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SYNTHESIS AND CHARACTERIZATION OF SCHIFF BASE SUBSTITUTED CARBAZOLE BEARING PYRIDOPYRIMIDINE COMPOUNDS

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ABSTRACT

The Schiff bases formation which is useful molecules both biologically and synthetically is one of the most important reactions in organic and medicinal chemistry. Available materials, catalyst-free and mild reaction conditions are essential to synthesize the Schiff bases in a good yield. In basic conditions, Schiff base substituted carbazole bearing pyridopyrimidine compounds **(4a-n)** were efficiently synthesized through corresponding benzaldehyde derivatives on treatment with 7- (4-amino-phenyl)-5-(9-ethyl-9H-carbazol-3-yl)- 1,3-dimethyl- 1H-pyrido [2,3-d] pyrimidine-2,4-dione in tetrahydrofuran under reflux in good yields. The structures of the synthesized compounds were identified by IR, ^{1}H NMR and ^{13}C NMR and elemental analysis.

Keywords: Carbazole, pyridopyrimidine, benzaldehyde, Schiff bases.

INTRODUCTION

Heterocyclic compounds, especially nitrogen containing, have been studied due to a variety of chemical and biological significance. In recent years, the pyrido-[2,3-d]-pyrimidine heterocyclic compounds that are annelated to a pyrimidine ring exhibit a wide range of biological and pharmacological properties[1-3]. The compounds show antitubercular[4], calcium channel blockers[5] antibacterial[6], antiviral[7], antifungal[8,9], antimalarial[10], antihypertensive[11], carbonic anhydrase inhibitors[12], analgesic and anti-inflammatory[13,14] properties. Among the compounds, pyrimidine and pyridine-containing compounds, have been the subject of expanding research efforts in organic and biological chemistry. Interestingly, pyrimidine compounds are also known for possessing antitumor, anticancer and antineoplastic potencies[15,16] and are very essential for synthetic drugs (e.g., barbituric acid derivatives), chemotherapeutic agents (e.g., sulfadiazine), and agricultural chemicals[17].

The formation of carbon-nitrogen bonds are the most important transformations in organic chemistry[18-24]. Traditionally, imines are synthesized from the dehydrative condensation of amines and carbonyl compounds in the presence of an acid catalyst[36,37] or by a number of catalytic and non-catalytic procedures, such as the self-condensation of amines upon oxidation[38,39], the oxidation of secondary amines[40,41] or directly from alcohols and amines via several tandem catalytic processes[42,43,44], mostly with homogeneous systems. Imines, in particular, are very important as electrophilic reagents in many organic reactions, such as reductions, additions, condensations and cycloadditions[25-35]. This study investigated 14 new Schiff base substituted carbazole bearing pyridopyrimidine compounds.

EXPERIMENTAL

Material and Methods

A SHIMADZU Prestige-21 (200 VCE) spectrometer measured the IR spectra. The ^{1}H and ^{13}C chemical shifts referenced to the internal deuterated solvent. Respectively, the measurements of the ^{1}H and ^{13}C

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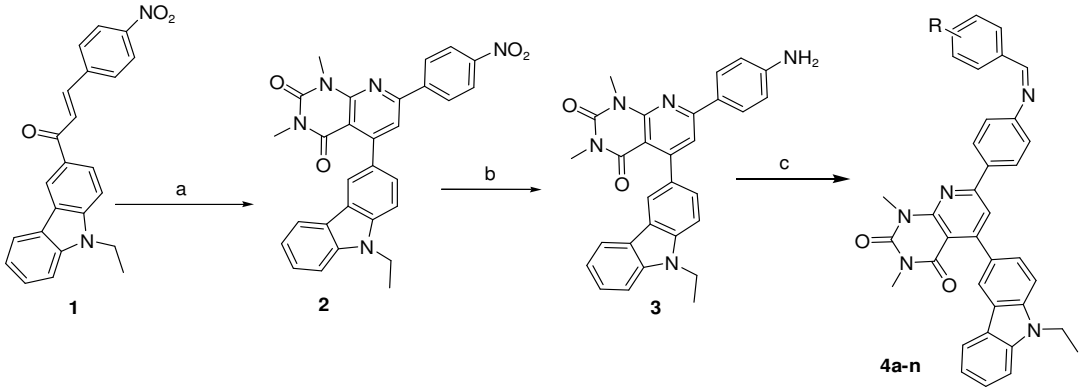
NMR spectra on spectrometer at VARIAN Infinity Plus 300 and at 75 Hz. The elemental analysis was carried out with a Leco CHNS-932 instrument. Melting points were taken on a Yanagimoto micro-melting point apparatus and are uncorrected. The preparation of the synthesis of carbazole containing pyridopyrimidine substituted Schiff base derivatives was completed in accordance with Scheme-1.



