DOI: 10.5281/zenodo.21471164

International Journal of Research and Applications
Jan - Mar © 2026 Transactions 13(49): 3901-3907

eISSN : 2349 – 0020
pISSN : 2394 – 4544
www.ijraonline.com

CHEMISTRY RESEARCH ARTICLE

Multi-step Synthesis and Characterization of novel 6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)-1*H*-benzo[d]imidazolescaffold

Srikanth Podishetty [1], Shabhari Prasad Suggala[2], Jagadeesh Kumar Ega [1*]

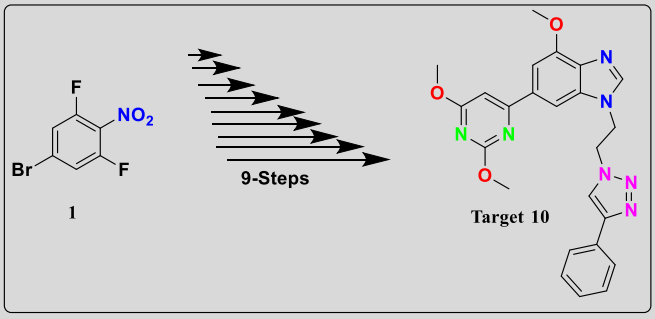
[1, 2, 1*] Chaitanya (Deemed to be University), (V) Himayathnagar, (M)Moinabad, (District) Ranga Reddy, Hyderabad -500075, Telangana, India.

*Email: jkjagadeeshkumare@gmail.com

ABSTRACT

At first5-bromo-1-fluoro-3-methoxy-2-nitrobenzene 2 formed from a stirred solution of 5-bromo-1, 3-difluoro-2-nitrobenzene 1 MeOH/ KOH to give ether via NPSRN. Compound 2 treated withtert-butyl (2-aminoethyl) carbamate under THF to yield Boc protected tert-butyl (2-((5-bromo-3-methoxy-2-nitrophenyl) amino) ethyl) carbamate 3.It is further with Zn dustNH4Cl under THF/H2O to give tert-butyl (2-((2-amino-5-bromo-3-methoxyphenyl) amino) ethyl) carbamate 4 through reduction. It is further interacted with triethyl orthoformate, PTSA catalytic amount to yield tert-butyl (2-(6-bromo-4-methoxy-1H-benzo[d]imidazol-1-yl) ethyl) carbamate 5 via cyclization. Furthermore, with Bis (pinacolato) diborane under dry Dioxane and PdCl2 (dppf)/ DCM to yield tert -butyl (2-(4-methoxy-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-benzo[d]imidazol-1-yl)ethyl) carbamate 6. Compound 6 charged with4-bromo-2,6-dimethoxypyrimidine followed by PdCl2 (dppf) CH2Cl2 to give tert-butyl (2-(6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl) ethyl) carbamate 7 through cross coupling. It is interacted with BBr3 which acts as Lewis acid under DCM to form 6-(1-(2-aminoethyl)-4-hydroxy-1H-benzo[d]imidazol-6-yl) pyrimidine-2, 4(1H, 3H)-dione hydrochloride 8. Then reaction mixture is charged witht-BuONO followed by 1.77 mmol TMSN3 drop-wise under CH3CN to give desired azide namely 1-(2-azidoethyl)-6-(2, 6-dimethoxypyrimidin-4-yl)-4-methoxy-1H-benzo[d]imidazole 9. Finally,label compound 9 under goes 3+2 cyclo addition with Phenyl acetylene in the presence of CuSO4.5H2O/ sodium ascorbate familiarly Sharpless catalyst which convert Cu (II) to Cu(I) during the course of the reaction to yield target 6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1-(2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethyl)-1H-benzo[d]imidazole 10 with an excellent yields depicted (Scheme I) in this manuscript viz click protocols.

Keywords: Boc protection, pyrimidine, benzo[d]imidazole, 1, 2, 3-triazole, Cyclization, PdCl2 (dppf), BBr3, TMSN3, 3+2 cyclo addition, coupling, deprotection.



