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# MULTIFARIOUS STAGE SYNTHESIS OF UNIQUELY SUBSTITUTED CHROMENO DERIVATIVES OF CARBOXY AND AMINO PYRIMIDINE

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**ABSTRACT**

A one-pot reaction of resorcinol, malononitrile and benzaldehyde in tracing amount of methanol and 0.1 % sodium carbonate solution and at room temperature on vigorous stirring given 2-amino-7-hydroxy-4-phenyl-4H-1-benzopyran-3-carbonitrile which on O-alkylation in presence of dry potassium carbonate in dry acetone at 70-80$^0$C with 1,2-chloroethyl pyrrolidine,1,2-chloroethyl piperidine, 1,2-cholro ethyl morpholine given ethoxy pyrollidine , ethoxypiperidine and ethoxymorpholine substituted benzopyran intermediates, which on further reaction with formic acid and urea, in specific reaction conditions cyclize the amino and carbonitrile part in substrate and converted into different novel chromeno carboxy and amino derivatives of pyrimidine.

**Keywords**: Urea, Formic acid, Pyrimidine, Pyrrolidine, Piperidine, Morpholine, Carboxy



## INTRODUCTION

Pyrimidine is the heterocyclic aromatic compound containing two nitrogen atoms at position 1 & 3 of the six-membered rings. Heterocyclic compounds containing pyrimidine ring are of a high-interest area of a chemist because they organize an imperative class of natural and imitation products, many of them exhibit useful biological activities and clinical applications.[1,2] Substituted pyrimidines occur very widely in a living organism and were some of the first compounds studied by organic chemist[3-5]. A pyrimidine has so many properties in conjoint with a pyrimidine, as the number of nitrogen atoms in the ring increases the ring pi electrons become less energetic and electrophilic aromatic substitution gets more difficult while nucleophilic aromatic substitution gets easier. In medicinal chemistry pyrimidine derivatives have a significant role for their therapeutic application.[6-8] During the last few years, so many pyrimidine products had been developed as chemotherapeutic agents and have found wide clinical application such as antifungal, antibacterial, anticancer, anti-inflammatory, antibiotic, anti- HIV, anesthetics and cardiac agent[9-18].Here we had reported a multiple-step synthesis of substituted chromeno derivatives of amino and carboxy pyrimidine ,these derivatives had synthesized in three-step reaction in which initial moiety had undergone knoevenagel condensation, trailed by Michael addition in which one-pot synthesis has been done in tracing amount of methanol and 0.1% aqueous solution of sodium carbonate and formed 2-amino-7-hydroxy 4-phenyl-4H-1-benzopyran-3-carbonitrile[19.] A knoevenagel condensation is a nucleophilic addition of an active hydrogen compounds to a carbonyl group followed by dehydration reaction in which a molecule of water is eliminated[20,21]. In this reaction carbonyl compound is usually aldehyde or ketone. The catalyst is generally weak base. Active hydrogen compounds like diethyl malonate, Meldrum's acid, ethyl acetoacetate, malonic acid, cyanoacetic acid, malononitrile etc.[22-24].Michael addition is suitable for the superior class of multiple additions. It is a convenient method for C-C bond formation. In the reaction, donors are active methylene' compounds such as malonates and nitroalkanes, and the acceptors are activated olefins such as α, β-unsaturated carbonyl compounds [26-28]. The second step reaction underwent O- alkylation in which 1, 2-chloroethyl-pyrrolidine,1, 2-chloroethylpiperidine or 1,2-chloroethylmorpholine act as an alkylating agent and –OH part of substrate


