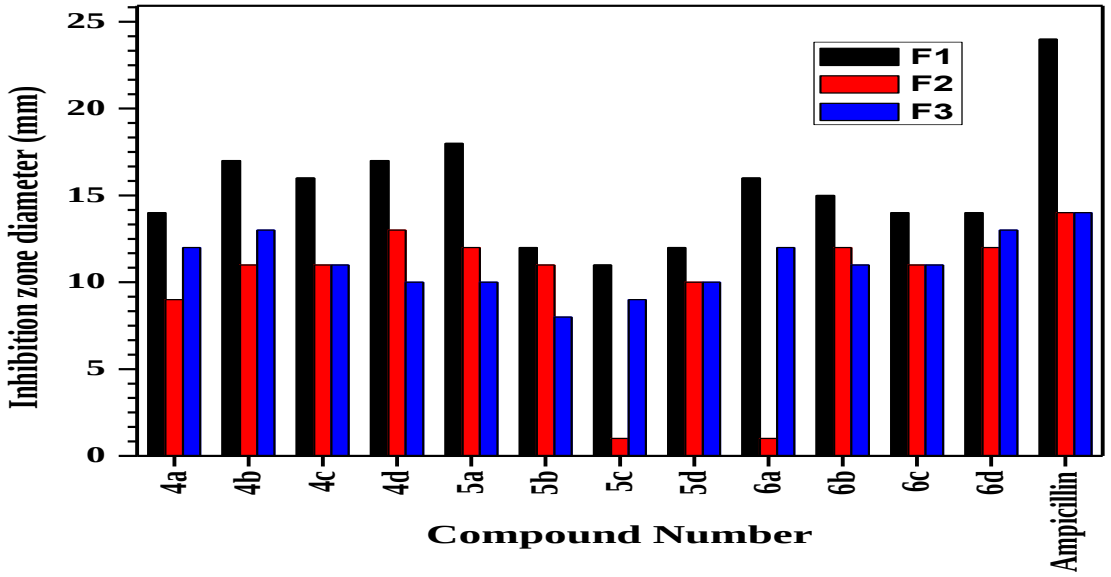


Figure 2: Antifungal activities of compounds **4**, **5** and **6**.

F1= *Aspergillus niger*, **F2**= *Penicillium sp*, **F3**= *Candida albicans*

Conclusion

A series of novel 2-(9-ethyl-9*H*-carbazol-3-yl)-4*H*-chromen-4-one derivatives (**4, 5** and **6**) were synthesized from 3-(9-ethyl-9*H*-carbazol-3-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one in approach of new antimicrobial agents. All compounds were examined for their *in vitro* antimicrobial activities against four bacteria and three fungi, showed moderate to promising antimicrobial activity as compared with standard drug ampicillin. Structure activity relationship (SAR) study of all compounds (**4, 5** and **6**) were taken into interpretation, it was observed that synthesized compounds having electron withdrawing groups like chloro and bromo attached to the phenyl ring showed excellent potential of antimicrobial activity. Also compounds containing moderate electron releasing group, methyl was able to produce moderate growth inhibitory activity against bacterial and fungal strains.

Experimental

The recorded melting points were determined in an open capillary and are uncorrected. IR spectra were recorded on PerkinElmer FTIR spectrophotometer from KBr pellets. ^{1}H NMR spectra were recorded on a Bruker Avance II 400 MHz device in $CDCl_3$, and ^{13}C NMR spectra were recorded at 125 MHz in $CDCl_3$ using tetramethylsilane (TMS) as internal standard.

The mass spectra were obtained by Waters mass spectrophotometer. Thin layer chromatography (TLC) was carried out on precoated silica gel aluminum plates to check compound purity.

In vitro antimicrobial assay

The antimicrobial activity was evaluated by the agar well diffusion method [26]. The activity was determined by measuring the diameter of inhibition zone (in mm). The samples of the tested compound concentrations (10–200 μg/mL) were loaded into wells on the plates. All solutions were prepared in DMSO, and pure DMSO was loaded as a control. The plates were incubated at 37 ºC for 24 h. and then were examined for the formation of inhibition zone diameter in mm and calculate their activity index (AI).