Compounds	R	Compounds	R	Compounds	R
4a	H	4f	4-CH_3	4k	2-NO_2
4b	4-NO_2	4g	3-Cl	4l	3,4-dichlor
4c	4-F	4h	3-Br	4m	2-Br
4d	4-OCH_3	4i	3,4-dimethoxy	4n	2,5-dimethoxy
4e	3-OCH_3	4j	3-CH_3		

Scheme-1: Synthetic route of Schiff Base Substituted Carbazole containing Pyrido-Pyrimidine Compounds. Reagents and Yields: (a) 6-Amino-1,3-Dimethyluracil, NaOH, EtOH, Reflux, 7 h, 90%; (b) $NiCl_2$, $NaBH_4$, THF, 0 °C, 8 h, 78%; (c) Aldehyde, Na_2CO_3, THF, 70 °C, 24 h, 72-88%.

Synthesis of Carbazole Substituted Pyridopyrimidine

A solution of nitrochalcone (was prepared according to the following procedures mentioned in literature [45]) (2.16 g, 5.84 mmol) in a mixture of ethanol (50 ml), 6-amino-1,3-dimethyluracil (0.89 g, 5.74 mmol) and sodium hydroxide (0.22 g, 5.5 mmol) was heated at reflux for 7 hours, quenched with water, filtered and recrystallized from diethyl ether.

General Procedure for the Synthesis of Amino Pyridopyrimidino Derivatives

$NaBH_4$ (1.23 g, 32.37 mmol) was added portionwise at 0 °C (ice bath) over 10 min to a solution of 5-(9-Ethyl-9H-carbazol-3-yl)-1,3-dimethyl-7-(4-nitro-phenyl)- 1H-pyrido [2,3-d] pyrimidine -2,4-dione **(2)** (1.5 g, 2.96 mmol) in anhydrous tetrahydrofuran and $NiCl_2$ (3.11 g, 23.92 mmol). Stirring was continuing for 30 min with cooling, followed by stirring at room temperature for 2 h. The mixture was evaporated off after the disappearing of the starting material. The black precipitate was dissolved in 1N HCl and then the acidic solution was alkalified by the addition of 1N NaOH. After completion of the reaction, it was extracted with ethyl acetate (20 ml) and washed with water and brine. The organic layer was dried over $MgSO_4$ and concentrated (rotary evaporator) to give the crude products.

General Procedure for Synthesis of Carbazole containing Pyridopyrimidino Substituted Imine Derivatives (4a-n)

A mixture of 7- (4-Amino-phenyl)-5- (9-ethyl-9H-carbazol-3-yl)- 1,3-dimethyl- 1H-pyrido [2,3-d] pyrimidine-2,4-dione **1** (0.8 g, 1.677 mmol) and benzaldehyde derivatives (0.6 ml, 5.143 mmol) in anhydrous tetrahidrofuran in presence of Na_2CO_3 (0.71 g, 6.454 mmol) was stirred at 70 ^{0}C for 24 hours. The solution was extracted with AcOEt with an aqoues phase. Organic phase was washed three times with water, dried with anhydrous magnesium sulphate and evaporated under reduced pressure.