Graphical Abstract

1. INTRODUCTION

Heterocyclic compounds havedynamic role in medicinal & agrochemical industries. In recent years it has been found that most vibrant and eye-catching heterocyclic compounds [1] are benzimidazole class of compounds. [2,3] Variety of this heterocyclic class of compounds shows anti-microbial activities which inhibits the diseases due to microbes,[4–9] anti-tubercular activities effective against tuberculosis[10]. Based on their strategies and applications benzimidazole derivatives became attention for organic chemists. The 2-subtitued benzimidazole scaffold as shown in (Fig: 1–3). [11–14] These heterocyclic compounds are also known to be present in biological structure-like hemoglobin [15] or chlorophyll [16–18]. By using several transition metals catalyzed [19] reactions carbon-nitrogen bond formation can be accomplished. In addition, making use of hyper valent iodine, carbon-hydrogen amidation was achieved. Iodine facilitated various reactions are established for making nitrogen comprising heterocyclic systems.[20,21] Development of C–N bond by using C–H amidation has been described rarely, may be because of nitrogen's weak nucleophilicity in amide substrates. From the extension of earlier work. [22]

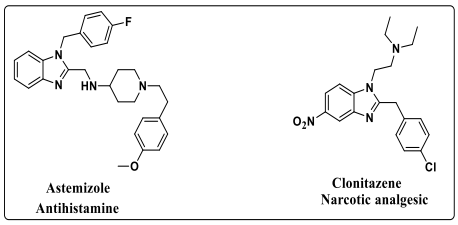


Fig 1: 2-substituted benzimidazoles as antihistamine & narcotic analgesics

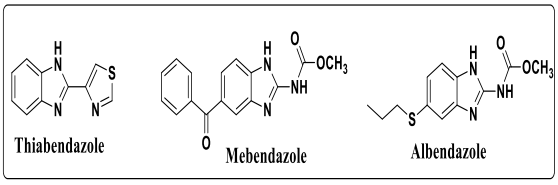


Fig 2: 2-substituted benzimidazoles as anthelmintic drugs

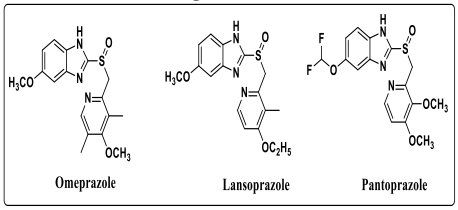


Fig-3: 2-substituted benzimidazoles as Antiulcer agents

2, 4 diamino pyrimidines and some 2- amino- 4 hydroxy pyrimidines are antagonists of folic acid. These pyrimidines were than eventually proved as inhibitors of the enzyme dihydrofolate reductase. Amongst the2, 4-diaminpyrimidine drugs, pyrimethamine is selective inhibitor of the DHFR of malarial plasmodia.[24] Trimethoprim, antibacterial drug.[23] Brodimoprim, is also found to be an effective antibacterial compound. Some new pyrimidine derivatives like 7-(2-methoxy phenyl)-3 methyl- 5-thioxo-5, 6-dihydro[1, 2, 4]-triazolo[4, 3-c] pyrimidine-8-carbo-nitrile acts as bacterial activity and anticancer activity [25]. (Shown in Fig: 4)

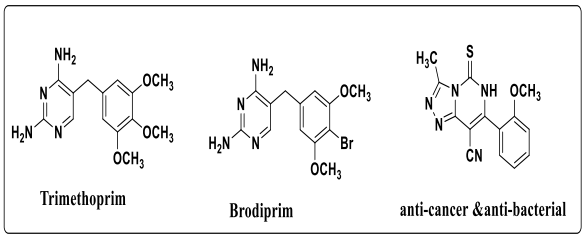


Fig 4: some biologically potent pyrimidine derivatives

The possibility to insert in simple and flexible ways functional negotiators in a straight line merged to the heterocycles, by means of click protocols for 1,2,3-triazole synthesis. These moieties are bioactive ability [26, 27]. (Shown in Fig: 5)