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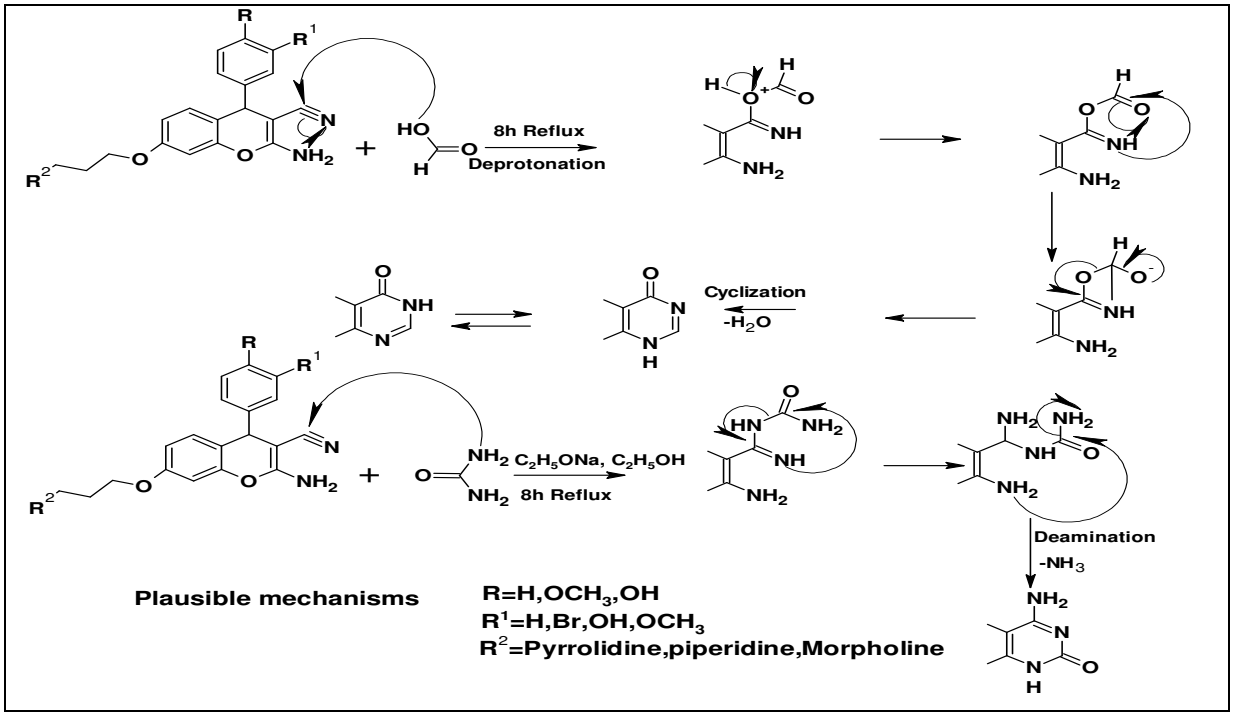
alkylate and given ether as a product. Alkylation is the transfer of an alkyl group from one molecule to another. The alkyl group may be transferred as an alkyl carbocation, a free radical, carbanion, or a carbine or their equivalents [29-30]. When the alkylating agent is an alkyl halide, the conversion is known as Williamson ether synthesis. Alcohols are also good alkylating agents in the presence of suitable acid/base catalysts[31-32].In the final step above synthesized compounds reacts with formic acid and urea in presence of tracing amount of sodium ethoxide as catalyst and ethanol as solvent at 70-80 $^0$C by constant stirring and reflux for 7-8 hours. In this step cyclization of amino and carbonitrile, part of substrate reacted and synthesized unique substituted chromeno derivatives of amine and carboxy substituted pyrimidine[33].




Scheme-1: Plausible Mechanism of Reaction

## EXPERIMENTAL

### Materials and Methods

Laboratory grade chemicals and solvent were bought from Sigma Aldrich and Merck and used without any further purification. The reaction was monitored by TLC using Merck's silica gel 60F254 aluminium sheets. Infrared spectra were recorded neatly on Agilent cary 630 spectrophotometer. High-resolution mass spectra were recorded on Agilent 6520(Q-TOF). NMR spectra were recorded on a Bruker Avance 400(FT NMR) DPX300MHz NMR spectrometer.

### General Procedure and Detection Method

### 2-Amino-7-hydroxy-4-phenyl-4*H*-1-benzopyran-3-carbonitrile (1a-4a)

A mixture of benzaldehyde, malononitrile and resorcinol in equal molar ratio dissolved in methanol (1.0 ml) in a round bottom flask. A solution of $Na_2CO_3$ (0.09 g, 0.8 mmol) in water (19.0 ml) then added to the round bottom flask and the resulting suspension was stirred at room temperature for 10 hours. The solid formed was filtered off, washed with water followed by cold methanol and dried in an oven at 100 $^0$C to given 2-amino-3-cyano-7-hydroxy-4-phenyl-4H-chromene in 85% yield. (Note- In the synthesis of 2a, 3a, 4a, on the place of benzaldehyde, 3-bromo, 3-methoxy and 4-methoxy benzaldehyde has been used.)

