Synthesis of New Imino Containing Tetrahydrochromeno[2,3-*d*] pyrimidines

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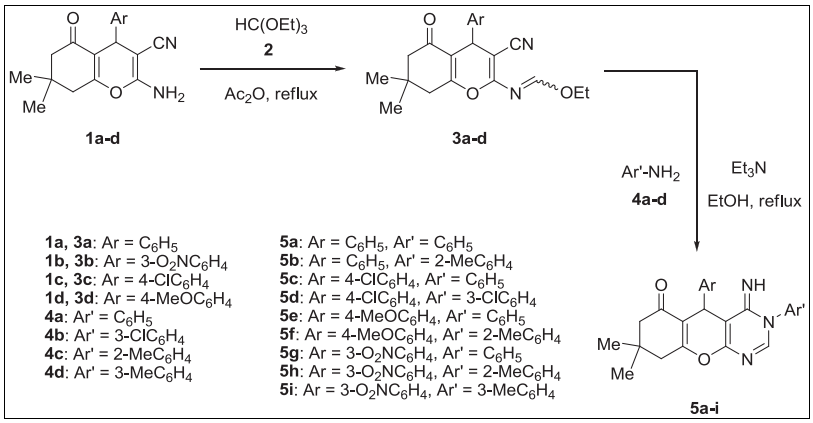


Some new derivatives of 3,5-diaryl-4-imino-5,7,8,9-tetrahydro-3*H*-chromeno[2,3-*d*]pyrimidine have been prepared through a condensation reaction of 2-amino-4-aryl-3-cyano-5,6,7,8-tetrahydrobenzo[*b*]pyrans with triethyl orthoformate in boiling acetic anhydride followed by cyclization with primary aryl amines in the presence of a few drops triethylamine as catalyst in refluxing ethanol. The products were characterized on the basis of IR, ^{1}H-NMR, and ^{13}C-NMR spectral and microanalytical data.

INTRODUCTION

The chromene moiety appears as an important structural component in both biologically active and natural compounds and is widely employed as cosmetics, pigments [1,2], and potential biodegradable agrochemicals [3]. It is known that certain chromenes possess important biological activities such as antioxidant [4], anticancer [5,6], anti-HIV [7], antiviral [8], antihypertensive [9], anticonvulsant [10], antileishmanial [11], TNF-α inhibitor [12], and antifungal [13] activity. This motif widely found in natural alkaloids, tocopherols, flavonoids, and anthocyanins [14], and several chromene derivatives have been proven to be efficient DNA polymerase β inhibitors [15] and apoptosis inducers [16]. On the other hand, a pyrimidine scaffold is the base of many bioactive molecules such as antitubercular [17], antibacterial [18,19], antitumor [20], antiinflammatory [21], antifungal [22], antiviral [23], and antileishmanial [24] agent.

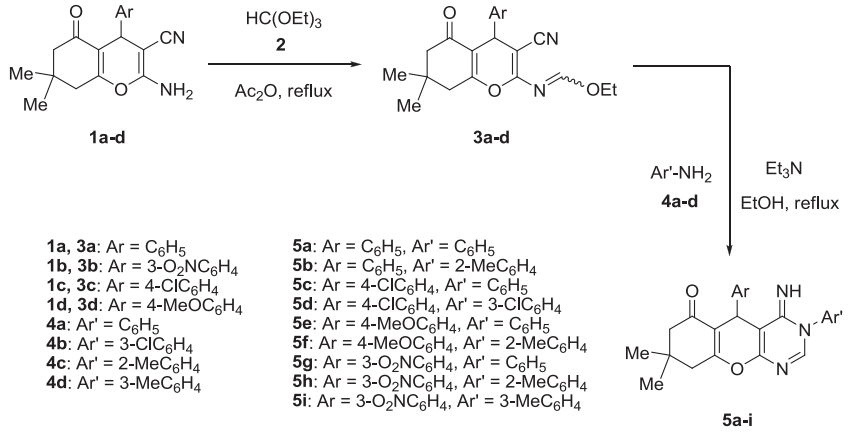
Chromeno[2,3-*d*]pyrimidines, which are constructed from two fused chromene and pyrimidine rings, have also generated great attention because of their interesting biological properties such as antitumor [25,26], antitubercular [27], antibacterial [28], antifungal [29], and antimicrobial [27,30] activity. In addition, these compounds exhibit excellent photophysical properties [31]. A perusal of literature reveals that there are a number of methods for the synthesis of chromeno[2,3-*d*]pyrimidines starting from chromene or pyrimidine moiety [32–36]. However, to the authors' knowledge, the synthesis of 4-imino tetrahydrochromeno[2,3-*d*]pyrimidine derivatives has been largely overlooked, and there is only one reference in the literature on the synthesis of these compounds [32].