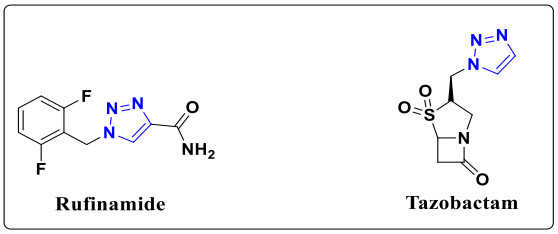


Fig: 5 Drugs containing 1, 2, 3-triazoles

Herein, we have described the synthesis of 6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)-1*H*-benzo[d]imidazole. (Shown in Fig: 6)

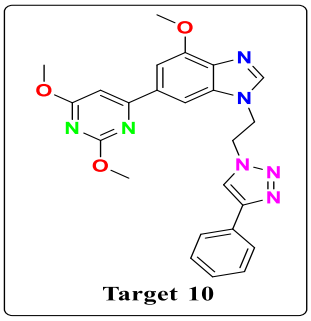
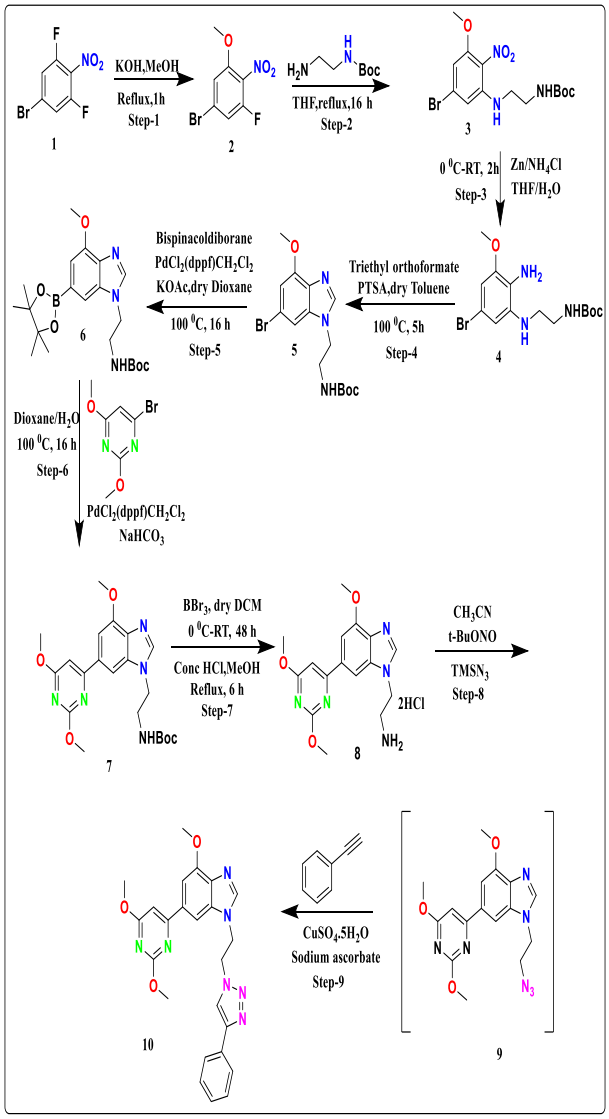


Fig: 6 Designed compound 10

2. EXPERIMENTAL

Melting points were determined using a Cintex melting point apparatus and are uncorrected. Thin-layer chromatography (TLC) was performed by using Merck silica gel 60 F254 precoated plates (0.25 mm) and column chromatography was performed by using Silica gel (particle size 100-200 mesh). ^{1}H NMR spectra were recorded on a Bruker AMX 400 MHz spectrometer, 100MHz for ^{13}C NMR spectra. Chemical shift values were given in ppm (δ) with TMS as an internal standard. Mass spectra were determined on Agilent LC-1100 (LC-MS) series instrument. Elemental analyses were performed on a Carlo Erba 106 and Perkin Elmer model 240 analyzers.