### 2-Amino-4-phenyl-7-[2-(pyrrolidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile (1b-4b)

A mixture of 2-amino-3-cyano-7-hydroxy-4-phenyl-4H-chromene (1a-4c) (0.264g, 1mmol), 1-(2-chloroethyl) pyrollidine .HCl (0.255 g, 1.5mmol) dry Potassium Carbonate (0.276g 2mmol) dissolved in 25 ml dry acetone in a 50 ml round bottom flask reflux the solution for 8 hours at 60-70 $^0$C tem. Cool the

solution at room temperature and filter, evaporate the acetone from the filtrate and collect the yellow crystalline compound. Monitor the compound by TLC with Methanol and benzene (2:8) and purify the compound through column chromatography on silica gel in a combination of ethyl acetate and hexane in 3:7.

**2-Amino-4-phenyl-7-[2-(piperidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile(1c-4c)**

A mixture of 2-amino-3-cyano-7-hydroxy-4-phenyl-4H-chromene (1a-4a) (0.264g, 1mmol), 1-(2-chloroethyl) Piperidine .HCl (0.276g, 1.5mmol) dry Potassium Carbonate (0.276g 2mmol) dissolved in 25 ml dry acetone in a 50 ml round bottom flask reflux the solution for 8 hours at 60-70 $^0$C tem. Cool the solution at room temperature and filter, evaporate the acetone from the filtrate and collect the light yellow crystalline compound. Monitor the compound by TLC with Methanol and benzene (2:8) and purify the compound through column chromatography on silica gel in a combination of ethyl acetate and hexane in 4:6.

**2-Amino-4-phenyl-7-[2-(morpholin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile(1d-4d)**

A mixture of 2-amino-3-cyano-7-hydroxy-4-phenyl-4H-chromene (1a-4a) (0.264g, 1mmol), 1-(2-chloroethyl) morpholine.HCl (0.279 g, 1.5mmol) dry Potassium Carbonate (0.276g 2mmol) dissolved in 25 ml dry acetone in a 50 ml round bottom flask reflux the solution for 8 hours at 60-70 $^0$C tem. Cool the solution at room temperature and filter, evaporate the acetone from the filtrate and collect the pale yellow crystalline compound. Monitor the compound by TLC with Methanol and benzene (2:8) and purify the compound through column chromatography on silica gel in a combination of ethyl acetate and hexane in 4:6.

**8-[2-(Pyrrolidin-1-yl)ethoxy]-5-phenyl-3,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-4-one(1e-4e)**

A mixture of compound2-amino-4-phenyl-7-[2-(pyrrolidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile (1b-4b) (2 mmol) and excess of formic acid was refluxed on an oil bath for 7-8 h under inert condition and reaction monitored by TLC in a combination of Chloroform: methanol in (7:3). After the completion of the reaction, the solvent was distilled off under reduced pressure, and obtained solid has purified by recrystallization in ethanol followed by column chromatography (silica gel) using hexane and ethyl acetate.

**8-[2-(Piperidin-1-yl)ethoxy] -5-phenyl-3,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-4-one (1f-4f)**

A mixture of compound 2-amino-4-phenyl-7-[2-(piperidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile(1c-4c) (2 mmol) and excess of formic acid were refluxed on oil bath for 7-8 h under inert condition. Reaction monitored by TLC in a combination of DCM: methanol in 7:3 After completion of the reaction, the solvent was distilled off under reduced pressure, obtained solid has purified by recrystallization in absolute ethanol followed by column chromatography (silica gel) using hexane and ethyl acetate.