These findings encouraged us to synthesize some new 4-imino tetrahydrochromeno[2,3-*d*]pyrimidine derivatives. Therefore, in continuation of our previous works in the synthesis of new heterocyclic compounds with potential biological activities [37–48], in this paper, we report a convenient synthesis of new 3,5-diaryl-4-imino-5,7,8,9-tetrahydro-3*H*-chromeno[2,3-*d*]pyrimidines **5a–i** through a condensation reaction of 2-amino-4-aryl-3-cyano-5,6,7,8-tetrahydrobenzo[*b*]pyrans **1a–d** with triethyl orthoformate **2** in boiling acetic anhydride obtaining compounds **3a–d** followed by cyclization with primary aryl amines **4a–d** in the presence of a catalytic amount of triethylamine in refluxing ethanol (Scheme 1).

RESULTS AND DISCUSSION

For our investigations, 2-amino-4-aryl-3-cyano-5,6,7,8-tetrahydrobenzo[*b*]pyrans **1a-d** were prepared according

Scheme 1. Synthesis of new 3,5-diaryl-4-imino-5,7,8,9-tetrahydro-3*H*-chromeno[2,3-d]pyrimidines.



to the literature procedure [49]. When these compounds were allowed to interact with excess triethyl orthoformate **2** in acetic anhydride at reflux temperature, condensation reaction occurred giving **3a–d**. The latter compounds were then reacted with primary aryl amines **4a–d** in the various catalyst-solvent systems at reflux temperature such as *t*-BuOK in *t*-BuOH, pyridine as both catalyst and solvent, Et_3N in EtOH, and also in EtOH in the absence of a base catalyst. Among them, the reactions were proceeded to give the good yields of the products 3,5-diaryl-4-imino-5,7,8,9-tetrahydro-3*H*-chromeno[2,3-d]pyrimidines **5a-i**, using triethylamine in refluxing ethanol.

The structural assignment of compounds **5a–i** was based upon spectral data and elemental analysis. For example, the ^{1}H-NMR spectrum of compound **5a** in DMSO-d_6 did not show the OEt signals of the precursor **3a** at $\delta = 1.20$ (t, $J = 6.7$ Hz, 3H), $\delta = 4.21$ (q, $J = 6.7$ Hz, 2H) ppm, but instead showed a signal at $\delta = 8.72$ (s, 1H) for NH group that is removed on deuteration, and other characteristic signals in aromatic region for new phenyl group indicating the formation of the tricyclic compound **5a**. The IR spectrum was devoid of the CN absorption band at 2209 cm^{-1} of the precursor but instead showed the NH absorption band at 3349 cm^{-1}, which shows the inclusion of the nitrile moiety in the cyclisation process. Further proof came from ^{13}C-NMR spectrum that showed the characteristic signals at δ 26.5, 28.7, 31.3, 32.0, and 50.1 ppm for aliphatic carbons as well as the other signals in the aromatic region and also carbonyl group. Also, this compound gave satisfactory elemental analysis data corresponding to the molecular formula $C_{25}H_{23}N_3O_2$ (Experimental).

CONCLUSION

In brief, we have synthesized some new 3,5-diaryl-4-imino-5,7,8,9-tetrahydro-3*H*-chromeno[2,3-*d*]pyrimidines in good yields through the condensation reaction of 2-amino-4-aryl-3-cyano-5,6,7,8-tetrahydrobenzo[*b*]pyrans with triethyl orthoformate in boiling acetic in the presence of a few drops triethylamine as catalyst in refluxing ethanol. The products were characterized on the basis of spectral and microanalytical data.

EXPERIMENTAL

Melting points were recorded on a Stuart SMP3 melting point apparatus. The IR spectra were obtained with KBr disks using a Tensor 27 Bruker spectrophotometer. The ^{1}H and ^{13}C-NMR spectra were recorded with Bruker 300 and 400 MHz spectrometers, using TMS as internal standard. Elemental analysis was performed on a Thermo Finnigan Flash EA microanalyzer.