3. RESULTS AND DISCUSSION



Scheme I: Synthesis of 6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)-1*H*-benzo[d]imidazole

Step 1: Synthesis of 5-bromo-1-fluoro-3-methoxy-2-nitrobenzene 2

To a stirred solution of 5-bromo-1, 3-difluoro-2-nitrobenzene**1** (3 g, 12.60 mmol) in MeOH (30 mL) was added KOH (635 mg, 11.34 mmol) and stirred the reaction mixture at reflux temperature for 1 h. Progress of the reaction was monitored by TLC. The reaction mixture was cooled to RT; the solvent was concentrated under reduced pressure. The obtained residue was dissolved in water (30 mL), extracted with DCM (3x20 mL). The combined organic layer was washed with brine (20 mL), dried over *anhydrous* sodium sulphate and concentrated under reduced pressure. The crude compound was purified by column chromatography (silica gel 230-240 mesh, eluted with pet ether) to afford 5-bromo-1-fluoro-3-methoxy-2-nitrobenzene**2** as off white solid (2.7 g, 85.7% yield).

Step 2: Synthesis of tert-butyl (2-((5-bromo-3-methoxy-2-nitrophenyl) amino) ethyl) carbamate 3

To a stirred solution of 5-bromo-1-fluoro-3-methoxy-2-nitrobenzene**2** (1.5 g, 6.0 mmol), *tert*-butyl (2-aminoethyl) carbamate (3.84 mL, 24.0 mmol) in THF (30 mL) and stirred the reaction mixture at reflux temperature for 16 h. The progress of the reaction was monitored by TLC. The reaction mixture was cooled to RT, quenched with water (30 mL), was extracted with EtOAc (3x15 mL). The combined organic layer was dried over *anhydrous* sodium sulphate and concentrated under reduced pressure. The crude compound was purified by column chromatography (silica gel 100-200 mesh, eluted with 20% EtOAc in Pet ether) to afford tert-butyl (2-((5-bromo-3-methoxy-2-nitrophenyl) amino) ethyl) carbamate**3** as Yellow solid (2.0 g, 85.4% yield).

Step 3: Synthesis of *tert*-butyl (2-((2-amino-5-bromo-3-methoxyphenyl) amino) ethyl) carbamate 4

To a stirred solution of tert-butyl (2-((5-bromo-3-methoxy-2-nitrophenyl) amino) ethyl) carbamate**3** (1 g, 2.56 mmol) in THF/H_2O (30 mL, 2:1 v/v) was added Zn dust (1.6 g, 25.64 mmol), NH_4Cl (680 mg, 12.82 mmol) at 0 °C and stirred the reaction mixture at RT for 2 h. The progress of the reaction was monitored by TLC. The reaction mixture was filtered through a pad of celite, washed with EtOAc (20 mL), extracted with water (20 mL). The combined organic layer was dried over *anhydrous* sodium sulphate and concentrated under reduced pressure. The crude

compound was purified by column chromatography (silica gel 230-400 mesh, eluted with 20% EtOAc in Pet ether) to afford tert-butyl (2-((2-amino-5-bromo-3-methoxyphenyl) amino) ethyl) carbamate**4** as brown solid (900 mg, 97.5% yield).

Step 4: Synthesis of *tert*-butyl (2-(6-bromo-4-methoxy-1*H*-benzo[d]imidazol-1-yl) ethyl) carbamate 5

To a stirred solution of tert-butyl (2-((2-amino-5-bromo-3-methoxyphenyl) amino) ethyl) carbamate **4**(900 mg, 2.5 mmol) in dry Toluene (15 mL) was added Triethyl orthoformate (0.45 mL, 2.75 mmol), PTSA (50 mg, catalytic amount) and stirred the reaction mixture at 100 °C temperature for 5 h. The progress of the reaction was monitored by TLC. The reaction mixture was cooled to RT; the solvent was concentrated under reduced pressure. The obtained residue was dissolved in water (20 mL), extracted with DCM (3x20 mL). The combined organic layer was washed with brine (10 mL), dried over *anhydrous* sodium sulphate and concentrated under reduced pressure. The crude compound was purified by column chromatography (silica gel 230-240 mesh, eluted with 2% MeOH in DCM) to afford tert-butyl (2-(6-bromo-4-methoxy-1*H*-benzo[d]imidazol-1-yl) ethyl) carbamate**5** as yellow solid (700 mg, 75.7% yield).