**8-[2-(Morpholin-1-yl)ethoxy]-5-phenyl-3,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-4-one(1g-4g)**

A mixture of compound 2-amino-4-phenyl-7-[2-(morpholin-1-yl) ethoxy]-4*H*-1-benzopyran-3-carbonitrile (1d-4d) (2 mmol) and excess of formic acid was refluxed on an oil bath for 7-8 h (monitored by TLC DCM: methanol; (7:3)) under inert condition. After completion of the reaction, the solvent was distilled off under reduced pressure, obtained solid has purified by recrystallization in absolute ethanol followed by column chromatography (silica gel) using hexane and ethyl acetate.

**4-Amino-8-[2-(pyrrolidin-1-yl)ethoxy]-5-phenyl-1,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-2-one (1h-4h)**

A mixture of compound 2-amino-4-phenyl-7-[2-(pyrrolidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile (1b-4b) and urea in ratio 2:2 in 50 ml round bottom flask then added 0.01 g of sodium ethoxide as a catalyst and add 20 ml ethanol, kept the mixture on vigorous stirring with reflux at 70-80 $^0$C for 7-8 hours. Reaction monitored by TLC in chloroform-methanol (6:4) after the completion of the reaction,

reaction mixture poured in crushed ice and neutralized with diluted HCl. The precipitated product has been collected by filtration and washed with water. The crude product purified by recrystallization in absolute ethanol and further purified by column chromatography on silica gel using DCM and Methanol.

**4-Amino-8-[2-(piperidin-1-yl)ethoxy]-5-phenyl-1,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-2-one (1i-4i)**

A mixture of compound 2-amino-4-phenyl-7-[2-(piperidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile(1c-4c) and urea in ratio 2:2 in 50 ml Round bottom flask then added 0.01 g of sodium ethoxide as a catalyst and added 20 ml ethanol, kept the mixture on vigorous stirring with reflux at 70-80 $^0$C for 7-8 hours. Reaction monitored by TLC in DCM methanol (5:5) after the completion of the reaction, reaction mixture poured in crushed ice and neutralized with diluted HCl. The precipitated product has been collected by filtration and washed with water. The crude product purified by recrystallization in absolute ethanol and further purified by column chromatography on silica gel using DCM and methanol.

**4-Amino-8-[2-(morpholin-1-yl)ethoxy]-5-phenyl-1,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-2-one (1j-4j)**

A mixture of compound 2-amino-4-phenyl-7-[2-(morpholin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile(1d-4d) and urea in ratio 2:2 in 50 ml Round bottom flask then added 0.01 g of sodium ethoxide as a catalyst and added 20 ml ethanol, kept the mixture on vigorous stirring with reflux at 70-80 $^0$C for 7-8 hours. Reaction monitored by TLC in DCM methanol (5:5) after the completion of the reaction, reaction mixture poured in crushed ice and neutralized with diluted HCl. The precipitated product has been collected by filtration and washed with water. The crude product purified by recrystallization in absolute ethanol and further purified by column chromatography on silica gel using DCM and methanol.

**Spectral Data of Selected Compounds**

**2-Amino-7-hydroxy-4-phenyl-4*H*-1-benzopyran-3-carbonitrile (1a)**

White amorphous solid, MP-230-235 $^0$C ; **IR (wave no.=cm$^{-1}$)** 3495(R-OH), 3332(R-NH$_2$), 2193(R-CN), 1652(C=CN vinyl nitrile), 1588-1406(C-C aromatic), **$^1$HNMR (400 MHz,DMSO)** 9.76 (s, Ar-OH ), 7.36-7.33 (t, J=12 Hz ) 7.26-7.20 (q, J= 8 Hz) 6.90-6.84 (t, J= 12) 6.55-6.52 (dd, J= 4Hz) 6.478-6.472 (d, J=2.4) 4.66 (s) **C$^{13}$ NMR (100 MHz,DMSO)** 160.23-160.20, 156.98, 148.82, 146.31, 129.88, 127.33 126.62, 113.75, 112.34, (C-C aromatic)120.60, (CN) 102.14 (C=C vinylic), 56.28(C-O). HRMS-EI (m=z) calcd. For $C_{16}H_{12}N_2O_2$ 264.2786, found 264.2886. Anal. calcd. C-72.72, H-4.58, N-10.60, found C-72.69,H-4.60,N-10.60