7-[4-(Benzylidene- amino)- phenyl]- 5 -(9-ethyl-9H-carbazol-3-yl)-1,3-dimethyl- 1H- pyrido [2,3-d]-pyrimidine-2,4-dione (4a)

It was obtained after recrystallization from diethylether to give as yellow crystals. Yield 76 %, m.p. 241.6 °C; IR (KBr, υ, cm^{-1}): 1660.7 (R_2C=N-R), 2956.9 (C=C, aromatic), 1703.1 (C=O) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.89 (1H, s, = CH), 8.59 (1H, s, = CH), 8.35-8.38 (1H, d, = CH), 8.19-8.22 (1H, d, = CH), 7.94-7.97 (1H, t, = CH), 7.64 (1H, s, = CH), 7.27-7.53 (12H, m, -Ar-H), 4.39-4.47 (2H, q, - CH_2), 3.97 (3H, s, - CH_3), 3.43 (3H, s, - CH_3), 1.47-1.51 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm) : 14.1, 28.7, 30.5, 37.7, 109.5, 110.1, 110.9, 111.1, 118.2, 119.8, 119.9, 120.2, 120.3, 120.7, 123.3 (2C), 123.7, 125.5, 125.6, 125.7, 128.1, 128.3, 128.9, 129.0, 131.7, 134.6, 136.4, 137.7, 137.9, 150.4, 151.9, 152.0, 157.6, 159.9, 160.8, 163.9. Anal. Calcd. for $C_{36}H_{29}N_5O_2$: C, 76.71; H, 5.19; N, 12.43. Found: C, 76.03; H, 4.88; N, 11.96.

5-(9- Ethyl- 9H- carbazol-3-yl)- 1,3-dimethyl-7- {4-[(4-nitro-benzylidene)-amino]- phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4b)

It was recrystallized from diethylether to give as orange crystals. Yield 75 %, m.p. 234.6°C; IR (KBr, υ, cm^{-1}): 1654.9 (R_2C=N-R), 3053.3 (C=C, aromatic), 1701.2 (C=O) , 1583.6 (NO_2) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.89 (1H, s, = CH), 8.67 (1H, s, = CH), 8.34-8.37 (1H, d, = CH), 8.11-8.14 (1H, d, = CH), 7.64 (1H, s, = CH), 7.27-7.54 (12H, m, -Ar-H), 4.40-4.45 (2H, q, - CH_2), 3.97 (3H, s, - CH_3), 3.43 (3H, s, - CH_3), 1.47-1.52 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm) : 14.2, 28.7, 30.4, 38.3, 105.6, 108.6, 109.9, 111.0, 112.9, 114.4, 118.9, 119.0, 119.9, 120.4, 120.6, 123.3, 123.4, 124.1, 124.2, 124.5, 125.8, 125.9, 127.6, 130.9, 131.5, 137.4, 137.7, 138.1, 139.8, 149.1, 150.7, 151.9, 154.4, 159.0, 160.3, 161.3. Anal. Calcd. for $C_{36}H_{28}N_6O_4$: C, 71.04; H, 4.64; N, 13.81.Found: C, 70.96; H, 4.57; N, 13.74.

5-(9-Ethyl- 9H- carbazol-3-yl)- 1,3-dimethyl-7- {4-[(4-fluoro-benzylidene)-amino]- phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4c)

It was obtained after recrystallization from diethylether to give as yellow crystals. Yield 77.9%, m.p. 256.5°C ; IR (KBr, υ, cm^{-1}): 1660.7 (R_2C=N-R), 3051.4 (C=C, aromatic), 1703.1 (C=O) , 1145.7 (C-F) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.89 (1H, s, = CH), 8.55 (1H, s, = CH), 8.34-8.37 (1H, d, = CH), 8.19-8.21 (1H, d, = CH),7.93-7.96 (1H, t, = CH), 7.63 (1H, s, = CH), 7.16-7.53 (11H, m, -Ar-H), 4.39-4.44 (2H, q, - CH_2), 3.97 (3H, s, - CH_3), 3.42 (3H, s, - CH_3), 1.46-1.51 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm) : 14.5, 28.7, 30.5, 37.9, 109.2, 110.0, 110.1, 110.2, 116.5, 116.8, 117.9, 118.6, 120.0, 120.1, 120.8, 120.9, 122.9, 123.2, 123.3, 125.6, 126.1, 126.9, 130.2, 130.9, 131.7, 131.8, 132.5, 133.2, 138.1, 138.9, 151.5, 151.6, 157.1, 159.5, 160.2, 161.0, 162.3. Anal. Calcd. for $C_{36}H_{28}FN_5O_2$: C, 74.34; H, 4.85; N, 12.04. Found: C, 74.26; H, 4.80; N, 12.01.