Step 5: Synthesis of *tert* -butyl (2-(4-methoxy-6-(4, 4, 5, 5-tetramethyl-1, 3, 2-dioxaborolan-2-yl)-1*H*-benzo[d]imidazol-1-yl) ethyl) carbamate 6

To a stirred solution of tert-butyl (2-(6-bromo-4-methoxy-1H-benzo[d]imidazol-1-yl)ethyl) carbamate**5** (700 mg, 1.89 mmol) in dry Dioxane (10 mL) was added Bis (pina-colato)diborane (480 mg, 1.89 mmol), Potassium acetate (556 mg, 5.67 mmol) and the reaction mixture was degassed with Argon gas for 10 min. After 10 min $PdCl_2$ (dppf). CH_2Cl_2 (77 mg, 0.09 mmol) was added and stirred the reaction mixture at 100 °C for 16 h. The reaction mixture was cooled to RT, filtered through a pad of celite, washed with EtOAc (2x10 mL). The combined organic layer was dried over *anhydrous* sodium sulphate and concentrated under reduced pressure. The crude compound was purified by column chromatography (Florisil silica gel 60-100 mesh, eluted with 1-2% MeOH in DCM) to afford tert-butyl (2-(4-methoxy-6-(4, 4, 5, 5-tetramethyl-1, 3, 2-dioxaborolan-2-yl)-1*H*-benzo[d]imidazol-1-yl) ethyl) carbamate**6** as off white solid (520 mg, 65% yield).

Step 6: Synthesis of *tert*-butyl (2-(6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1*H*-benzo[d]imidazol-1-yl) ethyl) carbamate 7

To a stirred solution of tert-butyl (2-(4-methoxy-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-benzo[d]imidazol-1-yl)ethyl)carbamate**6**(250 mg, 0.59mmol), 4-bromo-2,6-dimethoxypyrimidine (157 mg, 0.71 mmol) in Dioxane/water (5 mL, 4:1 v/v) was added $NaHCO_3$ (100 mg, 1.19 mmol) and the reaction mixture was degassed with Argon gas for 10 min. After 10 min $PdCl_2$ (dppf) CH_2Cl_2 (25 mg, 0.02 mmol) was added and stirred the reaction mixture at 100 °C for 16 h. The reaction mixture was cooled to RT, filtered through a pad of celite withEtOAc (30 mL); organic layer was washed with water (20 mL). Aqueous layer was extracted with EtOAc (2x 20 mL). The combined organic layer was dried over *anhydrous* sodium sulphate and concentrated under reduced Pressure. The crude compound was purified by column chromatography (silica gel 230-400 mesh, eluted with 1-2% MeOH in DCM) to afford tert-butyl (2-(6-(2, 6-dimethoxypyrimidin-4-yl)-4-methoxy-1*H*-benzo[d]imidazol-1-yl) ethyl) carbamate**7** as yellow solid (200 mg, 78% yield).

Step 7: Synthesis of 6-(1-(2-aminoethyl)-4-hydroxy-1*H*-benzo[d]imidazol-6-yl) pyrimidine-2, 4(1*H*, 3*H*)-dione hydrochloride 8

To a stirred solution of tert-butyl (2-(6-(2, 6-dimethoxypyrimidin-4-yl)-4-methoxy-1H-benzo[d]imidazol-1-yl) ethyl) carbamate**7** (200 mg, 0.466 mmol) in dry DCM (10 mL) was added BBr_3 (0.44 mL, 4.66 mmol) and stirred the reaction mixture at RT for 48 h. The progress of the reaction was monitored by LCMS. The reaction mixture was concentrated under reduced pressure. The residue was washed with diethyl ether (15 mL) and dried under vacuum to afford 1-(2-aminoethyl)-6-(2, 6-dimethoxypyrimidin-4-yl)-1*H*-benzo[d]imidazol-4-ol as Brown solid (160 mg, crude wt). The compound was used in the next step without any purification.
The crude compound (160 mg, 0.50 mmol) in MeOH (10 mL) was added Conc. HCl (10 mL) at RT and stirred the reaction mixture at reflux temperature for 6 h. The progress of the reaction was monitored by LCMS. The reaction mixture was cooled to RT and concentrated under reduced pressure. The obtained solid was washed with diethyl ether (3x10 mL), dried under vacuum to afford 6-(1-(2-aminoethyl)-4-hydroxy-1*H*-benzo[d]imidazol-6-yl) pyrimidine-2,

4(1*H*, 3*H*)-Dione hydrochloride **8** as off white solid (180 mg, 98% yield).