**2-Amino-4-phenyl-7-[2-(pyrrolidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile (1b)**

Brown color solid MP-265-272 IR- (wave no. cm$^{-1}$) 3334 (R-NH$_2$), 2188(R-CN), 1649(-C=CN), 1579-1400(C-C Aromatic) ,1336 (-C-OR, OR= ethoxypyrrolidine),1156,(C-N-C at pyrrolidine ring) **$^1$HNMR(300 MHz,CdCl$_3$)** 7.24-7.23 (t, J=1.2Hz), 7.21-7.20 (d, J=1.5 Hz), 7.18(s), 7.15-7.14 (t, J=1.35), 7.13-7.12 (t, J=5.4), 7.105-7.100 (d, J=1.5Hz), 6.76 (s), 6.73 (s), 6.54-6.53 (d, J=2.4Hz) ,6.519-6.510 (d, J=2.7Hz), 6.47-6.46 (d, J=2.7Hz), 4.18(s), 4.56(s), 4.00-3.96 (t, J=11.7), 2.83-2.79 (t, J=11.7Hz), 2.57-2.53 (t, J=12.9), 1.96(s), 1.89(s), 1.77-1.68 (m, J=7.5Hz), C$^{13}$ NMR (CDCl$_3$ 75.42 MHz) 159.50, 158.67, 149.31, 145.06, 130.34, 129.31, 128.90, 128.02, 127.29, 120.26, 115.16, 112.25, 102.13, 77.65, 77.23, 67.29, 60.67, 59.29, 54.96, 54.72, 40.61, 23.60, 1.16 calcd. $C_{16}H_{12}N_2O_3$, 361.43692, +ESISCAN-MS+362.18, Anal.calcd. C-73.11, H-6.41, N-8.16 found C-73.15, H-6.45, N-8.16

**2-Amino-4-phenyl-7-[2-(piperidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile (1c)**

Bright pink color solid MP:- 275-280 , IR (v~ cm-1) 3350(R-NH$_2$), 2240 (R-CN), 1639 (C=CN vinyl nitrile), 1589-1450 (C,C aromatic), 1302 (C-OR OR = ethoxypiperidine),1078 (C-N-C at piperidine ring), **$^1$H NMR (CdCl$_3$ 300MHz)** 7.26 -7.24,(t, J= 3 ), 7.214-7.209 (d= 1.5), 7.189 (s) , 7.15-7.14 (d, J= 3) , 6.77,(s) 6.75, (s) 6.547-6.539(d, J=2.4) , 6.519-6.510 (d, J= 2.7) 6.472-6.462 (d, J=2.7) 4.819 (s) , 4.565( s), 4.009- 3.966 (t, J= 6.9), 2.98 (s) 2.833-2.794 (t, J= (5.7), 2.576-2.533(q, J=6.45), 1.96(s), 1.89(s) **C$^{13}$ NMR (CDCl $_3$ 75.42 MHz)** 157.31, 155.55, 155.20, 131.06, 129.33, 129.10, 119.99, 115.16,

114.25, 104.25, 77.44, 77.23, 62.88, 61,86, 57.88, 55.09, 42.22, 34.55, 31.96 Calcd. $C_{23}H_{25}N_3O_2$ 375.4635, ESISCAN-MS+376.09, Anal.calcd.C-71.79, H-6.43, N-11.16, found C-71.83, H-6.44, N-11.19.

**2-Amino-4-phenyl-7-[2-(morpholin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile (1d)**
Yellow color solid: MP 275-280 $^0$C, IR (wave no. cm$^{-1}$) 3335(R-$NH_2$), 2198(R-CN), 1644(C=CN vinyl nitrile), 1599-1442(C-C aromatic),1335(C-OR where OR = ethoxymorpholine),1159(C-N-C at morpholine ring) **$^1$H NMR ($CdCl_3$ 300MHz)** 7.255-7.241 (t, J= 4.2), 7.112-7.090 (d, J=6.6), 7.009 (s) , 6.990-6.987 (d, J= 0.9), 6.88 (s), 6.76 (s), 6.455-6.454 (d, J=0.3), 6.424-6.420 (d J=1.2) 4.908 (s) ,4.670 (s),4.098-4.086 ( t, J=3.6), 2.992 (s) , 2.883-2.862 (t, J=6.3), 2.588-2.537 (q, J=7.65), 2.003 (s), 1.962 (s). 1.884 (s), **C$^{13}$ NMR ($CDCl_3$ 75.42 MHz)** 159.66 156.31, 153.55, 152.20, 135.96, 129.33, 129.10, 120.99, 115.16, 114.85, 104.25, 77.98, 77.23, 65.88, 61.86, 57.88, 55.70, 42.22, 39.33, 35.65, 31.22 Calcd. $C_{22}H_{23}N_3O_3$, 377.43632, ESISCAN-MS+377.47509, Anal.calcd.C-70.01, H-6.14, N-11.13 found C-70.83, H-6.22, N-11.15.