5-(9-Ethyl-9H-carbazol-3-yl)- 1,3-dimethyl-7-{4-[(4-methoxy-benzylidene)-amino]-phenyl}-1H-pyrido [2,3-d]-pyrimidine-2,4-dione (4d)

It was recrystallized from ether to give as yellow crystals. Yield 72.3 %, m.p. 257.3°C ; IR (KBr, υ, cm^{-1}): 1660.7 (R_2C=N-R), 2972.6 (C=C, aromatic), 1703.1 (C=O) , 2839.9 (O-CH_3) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.85 (1H, s, = CH), 8.49 (1H, s, = CH), 8.32-8.35 (1H, d, = CH), 8.17-8.19 (1H, d, = CH),7.87-7.89 (1H, t, = CH), 7.59 (1H, s, = CH), 7.23-7.51 (11H, m, -Ar-H), 4.35-4.41 (2H, q, - CH_2), 3.92 (3H, s, -OCH_3), 3.88 (3H, s, - CH_3), 3.39 (3H, s, - CH_3), 1.44-1.49 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm) : 14.1, 28.7, 30.5, 38.0, 55.7, 105.7, 108.9, 109.2, 114.4, 114.5, 118.2, 118.3, 119.8, 119.9, 120.2, 120.3, 120.7, 120.8, 120.9, 123.3, 123.5, 123.6, 125.6, 125.7, 126.4, 126.5, 128.2, 129.3, 129.5, 130.9, 151.9, 152.428, 153.546, 154.665, 160.3, 160.9, 162.5. Anal. Calcd. for $C_{37}H_{31}N_5O_3$: C, 74.86; H, 5.26; N, 11.80. Found : C, 74.82; H, 5.19; N, 11.74.

5-(9-Ethyl-9H-carbazol-3-yl)- 1,3-dimethyl-7-{4-[(3-methoxy-benzylidene)-amino]-phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4e)

It was obtained after recrystallization from diethylether to give as yellow crystals. Yield 75 % m.p. 225.7°C ; IR (KBr, υ, cm^{-1}): 1658.8 (R_2C=N-R), 2966.5 (C=C, aromatic), 1701.2 (C=O) , 2933.7 (O-

CH_3) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.89 (1H, s, = CH), 8.56 (1H, s, = CH), 8.34-8.38 (1H, d, = CH), 8.19-8.22 (1H, d, = CH), 7.63 (1H, s, = CH), 7.26-7.57 (12H, m, -Ar-H), 4.39-4.47 (2H, q, - CH_2), 3.97 (3H, s, -OCH_3), 3.92 (3H, s, - CH_3), 3.43 (3H, s, - CH_3), 1.47-1.51 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 14.1, 28.7, 30.4, 38.0, 55.7, 105.7, 109.1, 109.2, 112.2, 114.5, 118.6, 119.8, 119.9, 120.2, 120.3, 120.8, 120.9, 121.8, 122.7, 123.6, 123.7, 125.6, 125.7, 126.5, 126.6, 128.5, 129.8, 130.1, 137.9, 138.0, 151.9 (2C), 152.0, 155.3, 160.9, 161.0, 161.1. Anal. Calcd. for $C_{37}H_{31}N_5O_3$: C, 74.86; H, 5.26; N, 11.80. Found: C, 74.78; H, 5.21; N, 11.73.

5-(9-Ethyl-9H-carbazol-3-yl)- 1,3-dimethyl-7- {4-[(4-methyl-benzylidene)-amino]- phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4f)