General procedure for the synthesis of substituted 2-(9-ethyl-9H-carbazol-3-yl)-4H-chromen-4-one4:

Carbazole chalcones **3(a-d)** (1.70g, 5 mmol) in DMSO (10 mL)**,** a catalytic amount of I_2 (50 mg) was added. The mixture was heated at 140 $^{\circ}$C for 3h. The completion of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured into cold water. Product precipitated was filtered off, washed with sodium thiosulphate, dried and recrystallized from ethanol to obtain the compounds **4(a-d)** in pure form.

6-chloro-2-(9-ethyl-9*H*-carbazol-3-yl)-4*H*-chromen-4-one (4a): Pale yellow colored solid, Yield: 71 %, m.p.: 208-209 ºC, IR (KBr, cm^{-1}): 1627 (C=O), 1233 (C-O), 1134 (Ar-Cl). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.40 (t, 3H, CH_3), 4.47 (q, 2H, N-CH_2), 7.24 (m, 1H, C_3 proton of chromone ring), 7.33-7.59 (m, 4H, Ar-H), 7.67-8.08 (m, 2H, Ar-H), 8.10-8.20 (m, 3H, Ar-H), 8.65 (s, 1H, Ar-H). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 14.11, 37.83, 83.35, 109.49, 112.54, 121.17, 122.13, 122.50, 122.66, 123.61, 125.36, 128.11, 128.63, 129.81, 134.75, 134.84, 139.85, 142.48, 156.42, 168.33.170.67. MS (*m/z*): 374 (M+1).

6-bromo-2-(9-ethyl-9*H*-carbazol-3-yl)-4*H*-chromen-4-one (4b): Pale yellow colored solid, Yield: 68 %, m.p.: 182-183 ºC, IR (KBr, cm^{-1}): 1643 (C=O), 1232 (C-O), 1022 (Ar-Br). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.39 (t, 3H, CH_3), 4.52 (q, 2H, N-CH_2), 7.21 (m, 1H, C_3 proton of chromone ring), 7.30-7.57 (m, 3H, Ar-H), 7.71-8.08 (m, 3H, Ar-H), 8.30-8.35 (m, 3H, Ar-H), 9.0 (s, 1H, Ar-H). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm):14.21, 37.85, 83.45, 109.59, 112.55, 121.27, 122.23, 122.53, 122.62, 123.49, 125.34, 128.21, 128.53, 129.82, 134.73, 134.82, 139.87, 142.42, 156.49, 168.43, 170.89. MS (*m/z*): 418 (M+1).

2-(9-ethyl-9*H*-carbazol-3-yl)-7-methyl-4*H*-chromen-4-one (4c): Pale yellow colored solid, Yield: 69 %, m.p.: 148-149 ºC, IR (KBr, cm^{-1}): 1625 (C=O), 1230 (C-O).^{1}H NMR (400 MHz, DMSO-d_6δ, ppm): 1.36 (t, 3H, CH_3), 3.29 (s, 3H, Ar-CH_3), 4.49 (q, 2H, N-CH_2), 5.72 (s, 1H, C_3 proton of chromone ring), 7.34-7.73 (m, 2H, Ar-H), 8.00-8.62 (m, 4H, Ar-H), 8.97-9.81 (m, 4H, Ar-H). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm):14.10, 37.81, 83.39, 109.38, 112.37, 121.37, 122.20, 122.51, 122.59, 123.37, 125.44, 128.35, 128.62, 129.75, 134.69, 134.52, 139.79, 142.45, 156.40, 168.41, 170.76.MS (*m/z*): 354 (M+1).