Step 8: 1-(2-azidoethyl)-6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1*H*-benzo[d]imidazole 9

The compound **8** 1.48 mmol containing amine functionality was was dissolved in CH_3CN (2 mL) in a RB flask and cooled to 0°C in an ice bath. To this stirred mixture was added 2.22 mmol of *t*-BuONO followed by 1.77 mmol $TMSN_3$ drop-wise. The subsequent solution was stirred at RT for 1 h further followed by reaction mixture was focused under vacuum and the crude product was purified by silica gel chromatography (hexane) to give 1-(2-azidoethyl)-6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1*H*-benzo[d]imidazole**9**(200 mg, 79% yield).

Step 9: Synthesis of 6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)-1*H*-benzo[d]imidazole 10

The compound 9 was stirred at RT for 2 h in the presence of 0.54 mmol Phenyl acetylene, aq. solution (0.2 mL) 0.036 mmol of $CuSO_4.5H_2O$ and 0.108 mmol sodium ascorbate which is namely Sharpless catalyst were then added and the reaction was stirred the product was then precipitated with methanol to give the product an off white solid of 6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)-1*H*-benzo[d]imidazole**10**(248 mg, 82% yield).

CONCLUSION

In the current study, we have synthesized 6-(2,6-dimethoxypyrimidin-4-yl)-4-methoxy-1-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)ethyl)-1*H*-enzo[d]imidazolewith an excellent yields and high purity.

REFERENCES

1) Katritzky, A. R. *Handbook of Heterocyclic Chemistry*; Pergamon Press: New York, **1985**; 1–2.
2) Bisby, R. *FEBS Lett*, **1992**, 308, 107–107.
3) Pathan, S. I.;Chauhan, N. P. S.; Singh, G. P.*Synth. Commun*, **2020**, 50(9), 1251–1285.
4) Graßmanna, J.; Hippelia, S.; Dornischa, K.; Rohnerta, U. Beuscherb, N. Elstnera, E. *Arzneimittelforschung*, **2011**, 50, 135–139.
5) Aruoma, O.I. Free radicals, oxidative stress, and antioxidants in human health and disease. *J Amer Oil Chem Soc*, **1998**, 75, 199–212.
6) Abdel-Rahman, A. E.; Mahmoud, A. M.; El-Naggar, G. M.; El-Sherief, H. A. *Pharmazie*, **1983**, 38, 589–590.
7) Tahlan, S.; Kumar, S.; Kakkar, S.; Narasimhan, B. *BMC Chem*, **2019**, 13.
8) Ismail, P. S.; Vithal, R. A.; Singh, *G. P. Loc.***2020**, 17, 743–747.
9) Coburn, R. A.; Clark, M. T.; Evans, R. T.; Genco, R. J. *J. Med. Chem*, **1987**, 30, 205–208.
10) Chkirate, K.; Karrouchi, K.; Dege, N.; KheiraSebbar, N.; Ejjoummany, A.; Radi, S.; Adarsh, N. N.; Talbaoui, A.; Garcia, Y. *New J. Chem*, **2020**, 44, 2210–2221.
11) G. €oker, H.; Tunc¸Bilek, M.; Ayhan, G.; Altanlar, N. *Farmaco*, **1998**, 53, 415–420.
12) Ayhan-Kılcıgil, G.; Altanlar, N.; G€oker, H. *Il Farmaco*, **1999**, 54,562–565.
13) Soliman, F. S. G.; Rida, S. M.; Kappe, T. *Archiv Der Pharmazie*, **1984**, 317, 951–958.
14) Habib, N. S.; Abdel-Hamid, S.; El-Hawash, *M. Farmaco*, **1989**, 44, 1225–1232.
15) Antoci, V.; Cucu, D.; Zbancioc, G.; Mangalagiu, I. I. *Future Med. Chem*, **2020**, 12, 207–222.
16) Yadav, S.; Narasimhan, B.; Lim, S. M.; Ramasamy, K.; Vasudevan, M.; Shah, S. A. A.; Mathur, A. *Egypt. J. Basic Appl. Sci*, **2018**, 5, 100–109.
17) Surineni, G.; Gao, Y.; Hussain, M.; Liu, Z.; Lu, Z.; *Med ChemComm*, **2018**, 10, 49–60.
18) Keng Yoon, Y.; Ismail, R.;Osman, H.; Beevi, F. *Bio Med Res. Int*, **2013**, 1–6.
19) R_afols, C.; Bosch, E.;Ruiz, R.; Reis, M.; Martins, F. *J Chem Eng Data*, **2011**, 57,330–338.
20) Islam, I.; Skibo, E. B.; Dorr, R. T.; Alberts, D. S. *J. Med. Chem*, **1991**, 34, 2954–2961.
21) Kruse, L. I.; Ladd, D. L.; Faucette, L.;Johnson, R. *J. Med. Chem*, **1989**, 32, 409–417.
22) Habernickel, V. *J. Drugs made in German*, **1992**, 35, 97.
23) Nakano, H.; Inoue, T.; Kawasaki, N.; Miyataka, H.; Matsumoto, H.; Taguchi, T. Inagaki, N.; Nagai, H.; Satoh, T. *Chem. Pharm. Bul*, **1999**, 47, 1573–1578.
24) Welsh, A.; Rylands, L.; Arion, V.; Prince, S.; Smith, G. *Dalton Trans*, **2020**, 49, 1143–1156.
25) Varvaresou, A.; Siatra-Papastaikoudi, T.; Tsotinis, A.; *A. Farmaco*. **1998**, 53, 320–326.
26) Singh, G.; Sahota, H. K. *Plant Physiol. Biochem*, 2018, 132, 166–173.