It was recrystallized from diethylether to give as orange crystals. Yield 73.5 % m.p. 276.4°C ; IR (KBr, υ, cm^{-1}): 1658.8 (R_2C=N-R), 3049.5 (C=C, aromatic), 1703.1 (C=O) , 2951.1 (-CH_3) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.89 (1H, s, = CH), 8.55 (1H, s, = CH), 8.35-8.38 (1H, d, = CH), 8.19-8.22 (1H, d, = CH), 7.64 (1H, s, = CH), 7.26-7.85 (12H, m, -Ar-H), 4.41-4.44 (2H, q, - CH_2), 3.97 (3H, s, - CH_3), 3.43 (3H, s, - CH_3), 2.44 (3H, s, - CH_3), 1.46-1.51 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 14.1, 21.9, 28.7, 30.5, 38.1, 105.7, 109.0, 109.2, 118.2, 119.9, 120.3, 120.7, 120.9, 123.3, 123.7, 125.7, 126.5, 126.6, 128.3, 129.2, 129.3, 129.4, 129.8, 129.9, 133.9, 134.9, 137.5, 140.8, 141.8, 142.3, 151.9, 152.1, 152.3, 154.7, 160.3, 161.0, 161.1. Anal. Calcd. for $C_{37}H_{31}N_5O_2$: C, 76.93; H, 5.41; N, 12.12. Found: C, 76.85; H, 5.38; N, 12.04.

5-(9- Ethyl- 9H- carbazol-3-yl)- 1,3-dimethyl-7-{4-[(3-chlor-benzylidene)-amino]- phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4g)

It was obtained after recrystallization from diethylether to give as yellow crystals. Yield 88.2 %, m.p. 234.7°C ; IR (KBr, υ, cm^{-1}): 1658.8 (R_2C=N-R), 3061.0 (C=C, aromatic), 1701.2 (C=O) , 746.5 (C-Cl) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.89 (1H, s, = CH), 8.54 (1H, s, = CH), 8.35-8.38 (1H, d, = CH), 8.19-8.22 (1H, d, = CH), 7.63 (1H, s, = CH), 7.26-7.99 (12H, m, -Ar-H), 4.39-4.45 (2H, q, - CH_2), 3.97 (3H, s, - CH_3), 3.43 (3H, s, - CH_3), 1.47-1.51 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 14.1, 28.7, 30.5, 38.1, 108.9, 109.2, 109.3, 118.1, 119.9, 120.3, 120.7, 120.9, 121.0, 123.3 (2C), 123.7, 125.7, 126.6, 126.7, 127.5, 128.2, 128.6, 129.3, 129.8, 130.3, 133.2, 135.2, 138.2, 140.8, 141.8, 151.5, 151.9, 152.1, 160.3, 160.4, 161.0. Anal. Calcd. for $C_{36}H_{28}ClN_5O_2$: C, 72.29; H, 4.72; N, 11.71. Found: C, 72.05; H, 4.63; N, 11.59.

5-(9-Ethyl-9H-carbazol-3-yl)- 1,3-dimethyl-7- {4-[(3-brom-benzylidene)-amino]- phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4h)

It was recrystallized from diethylether to give as yellow crystals. Yield 85.2 %, m.p. 233.2°C ; IR (KBr, υ, cm^{-1}): 1658.8 (R_2C=N-R), 3057.2 (C=C, aromatic), 1703.1 (C=O) , 678.9 (C-Br) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.88 (1H, s, = CH), 8.52 (1H, s, = CH), 8.34-8.38 (1H, d, = CH), 8.19-8.22 (1H, d, = CH), 8.14 (1H, s, = CH), 7.63 (1H, s, = CH), 7.27-7.53 (11H, m, -Ar-H), 4.39-4.46 (2H, q, - CH_2), 3.96 (3H, s, - CH_3), 3.42 (3H, s, - CH_3), 1.46-1.51 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 14.1, 28.7, 30.5, 38.1, 105.7, 109.0, 109.2, 109.9, 118.1, 119.9, 120.3, 120.7, 120.9, 123.2, 123.3, 123.4, 123.7, 125.7, 126.6, 128.0, 128.2, 129.3, 130.6, 131.5, 134.5, 138.2, 138.4, 140.8, 141.8, 151.4, 151.9, 152.1, 154.4, 159.1, 160.3, 160.9. Anal. Calcd. for $C_{36}H_{28}BrN_5O_2$: C, 67.29; H, 4.39; N, 10.90. Found: C, 67.22; H, 4.35; N, 10.80.