**8-[2-(Pyrrolidin-1-yl)ethoxy]-5-phenyl-1,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-4-one (1e)** pale yellow color solid MP-285-290 IR- (wave no. cm$^{-1}$) 3384, (-NH stretching) 1705(>C=O), 1619,(CH=N at pyrimidine ring) 1566-1420(C-C Aromatic) ,1325,1320 (-C-OR, OR= ethoxypyrrolidine), 1477,1239(C-O-C at pyran ring) 1089 (C-N-C at pyrrolidine ring) ($^1$HNMR(300 MHz,$CdCl_3$) 8.22-8.19 (d J=9 Hz1 H –NH at pyrimidine ring),7.30-6.99 (m, J= 11.62, 8H, Ar-H), 7.19 (d, J=3, 1H,CH, at pyrimidine ring) 4.81(s,1H,pyran-CH), C$^{13}$ NMR ($CDCl_3$ 75.42 MHz) δ ppm 161(>C=O),159,(C-O-C at pyran ring ) 158.67, 150, ( CH=N at pyrimidine ring)149.31, 145.06, 130.34, 129.31, 128.90, 128.02, 127.29, 120.26, 115.16, 112.25, 102.13, 77.65, 77.23, 67.29, 60.67, 59.29,( C-O-C at -ethoxy C) 54.96, 54.72, 40.55(C-N-C at pyrolidine ring), 23.33 and 22.11( C-C at pyrolidine ring) calcd. $C_{23}H_{23}N_3O_3$, 389.17692, +ESISCAN-MS+390.18, Anal.calcd. C-70.95, H-5.91, N-10.79 found C-71.15, H-6.01, N-10.80

**8-[2-(Piperidin-1-yl)ethoxy]-5-phenyl-1,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-4-one (1f)** yellow color solid MP-290-295 IR- (wave no. cm$^{-1}$) 3389, (-NH streching) 1725(>C=O), 1601,(CH=N at pyrimidine ring) 1522-1420(C-C Aromatic) ,1365,1333 (-C-OR, OR= ethoxypiperidine), 1444,1245 (C-O-C at pyran ring),1110, (C-N-C at piperidine ring),($^1$HNMR(300 MHz,$CdCl_3$) 8.33-8.31 (d J=6 Hz1 H –NH at pyrimidine ring),7.41-7.21 (m, J= 7.5, 8H, Ar-H), 7.19-7.18 (d, J=3, 1H,CH, at pyrimidine ring) 4.79(s,1H,pyran-CH), C$^{13}$ NMR ($CDCl_3$ 75.42 MHz) δ ppm 166(>C=O),152,(C-O-C at pyran ring ) 159, 152, ( HC=N at pyrimidine ring)147, 144, 132, 129, 128, 127, 121, 116, 114, 77, 67, 60, 59,( $H_2C$-O-$CH_2$ at -ethoxy C) 54, 40,($H_2C$-N-$CH_2$ at piperidine ring), 23 and 22 ( $H_2C$-$CH_2$ at piperidine ring) calcd. $C_{24}H_{25}N_3O_3$, 402.98, +ESISCAN-MS+403.19, Anal.calcd. C-71.46, H-6.20, N-10.42 found C-71.33, H-6.10, N-10.77