2-(9-ethyl-9*H*-carbazol-3-yl)-4*H*-chromen-4-one(4d): Pale yellow colored solid, Yield: 70 %, m.p.: 134-135 ºC, IR (KBr, cm^{-1}): 1640 (C=O), 1232 (C-O), ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.37 (t, 3H, CH_3), 4.50 (q, 2H, N-CH_2), 7.20 (m, 1H, C_3 proton of chromone ring), 7.45-7.52 (m, 5H, Ar-H), 7.62-7.78 (m, 3H, Ar-H), 8.21-8.64 (m, 3H, Ar-H). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm):14.12, 37.82, 83.41, 109.42, 112.35, 121.27, 122.24, 122.55, 122.60, 123.43, 125.34, 128.25, 128.52, 129.85, 134.79, 134.82, 139.81, 142.40, 156.42, 168.43, 170.80. MS (*m/z*): 340 (M+1).

General procedure for the synthesis of 6-(9-ethyl-9H-carbazol-3-yl)-4-(2-hydroxyphenyl)pyrimidine-2(1H)-thione

A mixture of compounds **4(a-d)** (0.33g, 1mmol), thiourea (0.22g, 3mmol), and potassium hydroxide (0.27g, 5mmol) in ethanol (15 mL) was reflux for 4 h. Completion of reaction monitored by TLC, then the reaction mixture was allowed to cool and poured over crushed ice and neutralized with acetic acid, whereby a solid was precipitated, which was filtered off and recrystallized from ethanol to produce **5(a-d).**

4-(5-chloro-2-hydroxyphenyl)-6-(9-ethyl-9*H*-carbazol-3-yl) pyrimidine-2(1*H*)-thione (5a):
Green colored solid, Yield: 72 %, m.p.: 163-164 ºC, IR (KBr, cm^{-1}): 3388 (OH), 3062(NH), 1122 (Ar-Cl), 1256 (C=S).^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.47 (t, 3H, CH_3), 4.50 (q, 2H, N-CH_2), 6.87 (s, 1H, thiopyrimidine ring), 7.06-7.20 (m, 1H, Ar-H), 7.47-7.52 (m, 2H, Ar-H), 7.66-8.12 (m, 3H, Ar-H), 8.21-8.45 (m, 4H, Ar-H), 9.10 (s, 1H, NH), 14.39 (s, 1H, Ar-OH). ^{13}C NMR (125 MHz,$CDCl_3$, δ, ppm):13.87, 37.92, 106.05, 108.99, 109.10, 119.18, 119.74, 120.06, 120.74, 121.75, 122.82, 123.44, 124.01, 125.06, 125.19, 126.74, 130.94, 133.62, 140.62, 141.96, 154.68, 165.07, 177.15.MS (*m/z*): 432 (M+1).

4-(5-bromo-2-hydroxyphenyl)-6-(9-ethyl-9*H*-carbazol-3-yl) pyrimidine-2(1*H*)-thione (5b):
Green colored solid, Yield: 71 %, m.p.: 170-171 ºC, IR (KBr, cm^{-1}): 3383 (OH), 3055 (NH), 1074 (Ar-Br), 1269 (C=S). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.37 (t, 3H, CH_3), 4.49 (q, 2H, N-CH_2), 6.92 (s, 1H, thiopyrimidine ring), 7.24-7.37 (m, 3H, Ar-H), 7.48-7.51 (m, 2H, Ar-H), 7.58-7.76 (m, 3H, Ar-H), 8.08-8.20 (m, 2H, Ar-H), 8.76 (s, 1H, NH), 12.30 (s, 1H, Ar-OH). ^{13}C NMR (125 MHz,$CDCl_3$, δ, ppm):13.85, 37.90, 106.15, 108.90, 109.12, 119.15, 119.70, 120.04, 120.54, 121.65, 122.81, 123.42, 124.05, 125.07, 125.16, 126.70, 130.91, 133.60, 140.68, 141.92, 154.61, 165.02, 177.35.MS (*m/z*): 476 (M+1).