5-(9- Ethyl-9H- carbazol- 3- yl)- 1,3- dimethyl- 7-{ 4-[(3,4- dimethoxy-benzylidene)-amino]-phenyl} -1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4i)

It was recrystallized from diethylether to give as yellow crystals. Yield 75.9 % , m.p. 259.6°C ; IR (KBr, υ, cm^{-1}): 1656.9 (R_2C=N-R), 3049.5 (C=C, aromatic), 1701.2 (C=O) , 2933.7 (O-CH_3) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 9.03 (1H, s, = CH), 8.58 (1H, s, = CH), 8.37-8.39 (1H, d, = CH), 8.27-8.29 (1H, d, = CH),7.16-7.71 (12H, m, -Ar-H), 4.42-4.46 (2H, q, - CH_2), 3.86 (6H, s, -OCH_3), 3.71 (3H, s, - CH_3), 3.09 (3H, s, - CH_3), 1.32-1.36 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 14.4, 28.6, 30.4, 37.9, 56.1, 56.5, 105.4, 109.7, 109.8, 109.9, 110.1, 111.9, 113.3, 117.6, 117.7, 119.9 (2C), 120.5, 120.7, 121.5, 123.1, 123.2, 124.9, 125.8, 125.9, 126.8, 128.4, 130.1, 130.2, 130.3, 140.8, 141.6, 149.7, 149.8, 154.8,

158.8, 160.5, 160.8. Anal. Calcd. for $C_{38}H_{33}N_5O_4$: C, 73.18; H, 5.33; N, 11.23. Found: C, 73.16; H, 5.29; N, 11.11.

5-(9-Ethyl-9H-carbazol-3-yl)- 1,3-dimethyl-7- {4-[(3-methyl-benzylidene)- amino]-phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4j)

It was obtained after recrystallization from diethylether to give as yellow crystals. Yield 79.1 %, m.p. 226.6°C ; IR (KBr, υ, cm^{-1}): 1658.8 (R_2C=N-R), 3049.5 (C=C, aromatic), 1701.2 (C=O) , 2960.7 (-CH_3) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 9.09 (1H, s, = CH), 8.67 (1H, s, = CH), 8.42-8.45 (1H, d, = CH), 8.29-8.33 (1H, d, = CH), 7.18-7.82 (13H, m, -Ar-H), 4.44-4.50 (2H, q, - CH_2), 3.75 (3H, s, - CH_3), 3.15 (3H, s, - CH_3), 2.41 (3H, s, - CH_3), 1.32-1.36 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 14.5, 21.6, 28.6, 30.4, 37.9, 105.6, 109.9, 110.0, 110.1, 117.7, 117.8, 120.0, 120.1, 120.8, 120.9, 121.5, 121.6, 123.2, 123.3, 126.8, 126.9, 128.1, 129.4, 129.6, 129.7, 130.2, 130.4, 135.9, 136.7, 138.8, 141.7, 151.7, 151.9, 154.1, 159.4, 160.4, 161.4. Anal. Calcd. for $C_{37}H_{31}N_5O_2$: C, 76.93; H, 5.41; N, 12.12. Found: C, 76.89; H, 5.39; N, 12.10.

5-(9- Ethyl- 9H- carbazol-3-yl)- 1,3-dimethyl-7-{4-[(2-nitro-benzylidene)-amino]- phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4k)

It was recrystallized from diethylether to give as brown crystals. Yield 87.2 %, m.p. 285.9°C ; IR (KBr, υ, cm^{-1}): 1656.9 (R_2C=N-R), 3047.5 (C=C, aromatic), 1703.1 (C=O) , 1583.6 (NO_2) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 9.07 (1H, s, = CH), 8.88 (1H, s, = CH), 8.34-8.36 (1H, d, = CH), 8.18-8.21 (1H, d, = CH), 8.09-8.12 (1H, d, = CH), 7.62 (1H, s, = CH), 7.26-7.80 (11H, m, -Ar-H), 4.39-4.46 (2H, q, - CH_2), 3.96 (3H, s, - CH_3), 3.42 (3H, s, - CH_3), 1.46-1.51 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 14.1, 28.7, 30.5, 38.1, 105.7, 109.0, 109.2, 118.1, 119.9, 120.3, 120.9, 121.1, 123.3, 123.7, 124.8, 125.7, 126.6, 128.2, 129.4, 129.8, 130.0, 130.1, 131.4, 131.5, 133.8, 133.9, 138.8, 140.8, 141.9, 149.5, 151.9, 152.1, 154.3, 160.4, 160.9, 161.0. Anal. Calcd. for $C_{36}H_{28}N_6O_4$: C, 71.04; H, 4.64; N, 13.81. Found: C, 70.96; H, 4.56; N, 13.73.