General procedure for the synthesis of compounds 3a–d. A mixture of the respective tetrahydrobenzo[*b*]pyran **1a–d** (2 mmol) and excess triethyl orthoformate **2** (2 mL) in acetic anhydride (1 mL) was heated under reflux for 5–6 h. Upon completion, the mixture was poured onto crushed ice. Then, the precipitate was collected and recrystallized from ethanol (96%) to afford compounds **3a–d** in high yields.

Ethyl* N-*(3-cyano-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4*H*-chromen-2-yl)formimidate (3a). Yield (88%); mp 201–203°C; IR (KBr, cm^{-1}): 2209 (CN), 1664 (C = O), $^{-1}$H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.89 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 1.20 (t, $J = 6.7$ Hz, 3H, CH_3), 2.12 (AB_q, $\Delta v = 48.3$ Hz, $J_{AB} = 16.0$ Hz, 2H, CH_2), 2.42 (s, 2H, CH_2), 4.21 (q, $J = 6.7$ Hz, 2H, OCH_2), 4.32 (s, 1H, CH), 7.10–7.30 (m, 5H, Ph), 8.46 (s, 1H, N = CH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 13.8, 27.0, 28.3, 31.9, 37.1, 50.0, 64.1, 82.5, 111.6, 117.2, 127.2, 127.7, 128.6, 142.8, 156.0, 162.0, 163.0, 195.8; *Anal*. Calcd for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.33; N, 7.99, Found: C, 72.12; H, 6.41; N, 7.81.

Ethyl* N-*(3-cyano-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromen-2-yl)formimidate (3b). Yield (85%); mp 168–170°C; IR (KBr cm^{-1}): 2208 (CN), 1668 (C=O), 1511 and 1364 (NO_2), ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.87 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 1.18 (t, J=6.9 Hz, 3H, CH_3), 2.10 (AB_q, $\Delta\nu$=51.7 Hz, J_{AB}=16.1 Hz, 2H, CH_2), 2.39 (s, 2H, CH_2), 4.19 (q, J=6.9 Hz, 2H, OCH_2), 4.59 (s, 1H, CH), 7.55 (t, J=7.7 Hz, 1H, arom-H), 7.66 (d, J=7.4 Hz, 1H, arom-H), 7.98 (s, 1H, arom-H), 8.01 (d, J=8.1 Hz, 1H, arom-H), 8.47 (s, 1H, N=CH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 13.8, 26.9, 28.2, 31.9, 36.7, 49.9, 64.2, 81.3, 110.7, 116.9, 122.3, 122.4, 130.2, 134.7, 145.0, 147.9, 156.6, 162.5, 163.6, 195.8; *Anal*. Calcd for $C_{21}H_{21}N_3O_5$: C, 63.79; H, 5.35; N, 10.63, Found: C, 63.94; H, 5.28; N, 10.49.

Ethyl* N-*(4-(4-chlorophenyl)-3-cyano-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromen-2-yl)formimidate (3c). Yield (92%); mp 177-179 °C; IR (KBr cm^{-1}): 2212 (CN), 1675 (C=O), ^{1}H-NMR (300 MHz, DMSO-d_6, δ ppm): 0.98 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.31 (t, J=7.2 Hz, 3H, CH_3), 2.21 (AB_q, $\Delta\nu$=35.7 Hz, J_{AB}=15.9 Hz, 2H, CH_2), 2.59 (s, 2H, CH_2), 4.31 (q, J=7.2 Hz, 2H, OCH_2), 4.47 (s, 1H, CH), 7.29 (d, J=8.4 Hz, 2H, arom-H), 7.41 (d, J=8.4 Hz, 2H, arom-H), 8.57 (s, 1H, N=CH); ^{13}C-NMR (75 MHz, DMSO-d_6, δ ppm): 14.3, 27.5, 28.6, 32.4, 37.0, 50.4, 64.6, 82.4, 111.7, 117.5, 129.0, 130.1, 132.3, 142.3, 156.7, 162.6, 163.5, 196.2; *Anal*. Calcd for $C_{21}H_{21}ClN_2O_3$: C, 65.54; H, 5.50; N, 7.28, Found: C, 65.41; H, 5.62; N, 7.42.