6-(9-ethyl-9*H*-carbazol-3-yl)-4-(2-hydroxy-5-methylphenyl) pyrimidine-2(1*H*)-thione (5c):
Green colored solid, Yield: 70 %, m.p.: 189-109 ºC, IR (KBr, cm^{-1}): 3385 (OH), 3053 (NH), 1233(C=S). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm):1.35 (t, 3H, CH_3), 1.66 (s, 3H, Ar-CH_3), 4.44 (q, 2H, N-CH_2), 6.93 (s, 1H, thiopyrimidine ring), 7.23-7.39 (m, 2H, Ar-H), 7.56-8.01 (m, 3H, Ar-H), 8.16-8.68 (m, 5H, Ar-H),

8.83 (s, 1H, NH), 10.08 (s, 1H, Ar-OH). ^{13}C NMR (125 MHz,$CDCl_3$, δ, ppm):14.31, 37.89, 106.24, 108.91, 109.17, 119.16, 119.72, 120.14, 120.24, 121.62, 122.71, 123.42, 124.15, 125.17, 125.13, 126.74, 130.91, 133.62, 140.65, 141.90, 154.63, 165.12, 177.34.MS (*m/z*): 412 (M+1).

6-(9-ethyl-9*H*-carbazol-3-yl)-4-(2-hydroxyphenyl) pyrimidine-2(1*H*)-thione (5d):

Green colored solid, Yield: 68 %, m.p.: 141-142 ºC, IR (KBr, cm^{-1}): 3378 (OH), 3059 (NH), 1260 (C=S). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.38 (t, 3H, CH_3), 4.50 (q, 2H, N-CH_2), 6.98 (s, 1H, thiopyrimidine ring), 7.25-7.49 (m, 3H, Ar-H), 7.55-8.21 (m, 4H, Ar-H), 8.50-8.78 (m, 4H, Ar-H), 8.89 (s, 1H, NH), 10.28 (s, 1H, Ar-OH). ^{13}C NMR (125 MHz,$CDCl_3$, δ, ppm):14.41, 37.79, 106.28, 108.81, 109.27, 119.36, 119.52, 120.34, 120.26, 121.64, 122.72, 123.44, 124.25, 125.15, 125.17, 126.76, 130.90, 133.64, 140.75, 141.91, 154.68, 165.32, 177.64.MS (*m/z*): 383 (M+1).

General procedure for the synthesis of 4-chloro-2-(6-(9-ethyl-9H-carbazol-3-yl)-1,2-dihydro-2-iminopyrimidin-4-yl)phenol

A mixture of compounds **4(a-d)** (0.33g, 1mmol),ethanol (10 mL), guanidine hydrochloride (0.19g, 2mmol) and potassium hydroxide (0.16g, 3mmol) were refluxed for 6 h. After completion of the reaction (monitored by TLC), cooled and poured over crushed ice, neutralized with acetic acid. The obtained precipitate was collected by filtration, dried and recrystallized from ethanol to afford pure compounds **6(a-d)**.

4-chloro-2-(6-(9-ethyl-9*H*-carbazol-3-yl)-1,2-dihydro-2-iminopyrimidin-4-yl)phenol (6a):

Brown color solid, Yield: 71 %, m.p.: 160-161 ºC, IR (KBr, cm^{-1}): 3385 (OH), 3062 (NH), 1330 (C=N), 1140 (Ar-Cl). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.47 (t, 3H, CH_3), 4.42 (q, 2H, N-CH_2), 5.36 (s, 1H, iminopyrimidine ring), 6.93-7.17 (m, 3H, Ar-H), 7.26-7.49 (m, 4H, Ar-H), 7.56-8.29 (m, 3H, Ar-H), 8.62 (m, 1H, NH), 8.92 (s, 1H, NH), 13.02 (s, 1H, Ar-OH). ^{13}C NMR (125 MHz,$CDCl_3$, δ, ppm):13.83, 37.88, 105.99, 108.07, 109.10, 117.87, 119.20, 119.54, 119.73, 120.60, 120.84, 122.85, 123.49, 123.83, 125.19, 126.10, 126.10, 126.49, 127.91, 128.94, 133.65, 140.62, 143.14. MS (*m/z*): 415 (M+1).