5-(9-Ethyl-9H-carbazol-3-yl)-1,3-dimethyl-7-{4-[(3,4-dichloro-benzylidene)-amino]-phenyl} -1H-pyrido [2,3-d]-pyrimidine-2,4-dione (4l)

It was recrystallized from diethylether to give as brown crystals. Yield 86.4 % , m.p. 228.3°C ; IR (KBr, υ, cm^{-1}): 1658.8 (R_2C=N-R), 3047.5 (C=C, aromatic), 1699.3 (C=O) , 746.5 (C-Cl) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.88 (1H, s, = CH), 8.49 (1H, s, = CH), 8.34-8.37 (1H, d, = CH), 8.18-8.21 (1H, d, = CH), 8.06 (1H, s, = CH), 7.62 (1H, s, = CH), 7.26-7.77 (10H, m, -Ar-H), 4.39-4.46 (2H, q, - CH_2), 3.96 (3H, s, - CH_3), 3.42 (3H, s, - CH_3), 1.46-1.51 (3H, t, - CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 14.1, 28.7, 30.5, 38.1, 105.7, 109.0, 109.2, 109.9, 118.1, 119.9, 120.3, 120.7, 120.9, 121.0, 123.3, 123.7, 125.7, 126.5, 126.6, 128.2, 129.4, 130.4, 131.1, 133.5, 135.7, 136.3, 138.4, 140.8, 141.9, 151.1, 151.9, 152.1, 154.4, 160.3, 160.6, 160.9. Anal. Calcd. for $C_{36}H_{27}Cl_2N_5O_2$: C, 68.36; H, 4.30; N, 11.07. Found: C, 68.33; H, 4.29; N, 11.04.

5-(9- Ethyl- 9H- carbazol-3-yl)- 1,3-dimethyl-7-{4-[(2-bromo-benzylidene)-amino]- phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4m)

It was obtained after recrystallization from diethylether to give as orange crystals. Yield 72.6 %, m.p. 247.8°C ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm): 9.15 (1H, s, =CH), 8.89 (1H, s, =CH), 8.46-8.49 (1H, d, =CH), 8.32-8.35 (1H, d, =CH), 8.19-8.21 (1H, d, =CH), 7.84 (1H, s, =CH), 7.50-7.79 (9H, m, -Ar-H), 7.36-7.38 (1H, t, =CH), 7.26-7.28 (1H, t, =CH), 4.46-4.51 (2H, q, -CH_2), 3.79 (3H, s, -CH_3), 3.19 (3H, s, -CH_3), 1.33-1.38 (3H, t, -CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 13.9, 28.4, 30.2, 37.8, 105.4, 108.7, 108.9, 117.8, 119.6, 119.9, 120.6, 120.7, 120.8, 121.2, 122.9, 123.3, 125.4, 125.5, 126.3, 126.6, 127.7, 127.9, 129.0, 129.1, 132.5, 133.2, 134.5, 137.9, 140.5, 141.5, 151.3, 151.6, 154.1, 159.6, 159.9, 160.7. Anal. Calcd. for $C_{36}H_{28}BrN_5O_2$: C, 67.29; H, 4.39; N, 10.90. Found: C, 67.22; H, 4.36; N, 10.86.