Ethyl* N-*(3-cyano-4-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromen-2-yl)formimidate (3d). Yield (90%); mp 158–160°C; IR (KBr cm^{-1}): 2207 (CN), 1669 (C=O), ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.97 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.29 (t, J=7.1 Hz, 3H, CH_3), 2.19 (AB_q, $\Delta\nu$=50.1 Hz, J_{AB}=16.1 Hz, 2H, CH_2), 2.56 (s, 2H, CH_2), 3.72 (s, 3H, OCH_3), 4.29 (q, J=7.1 Hz, 2H, OCH_2), 4.35 (s, 1H, CH), 6.88 (d, J=8.5 Hz, 2H, arom-H), 7.14 (d, J=8.5 Hz, 2H, arom-H), 8.53 (s, 1H, N=CH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 13.8, 26.9, 28.3, 31.9, 36.2, 50.0, 55.0, 64.0, 82.7, 111.8, 113.9, 117.3, 117.4, 128.8, 155.8, 158.3, 161.8, 162.6, 195.7; *Anal*. Calcd for $C_{22}H_{24}N_2O_4$: C, 69.46; H, 6.36; N, 7.36, Found: C, 69.29; H, 6.49; N, 7.26.

General procedure for the synthesis of 3,5-diaryl-4-imino-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidines 5a–i. To a solution of the primary aryl amine **4a–d** (1 mmol) in ethanol (20 mL) in the presence of three drops triethylamine as catalyst, compounds **3a–d** (1 mmol) was added. The reaction mixture was heated under reflux for 5–6 h. After the completion of the reaction (monitored by TLC), the mixture was cooled to room temperature. The crude product was collected and recrystallized from ethyl acetate/n-hexane (1:3) to afford compounds **5a–i** in good yields.

4-imino-8,8-dimethyl-3,5-diphenyl-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidin-6(4*H*)-one (5a). Yield (77%); mp 272–275°C; IR (KBr cm^{-1}): 3349 (NH), 1637 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.92 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 2.13 (d, J=16.0 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.34 (d, J=16.0 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.65 (AB_q, $\Delta\nu$=30.3 Hz, J_{AB}=17.6 Hz, 2H, CH_2), 5.46 (s, 1H, CH), 7.02 (t, J=6.8 Hz, 1H, arom-H), 7.14 (t, J=6.7 Hz, 1H, arom-H), 7.20–7.30 (m, 4H, arom-H), 7.39 (d, J=7.0 Hz, 2H, arom-H), 7.55 (d, J=7.4 Hz, 2H, arom-H), 8.29 (s, 1H, N=CH), 8.72 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 26.5, 28.7, 31.3, 32.0, 50.1, 99.8, 114.2, 121.7, 123.4, 126.9, 127.9, 128.3, 128.4, 139.2, 143.2, 156.0, 158.9, 161.3, 164.0, 195.9; *Anal*. Calcd for $C_{25}H_{23}N_3O_2$: C, 75.54; H, 5.83; N, 10.57, Found: C, 75.39; H, 5.75; N, 10.68.

4-imino-8,8-dimethyl-3-(2-methylphenyl)-5-phenyl-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidin-6(4*H*)-one (5b). Yield (74%); mp 240–241°C; IR (KBr cm^{-1}) 3418 (NH), 1660 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.91 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.58 (s, 3H, CH_3), 2.11 (d, J=16.2 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.32 (d, J=16.2 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.58 (AB_q, $\Delta\nu$=33.2 Hz, J_{AB}=15.4 Hz, 2H, CH_2), 5.21 (s, 1H, CH), 7.05–7.20 (m, 5H, arom-H), 7.24 (t, J=7.7 Hz, 2H, arom-H), 7.30–7.40 (m, 2H, arom-H), 8.07 (s, 1H, N=CH), 8.44 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 17.5, 26.7, 28.8, 32.0, 32.2, 50.3, 98.9, 114.4, 126.3, 127.1, 127.2, 127.3, 128.3, 128.4, 130.5, 134.8, 137.3, 143.1, 156.4, 160.1, 161.3, 164.2, 196.3; *Anal*. Calcd for $C_{26}H_{25}N_3O_2$: C, 75.89; H, 6.12; N, 10.21, Found: C, 76.08; H, 6.06; N, 10.34.

5-(4-chlorophenyl)-4-imino-8,8-dimethyl-3-phenyl-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidin-6(4*H*)-one (5c). Yield (81%); mp 256–258°C; IR (KBr cm^{-1}) 3435 (NH), 1657 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.92 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 2.14 (d, J=16.0 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.35 (d, J=16.0 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.63 (AB_q, $\Delta\nu$=32.9 Hz, J_{AB}=17.7 Hz, 2H, CH_2), 5.49 (s, 1H, CH), 7.03 (t, J=7.4 Hz, 2H, arom-H), 7.25–7.35 (m, 3H, arom-H), 7.41 (d, J=8.4 Hz, 2H, arom-H), 7.55 (d, J=7.6 Hz, 2H, arom-H), 8.31 (s, 1H, N=CH), 8.76 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 26.5, 28.6, 30.8, 32.0, 50.0, 99.3, 113.9, 121.9, 123.5, 128.3, 128.4, 129.8, 131.5, 139.1, 142.1, 156.2, 158.9, 161.4, 164.2, 195.9; *Anal*. Calcd for $C_{25}H_{22}ClN_3O_2$: C, 69.52; H, 5.13; N, 9.73, Found: C, 69.67; H, 5.19; N, 9.61.