4-bromo-2-(6-(9-ethyl-9*H*-carbazol-3-yl)-1,2-dihydro-2-iminopyrimidin-4-yl)phenol (6b):

Brown color solid, Yield: 69 %, m.p.: 156-157 ºC, IR (KBr, cm^{-1}): 3380 (OH), 3051 (NH), 1329 (C=N), 1022 (Ar-Br), ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.44 (t, 3H, CH_3), 4.43 (q, 2H,N- CH_2), 5.37 (s, 1H, iminopyrimidine ring), 6.92-7.20 (m, 3H, Ar-H), 7.24-7.48 (m, 4H, Ar-H), 7.54-8.28 (m, 3H, Ar-H), 8.60 (m, 1H, NH), 8.90 (s, 1H, NH), 13.01 (s, 1H, Ar-OH).^{13}C NMR (125 MHz,$CDCl_3$, δ, ppm):13.80, 37.84, 105.97, 108.17, 109.12, 117.88, 119.21, 119.55, 119.74, 120.63, 120.82, 122.81, 123.47, 123.85, 125.29, 126.12, 126.41, 126.69, 127.90, 128.92, 133.64, 140.61, 143.45. MS (*m/z*): 459 (M+1).

2-(6-(9-ethyl-9*H*-carbazol-3-yl)-1,2-dihydro-2-iminopyrimidin-4-yl)-4-methylphenol(6c):

Brown color solid, Yield: 67 %, m.p.: 148-149 ºC, IR (KBr, cm^{-1}): 3382 (OH), 3072 (NH), 1340 (C=N), ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.41 (t, 3H, CH_3), 2.30 (s, 3H, Ar-CH_3), 4.46 (q, 2H, N-CH_2), 5.39 (s, 1H, iminopyrimidine ring), 6.96-7.25 (m, 3H, Ar-H), 7.34-7.49 (m, 3H, Ar-H), 7.52-8.48 (m, 4H, Ar-H), 8.66 (m, 1H, NH), 8.89 (s, 1H, NH), 12.90 (s, 1H, Ar-OH).^{13}C NMR (125 MHz,$CDCl_3$, δ, ppm):13.79, 37.78, 105.90, 108.27, 109.12, 117.81, 119.27, 119.74, 119.83, 120.62, 120.81, 122.85, 123.59, 123.89, 125.29, 126.14, 126.34, 126.55, 127.90, 128.94, 133.62, 140.71, 143.84. MS (*m/z*): 395 (M+1).

2-(6-(9-ethyl-9*H*-carbazol-3-yl)-1,2-dihydro-2-iminopyrimidin-4-yl)phenol (6d):

Brown color solid, Yield: 70 %, m.p.: 123-124 ºC, IR (KBr, cm^{-1}): 3395 (OH), 3070 (NH), 1338 (C=N). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.47 (t, 3H, CH_3), 4.49 (q, 2H, N-CH_2), 5.49 (s, 1H, iminopyrimidine ring), 6.91-7.23 (m, 4H, Ar-H), 7.34-7.48 (m, 4H, Ar-H), 7.50-8.49 (m, 3H, Ar-H), 8.65 (m, 1H, NH), 8.90 (s, 1H, NH), 12.89 (s, 1H, Ar-OH). ^{13}C NMR (125 MHz,$CDCl_3$, δ, ppm):13.77, 37.93, 105.89, 108.37, 109.22, 117.12, 119.25, 119.71, 119.80, 120.64, 120.84, 122.82, 123.52, 123.86, 125.24, 126.34, 126.84, 126.75, 127.91, 128.90, 133.60, 140.74, 143.89. MS (*m/z*): 381 (M+1).

Acknowledgements

The Authors are very much grateful to the Head, Department of Chemistry, S.S.G.M College, Kopargaon and A.C.S College, Satral for providing the laboratory facilities.

References

[1] Nam, D. H.; Lee, K. Y.; Moon, C. S.; Lee, Y. S. *Eur. J. Med. Chem*. **2010,** *45*, 4288.