The structures of the products have been elucidated on the basis of ^{1}H NMR, ^{13}C NMR MS data and elemental analysis.

Table 1: Analytical data of compounds (2-10)

Entry	Mol. Formulae	Found (%) (Calcd)		
		C	H	N
1	$C_7H_5BrFNO_3$	33.75 (33.63	2.03 2.02	5.62 5.60)
2	$C_{14}H_{20}BrN_3O_5$	43.21 (43.09	5.18 5.17	10.79 10.77)
3	$C_{14}H_{22}BrN_3O_3$	46.76 (46.68	6.17 6.16	11.68 11.66)
4	$C_{15}H_{20}BrN_3O_3$	48.78 (48.66	5.46 5.45	11.37 11.35)
5	$C_{21}H_{32}BN_3O_5$	60.56 (60.44	7.74 7.73	10.09 10.07)
6	$C_{21}H_{27}N_5O_5$	58.85 (58.73	6.35 6.34	16.33 16.31)
7	$C_{16}H_{19}N_5O_3$	58.47 (58.35	5.82 5.81	21.28 21.26)
8	$C_{16}H_{17}N_7O_3$	54.27 (54.08	4.83 4.82	27.61 27.59)
9	$C_{24}H_{23}N_7O_3$	63.13 (63.01	5.08 5.07	21.45 21.43)

Table 2: Spectral data of synthesized compounds (2-10)