3-(3-chlorophenyl)-5-(4-chlorophenyl)-4-imino-8,8-dimethyl-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidin-6(4*H*)-one (5d). Yield (75%); mp 235–237°C; IR (KBr cm^{-1}) 3376

(NH), 1656 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.92 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 2.15 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.35 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.65 (AB_q, $\Delta\nu$=31.6 Hz, J_{AB}=17.5 Hz, 2H, CH_2), 5.51 (s, 1H, CH), 7.08 (d, J=7.7 Hz, 1H, arom-H), 7.25–7.35 (m, 3H, arom-H), 7.39 (d, J=8.3 Hz, 2H, arom-H), 7.55 (t, J=6.7 Hz, 1H, arom-H), 7.79 (d, J=6.4 Hz, 1H, arom-H), 8.39 (s, 1H, N=CH), 8.92 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 26.7, 28.7, 30.1, 32.1, 50.4, 114.5, 120.0, 120.9, 123.2, 127.3, 128.1, 128.7, 129.0, 130.4, 130.8, 131.9, 140.0, 143.3, 156.2, 159.0, 164.3, 196.4; *Anal*. Calcd for $C_{25}H_{21}Cl_2N_3O_2$: C, 64.39; H, 4.54; N, 9.01, Found: C, 64.20; H, 4.63; N, 9.12.

4-imino-5-(4-methoxyphenyl)-8,8-dimethyl-3-phenyl-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidin-6(4H)-one (5e). Yield (79%); mp 240–241°C; IR (KBr cm^{-1}) 3435 (NH), 1656 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.93 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 2.13 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.33 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.64 (AB_q, $\Delta\nu$=32.6 Hz, J_{AB}=17.5 Hz, 2H, CH_2), 3.65 (s, 3H, OCH_3), 5.39 (s, 1H, CH), 6.79 (d, J=8.5 Hz, 2H, arom-H), 7.02 (t, J=7.2 Hz, 1H, arom-H), 7.25–7.35 (m, 4H, arom-H), 7.57 (d, J=8.0 Hz, 2H, arom-H), 8.29 (s, 1H, N=CH), 8.68 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 26.5, 28.6, 30.4, 31.9, 50.1, 54.9, 100.0, 113.6, 114.4, 121.6, 123.3, 128.4, 128.9, 135.2, 139.2, 155.8, 157.9, 158.8, 161.2, 163.6, 195.8; *Anal*. Calcd for $C_{26}H_{25}N_3O_3$: C, 73.05; H, 5.89; N, 9.83, Found: C, 73.22; H, 5.81; N, 9.72.

4-imino-5-(4-methoxyphenyl)-8,8-dimethyl-3-(2-methylphenyl)-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidin-6(4H)-one (5f). Yield (76%); mp 212–214°C; IR (KBr cm^{-1}) 3400 (NH), 1654 (C=O); ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.93 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.66 (s, 3H, CH_3), 2.13 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.32 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.62 (AB_q, $\Delta\nu$=27.4 Hz, J_{AB}=16.5 Hz, 2H, CH_2), 3.67 (s, 3H, OCH_3), 5.18 (s, 1H, CH), 6.81 (d, J=8.3 Hz, 2H, arom-H), 7.10–7.20 (m, 4H, arom-H), 7.29 (d, J=8.3 Hz, 2H, arom-H), 8.09 (s, 1H, N=CH), 8.41 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 17.4, 26.5, 28.6, 30.9, 31.9, 50.1, 55.0, 98.8, 113.4, 114.3, 125.9, 126.0, 127.0, 129.2, 130.2, 134.4, 134.9, 137.2, 156.0, 158.0, 159.8, 161.1, 163.5, 195.8; *Anal*. Calcd for $C_{27}H_{27}N_3O_3$: C, 73.45; H, 6.16; N, 9.52, Found: C, 73.31; H, 6.09; N, 9.63.