5-(9-Ethyl- 9H- carbazol-3-yl)-1,3-dimethyl-7-{4-[(2,5-dimethoxy-benzylidene)-amino]-phenyl}-1H-pyrido[2,3-d]-pyrimidine-2,4-dione (4n)

It was recrystallized from diethylether to give as orange crystals. Yield 84.3 % , m.p. 276.1°C ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm): 9.16 (1H, s, =CH), 8.91 (1H, s, =CH), 8.48-8.50 (1H, d, =CH), 8.33-8.36

(1H, d, =CH), 7.85 (1H, s, =CH), 7.15-7.77 (11H, m, -Ar-H), 4.48-4.54 (2H, q, -CH_2), 3.88 (6H, s, =CH_3), 3.81 (3H, s, -CH_3), 3.22 (3H, s, -CH_3), 1.33-1.38 (3H, t, -CH_3). ^{13}CNMR (300 MHz, $CDCl_3$, δ, ppm): 14.1, 28.7, 30.5, 38.1, 56.2, 56.5, 105.7, 109.0, 109.2, 110.5, 113.1, 118.2, 119.9, 120.2, 120.3, 120.9, 121.0, 123.3, 123.7, 125.3, 125.7, 126.6, 128.3, 128.5, 129.2, 131.5, 137.4, 140.8, 141.8, 151.9, 152.1, 152.8, 153.9, 154.6, 154.7, 157.2, 160.3, 161.0. Anal. Calcd. for $C_{38}H_{33}N_5O_4$: C, 73.18; H, 5.33; N, 11.23. Found: C, 73.13; H, 5.29; N, 11.17.

RESULTS AND DISCUSSION

The synthesis of pyridopyrimidine derivatives of carbazole containing nitro, amino and imino groups have resulted in a good yield. The nitro chalcone derivative (**1**) was prepared in a good yield according to the following procedures mentioned in literature[45] and it was converted to the pyridopyrimidine derivatives (**2**) using 6-amino-1,3-dimethyluracil with NaOH as a base catalyst in ethanol. In anhydrous tetrahydrofuran using nickel (II) chloride, the nitro compound was reducted to the compound bearing amino group **(3).** The amino pyridopyrimidine compound reacted with various benzaldehyde derivatives form series of different compounds (**4a-n**) in ethanol in high yield.

The structures of the prepared compounds (**4a-n**) were deduced from their elemental analysis data, and from their IR, ^{1}H-NMR and ^{13}C-NMR spectra.The IR spectra of all the compounds showed a characteristic mode at 1660.7 cm^{-1} which may be resulted from vibrations of group R_2C=N-R. The characteristic modes at 3050 cm^{-1} and 1703.1 cm^{-1} resulted from aromatic stretching frequencies and a corresponding carbonyl group. The absorption band at 1145.7 cm^{-1} indicated the presence of C-F group for the compound **4c**. The compounds **4b** and **4k** showed a characteristic mode at around 1583 cm^{-1} which may be resulted from vibrations of NO_2 group. The C-Cl bond stretching frequencies appeared around 746 cm^{-1} for **4c** and **4l**. In the ^{1}H-NMR spectrum of the compounds, aromatic protons were appeared around δ7.20–9.0 ppm. The spectrum also displayed a singlet at δ 8.59 ppm (s, 1H) assigned for group (–N=CH), absorption signals around δ 3.43 ppm and δ 3.97 ppm correspond to the six protons of the two groups N-CH_3, a quartet between δ 4.39-4.47 ppm (q, 2H) assigned for CH_2 protons and a triplet in the range δ 1.47-1.51 ppm (t,3H) correspond to CH_3 protons. Singlet for the protons of the methoxy group is observed in the area of around 3,92 ppm for the compounds **4d, 4e, 4i** and **4n.** From the ^{13}C NMR spectra, two signals from the carbonyl groups present in the pyrimidine ring were observed respectively around 160 and 151 ppm. The characteristic signals for C=N, C-NO_2, OCH_3, CH_2 and CH_3 groups are respectively around 160, 140, 55, 38 and 14 ppm respectively. Also the spectrum displayed two signals at 30.5 and 28.7 ppm for the carbon atoms of N-CH_3 groups. The obtained structures are confirmed based on IR, ^{1}H NMR and ^{13}C NMR spectra and the results obtained from the elemental analysis have been consistent with the composition of the newly synthesized compounds.

CONCLUSION

The new Schiff bases which have carbazole bearing pyridopyrimidine group have been reported as one of the most important reactions in organic and medicinal chemistry. The pyridopyrimidine motif is widely used in many organic compounds, and drug activity was related to biological activities. The synthesis procedures were performed under mild reaction conditions, in the absence of the catalyst providing the corresponding products in a good yield.

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