Entry	^{1}H NMR (400 MHz, DMSO-d6) (δ, ppm)	^{13}CNMR (100 MHz, DMSO-d6) (δ, ppm)	MS (LCMS): *m/z*
1	7.57 (dd, J = 9.4, 1.8 Hz, 1H), 7.50 (br-s, 1H), 3.96 (s, 3H).	159.61, 157.52, 129.01, 127.98, 113.16, 56.78.	248.94
2	6.95 (t, J = 5.7 Hz, 1H), 6.72 (br-S, 1H), 6.61 (d, J = 1.8 Hz, 1H), 6.40 (t, J = 5.5 Hz, 1H), 3.80 (s, 3H), 3.17 (q, J = 6.0 Hz, 2H), 3.06 (q, J = 6.2 Hz, 2H), 1.36 (s, 9H).	159.20, 157.34, 144.98, 129.40, 126.75, 109.92, 105.84, 80.65, 56.78, 44.48, 39.93, 28.41.	389.06
3	6.90 (t, J = 5.7 Hz, 1H), 6.43 (d, J = 2.0 Hz, 1H), 6.31 (br-s, 1H), 4.78 (t, J = 5.5 Hz, 1H), 4.13 (s, 2H), 3.72 (s, 3H), 3.15-3.00 (m, 4H), 1.38 (s, 9H).	157.34, 147.54, 131.68, 110.74, 109.03, 105.19, 80.65, 56.78, 44.48, 39.93, 28.41.	359.08
4	8.02 (s, 1H), 7.39 (s, 1H), 6.95 (t, J = 5.9 Hz, 1H), 6.83 (s, 1H), 4.21 (t, J = 5.8 Hz, 2H), 3.92 (s, 3H), 3.26 (m, J = 5.7 Hz, 2H), 1.28 (s, 9H).	157.34, 149.37, 139.41, 133.28, 132.54, 117.04, 109.42, 80.65, 56.78, 46.45, 39.13, 28.41.	369.07
5	8.08 (s, 1H), 7.47 (s, 1H), 6.95 (t, J = 5.9 Hz, 1H), 6.92 (s, 1H), 4.27 (t, J = 5.7 Hz, 2H), 3.92 (s, 3H), 3.28 (q, J = 5.7 Hz, 2H), 1.30 (s, 12H), 1.28 (s, 9H).	157.34, 152.94, 139.41, 134.29, 132.46, 127.90, 113.95, 113.28, 87.48, 80.65, 56.78, 46.45, 39.13, 28.41, 24.69.	417.24
6	8.42 (s, 1H), 8.04 (s, 1H), 7.27 (s, 1H), 6.97(t, J = 5.8 Hz, 1H), 6.84 (s, 1H), 4.25 (t, J = 5.9 Hz, 2H), 3.94 (m, 9H), 3.29 (q, J = 5.9 Hz, 2H), 1.22 (s, 9H).	170.50, 166.49, 164.84, 157.34, 151.24, 139.41, 134.63, 128.00, 127.02, 114.07, 110.02, 99.88, 80.65, 56.78, 54.17, 53.74, 46.45, 39.13, 28.41.	429.20
7	11.32(s, 2H, D_2O exchangeable), 10.8 (br-s, 1H, D_2O exchangeable), 9.1 (br-s, 1H), 8.24 (br-s, 3H, D_2O exchangeable), 8.13 (br-s, 1H, D_2O exchangeable), 7.72 (d, J = 5.7 Hz, 1H), 7.48 (s, 1H), 7.19 (s, 1H), 4.65 (t, J = 6.0 Hz, 2H), 3.35 (m, 2H).	170.50, 166.49, 164.84, 151.24, 139.41, 134.63, 128.00, 127.02, 114.07, 110.02, 99.88, 56.78, 54.17, 53.74, 48.48, 39.59.	329.15

8	7.80 (s, 1H), 7.65 (s, 1H), 7.11 (s, 1H), 6.88 (s, 1H), 4.30 (t, *J* = 7.3 Hz, 1H), 4.12 (t, *J* = 7.4 Hz, 1H), 3.97 (s, 3H), 3.87 – 3.57 (m, 8H).	170.50, 166.49, 164.84, 151.24, 139.41, 134.63, 128.00, 127.02, 114.07, 110.02, 99.88, 56.78, 54.17, 53.74, 50.09, 46.94.	355.14
9	7.90 (d, *J* = 64.1 Hz, 2H), 7.67 – 7.09 (m, 7H), 6.89 (s, 1H), 4.54 (ddt, *J* = 94.5, 47.8, 4.6 Hz, 4H), 4.10 – 3.75 (m, 9H).	170.50,166.49,164.84,151.24,149.56,139.41,134.63,130.41,128.86,128.00,127.73,127.02,126.28,125.77,114.07,110.02,99.88,56.78, 54.17, 53.74, 48.73, 44.00.	457.19