4-imino-8,8-dimethyl-5-(3-nitrophenyl)-3-phenyl-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidin-6(4H)-one (5g). Yield (75%); mp 259–261°C; IR (KBr cm^{-1}) 3314 (NH), 1641 (C=O), 1529 and 1347 (NO_2); ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.90 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 2.14 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.35 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.66 (AB_q, $\Delta\nu$=26.3 Hz, J_{AB}=17.8 Hz, 2H, CH_2), 5.66 (s, 1H, CH), 7.02 (t, J=7.2 Hz, 1H, arom-H), 7.26 (t, J=7.7 Hz, 2H, arom-H), 7.50-7.60 (m, 3H, arom-H), 7.75 (d, J=7.6 Hz, 1H, arom-H), 8.02 (d, J=7.7 Hz, 1H, arom-H), 8.33 (s, 1H, arom-H), 8.45 (s, 1H, N=CH), 8.91 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 26.4, 28.6, 31.1, 32.1, 49.9, 98.6, 113.4, 122.0, 122.1, 123.0, 123.7, 128.4, 130.1, 134.4, 138.9, 145.1, 147.5, 156.5, 158.9, 161.5, 164.7, 196.0; *Anal*. Calcd for $C_{25}H_{22}N_4O_4$: C, 67.86; H, 5.01; N, 12.66, Found: C, 68.01; H, 5.12, N; 12.54.

4-imino-8,8-dimethyl-3-(2-methylphenyl)-5-(3-nitrophenyl)-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidin-6(4H)-one (5h). Yield (72%); mp 222–225°C; IR (KBr cm^{-1}) 3313 (NH), 1638 (C=O), 1527 and 1333 (NO_2); ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.91 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 1.59 (s, 3H, CH_3), 2.15 (d, J=16.2 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.35 (d, J=16.2 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.67 (AB_q, $\Delta\nu$=23.7 Hz, J_{AB}=17.9 Hz, 2H, CH_2), 5.43 (s, 1H, CH), 7.05–7.20 (m, 4H, arom-H), 7.58 (t, J=7.7 Hz, 1H, arom-H), 7.73 (d, J=7.2 Hz, 1H, arom-H), 8.07 (d, J=7.6 Hz, 1H, arom-H), 8.13 (s, 1H, arom-H), 8.45 (s, 1H, N=CH), 8.67 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 17.1, 26.5, 28.5, 31.6, 31.9, 49.9, 97.4, 113.3, 121.9, 123.4, 126.1, 126.2, 127.3, 128.6, 129.9, 130.2, 134.6, 137.0, 145.0, 147.3, 156.7, 159.9, 161.2, 164.5, 195.9; *Anal*. Calcd for $C_{26}H_{24}N_4O_4$: C, 68.41; H, 5.30; N, 12.27, Found: C, 68.20; H, 5.37; N, 12.33.

4-imino-8,8-dimethyl-3-(3-methylphenyl)-5-(3-nitrophenyl)-5,7,8,9-tetrahydro-3H-chromeno[2,3-d]pyrimidin-6(4H)-one (5i). Yield (70%); mp 213–215°C; IR (KBr cm^{-1}) 3363 (NH), 1641 (C=O), 1568 and 1350 (NO_2); ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 0.91 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 2.15 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.24 (s, 3H, CH_3), 2.36 (d, J=16.1 Hz, 1H, one proton of diastereotopic protons in CH_2), 2.67 (AB_q, $\Delta\nu$=27.1 Hz, J_{AB}=17.7 Hz, 2H, CH_2), 5.64 (s, 1H, CH), 7.15 (t, J=7.9 Hz, 1H, arom-H), 7.25–7.35 (m, 3H, arom-H), 7.56 (t, J=7.9 Hz, 1H, arom-H), 7.73 (d, J=7.7 Hz, 1H, arom-H), 8.02 (d, J=8.0 Hz, 1H, arom-H), 8.32 (s, 1H, arom-H), 8.43 (s, 1H, N=CH), 8.81 (s, 1H, NH); ^{13}C-NMR (100 MHz, DMSO-d_6, δ ppm): 21.1, 26.4, 28.6, 31.1, 32.0, 49.9, 98.5, 113.4, 119.3, 122.0, 122.6, 122.9, 124.4, 128.2, 130.1, 134.3, 137.6, 138.8, 145.1, 147.4, 156.5, 159.0, 161.4, 164.6, 195.9; *Anal*. Calcd for $C_{26}H_{24}N_4O_4$: C, 68.41; H, 5.30; N, 12.27, Found: C, 68.59; H, 5.39; N, 12.18.

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