[2] Ibrahim, M. A.; Ali, T. E.; Alnamer, Y. A.; Gabr, Y. A. *ARKIVOC* **2010**,*i*, 98.
[3] Rocha-Pereira, J.; Cunha, R.; Pinto, D. C. G. A.; Silva, A. M. S.; Nascimento, M. S. J. *Bioorg. Med. Chem*. **2010**, *18*, 4195.
[4] Zhao, Li. Y.; Xiang, N.; Yang, L.; Wang, F.; Yang, G.; Wang, Z. *Heterocycles* **2014**, *89*, 2771.
[5] Ghosh, C. K. *Heterocycles* **2004**, *63*, 2875.
[6] Plaskon, A. S.; Grygorenko, O. O.; Ryabukhin, S. V. *Tetrahedron* **2012**, *68*, 2743.
[7] Sosnovskikh, V. Y.; Irgashev, R. A.; Kodess, M. I. *Tetrahedron* **2008**, *64*, 2997.
[8] Budzisz, E.; Miemicka, M.; Lorenz, I. P.; Mayer, P.; Krajewska, U.; Rozalski, M. *Polyhedron* **2009**, *28*, 637.
[9] Sosnovskikh, V. Y.; Korotaev, V. Y.; Barkov, A. Y.; Sokovnina, A. A.; Kodess, M. I. *J. Fluorine Chem*. **2012**, *141*, 58.
[10] Koo, J. *J. Pharm. Sci*. **1964,** *53(11)*, 1329.
[11] Koo, J. *J. Org. Chem.* **1961**, *26*, 635.
[12] Prakash, O.; Kumar R.; Prakash, V. *Eur. J. Med. Chem*. **2008**, *43*, 435.
[13] Michalis, A.; Terzidis, Constantinos A. T.; Julia, S. S. *ARKIVOC* **2008**, *xiv*, 132.
[14] Dongamanti, A.; Sidda, R.; Bommidi, V. L.; Arram, G. *J. Serb. Chem. Soc.***2015**, *8(11)*, 1361.
[15] Bergman, J.; Peloman, B. *Pure Appl. Chem.***1990**, *62*, 1967.
[16] Knolker, H.; Reddy, K. *Chem. Rev.* **2002**, *102*, 4303.
[17] Gluszynska, A. *Eur. J. Med. Chem.* **2015**, *94*, 405.
[18] Amr, A. E.; Abdalla, M. M. *Bioorg. Med. Chem*. **2006**, *14*, 4341.
[19] Supaluk, P.; Apilak, W.; Chanin, N.; Maneekarn, C.; Nirun, S.; Somsak, R.; Virapong, P. *Eur. J. Med. Chem*. **2011**, *46*, 738.
[20] Kaur, R.; Chaudhary, S.; Kumar, K.; Manish, K.; Gupta, M. K.; Rawal, R. K. *Eur. J. Med. Chem*. **2017**, *132*, 108.
[21] Larry, T. Pierce.; Michael, M. Cahill.; Hannah, J. Winfield.; Florence, O. McCarthy. *Eur. J. Med. Chem*. **2012**, *56*, 292.
[22] Kadnor, V. A.; Shirole, G. D.; Mhaske, G. R.; Shelke, S. N. *Indian J. Heterocyclic Chem.* **2017**, *27*, 59.
[23] Shelke, S.; Mhaske, G.; Gadakh, S.; Gill, C. *Bioorg. Med. Chem. Lett*. **2010**, *24(20)*,7200.
[24] Shelke, S.; Mhaske, G.; Bonifácio Vasco, D. B.; Gawande, M. *Bioorg. Med. Chem. Lett.* **2012**, *17(22)*, 5727.
[25] Shelke, S.; Salunkhe, N.; Sangale, S.; Bhalerao, S.; Naik, N.; Mhaske, G.; Jadhav, R.; Karale, B. *J. Korean Chem. Soc*. **2010,***54*, 59.
[26] Keche, A. P.; Hatnapure, G. D.; Tale, R.T.; Rodge, A. H.; Birajdar, S. S.; Kamble, V. M. *Med. Chem. Res.***2013**, *22*, 14.