**8-[2-(Morpholin-1-yl)ethoxy]-5-phenyl-1,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-4-one(1g)**
Dark yellow color solid MP-290-295 IR- (wave no. cm$^{-1}$) 3372, (-NH streching) 1719(>C=O), 1622,(CH=N at pyrimidine ring) 1576-1499(C-C Aromatic) ,1367,1321 (-C-OR, OR= ethoxymorpholine), 1423,1277 (C-O-C at pyran ring), 1120, (C-N-C at morpholine) ($^1$HNMR(300 MHz,$CdCl_3$) 8.43-8.41 (d J=6 Hz 1H –NH at pyrimidine ring),7.39-7.22 (m, J= 6.3, 8H, Ar-H), 7.22-7.21 (d, J=3, 1H,CH, at pyrimidine ring) 4.79(s,1H,pyran-CH), C$^{13}$ NMR ($CDCl_3$ 75.42MHz) δppm 161(>C=O), 151,(C-O-C at pyran ring ) 159, 151, ( HC=N at pyrimidine ring) ,148, 145, 131, 129, 128, 127, 121, 116, 114, 77, ( $H_2C$-O-$CH_2$ at morpholine ring)67, 60, 59,( C-O-$CH_2$ at -ethoxy C) 54, 40,($H_2C$-N-$CH_2$ at morpholine ring), 23-21 calcd. $C_{23}H_{23}N_3O_4$, 405.17, +ESISCAN-MS+406.17, Anal.calcd. C-68.14, H-5.69, N-10.37 found C-68.33, H-5.44, N-10.89

**4-Amino-8-[2-(pyrrolidin-1-yl)ethoxy]-5-phenyl-1,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-2-one (1h)**
Bright Orange color solid MP-290-295 IR- (wave no. cm$^{-1}$) 3340 (-NH stretching at $NH_2$), 3384, (-NH stretching) 1705(>C=O), 1619,(CH=N at pyrimidine ring)1613,1509, (C=N at pyrimidine ring), 1566-

1420 (C-C Aromatic) ,1345,1340 (-C-OR, OR= ethoxypyrrolidine), 1333, 1315, 1239, (C-O-C at pyran ring) 1202, (C-N-C at pyrrolidine ring ), ($^1$HNMR(300 MHz,$CdCl_3$) 8.22-8.19 (d J=9 Hz 1H –NH at pyrimidine ring),8.12 (s,1H, -NH at pyrimidine ring ) 8.00(s, 2H,-$NH_2$) 7.30-6.99 (m, J= 11.62, 8H, Ar-H), 7.19 (d, J=3, 1H,CH, at pyrimidine ring) 4.81(s,1H,pyran-CH),3.88-3.87(d, J=3) $C^{13}$ NMR ($CDCl_3$ 75.42MHz) δ ppm 161(>C=O),159,(C-O-C at pyran ring ) 158.67, 150, ( CH=N at pyrimidine ring)149.31, 145.06, 130.34, 129.31, 128.90, 128.02, 127.29, 120.26, 115.16, 112.25, 102.13, 77.65, 77.23, 67.29, 60.67, 59.29,( C-O-C at -ethoxy C) 54.96, 54.72, 40.55(C-N-C at pyrolidine ring), 23.33 and 22.11( C-C at pyrolidine ring) calcd. $C_{23}H_{24}N_4O_3$, 404.43692, +ESISCAN-MS+405.50, Anal.calcd. C-68.31, H-5.94, N-13.86 found C-68.24, H-5.93, N-13.84

**4-Amino-8-[2-(piperidin-1-yl)ethoxy]-5-phenyl-1,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-2-one (1i)** orange color solid MP-290-295 IR- (wave no. $cm^{-1}$) 3499 (-NH stretching at -$NH_2$), 3389, (-NH stretching at pyrimidine ring ) 1625(>C=O), 1601,(CH=N at pyrimidine ring) ,1522-1420(C-C Aromatic) ,1365,1333 (-C-OR, OR= ethoxypiperidine), 1444,1245 (C-O-C at pyran ring), 1150 (C-N-C at piperidine ring) ($^1$HNMR(300 MHz,$CdCl_3$) ,8.33-8.31 (d J=6 Hz1 H –NH at pyrimidine ring),7.41-7.21 (m, J= 7.5, 8H, Ar-H), 7.19-7.18 (d, J=3, 1H,CH, at pyrimidine ring), 4.79 (s,1H,pyran-CH), $C^{13}$ NMR ($CDCl_3$ 75.42MHz) δ ppm 166 (>C=O),152 (C-O-C at pyran ring) 159, 152, (HC=N at pyrimidine ring) 147, 144, 132, 129, 128, 127, 121, 116, 114, 77, 67, 60, 59,( $H_2C$-O-$CH_2$ at -ethoxy C) 54, 40,($H_2C$-N-$CH_2$ at piperidine ring), 23 and 22 ( $H_2C$-$CH_2$ at piperidine ring) calcd. $C_{24}H_{25}N_4O_3$, 418.48, +ESISCAN-MS +419.02, Anal.calcd. C-68.88, H-6.26, N-13.39 found C-68.33, H-6.10, N-13.77

**4-Amino-8-[2-(morpholine-1-yl)ethoxy]-5-phenyl-1,5-dihydro-4*H*-chromeno[2,3-*d*]pyrimidin-2-one (1j-4j)** orange color solid MP-290-295 IR- (wave no. $cm^{-1}$) 3443 (-NH stretching at -$NH_2$), 3372, (-NH stretching) 1689(>C=O), 1602,(CH=N at pyrimidine ring) 1506-1494(C-C Aromatic) ,1360,1321 (-C-OR, OR= ethoxymorpholine), 1423,1277 (C-O-C at pyran ring), 1243 (C-N-C at morphline ring) ($^1$HNMR(300 MHz,$CdCl_3$) 8.43-8.41 (d J=6 Hz1 H –NH at pyrimidine ring),7.39-7.22 (m, J= 6.3, 8H, Ar-H), 7.22-7.21 (d, J=3, 1H,CH, at pyrimidine ring) 4.79(s,1H,pyran-CH), $C^{13}$ NMR ($CDCl_3$ 75.42 MHz) δppm 161(>C=O), 151,(C-O-C at pyran ring ) 159, 151, ( HC=N at pyrimidine ring) ,148, 145, 131, 129, 128, 127, 121, 116, 114, 77, ( $H_2C$-O-$CH_2$ at morpholine ring) 67, 60, 59,( C-O-$CH_2$ at -ethoxy C) 54, 40,($H_2C$-N-$CH_2$ at morpholine ring), 23-21 calcd. $C_{23}H_{23}N_3O_4$, 420.46, +ESISCAN-MS +421.01, Anal.calcd. C-65.70, H-5.75, N-13.33 found C-65.33, H-5.44, N-13.89

## RESULTS AND DISCUSSION

It was a multiple-step reaction in which has been completed in three steps in first step active methylene compounds (malononitrile) reacted with carbonyl compounds (benzaldehyde and substituted benzaldehyde) in presence of tracing amount of methanol and weakly basic medium (Aq. $Na_2CO_3$) and formed Benzylidinepropanedinitrile by loss of a water molecule. Above Benzylidinepropanedinitrile again react with Resorcinol and formed [(2,4-dihydroxy phenyl)(phenyl)methyl]propanedinitrile which on cyclization given 7-hydroxy-2-imino-4-phenyl-3,4-dihydro-2H-1-benzopyran-3-carobonitrile by hydrogen shift it converted into 2-amino-7-hydroxy-4-phenyl-4*H*-1-benzopyran-3-carbonitrile**,** in the second step above formed compounds reacted with pyrrlidine, piperidine, and morpholine substituted alkyl halide, in presence Dry.$K_2CO_3$) in dry acetone as medium converted into novel 2-amino-4-phenyl-7-[2-(pyrrolidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile**,** 2-amino-4-phenyl-7-[2-(peperidin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile, 2-amino-4-phenyl-7-[2-(morpholin-1-yl)ethoxy]-4*H*-1-benzopyran-3-carbonitrile and their derivatives. In the third step these formed compounds reacted with access formic acid or urea on refluxed and stirring given refined chromeno, carboxy and amine derivatives of pyrimidine. This was a high yield, stress free step reaction, Simple reaction condition and easily available catalyst made it favorable for synthesis.

## CONCLUSION

Presence of pyrimidine ring in structure create a strong expectation of positive biological activity in the compounds Overall it was most likely synthesis because of high yield, easy steps, and using of simple and easy available compounds which turned into novel compounds.

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