RSC Advances

PAPER

View Article Online
View Journal | View Issue

Cite this: *RSC Adv.*, 2014, **4**, 60640

Received 3rd September 2014
Accepted 31st October 2014

DOI: 10.1039/c4ra09729g

www.rsc.org/advances

Synthesis of symmetrical and unsymmetrical bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes†

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Some novel symmetrical bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes were synthesized *via* diheteroarylation of sp^3 CH bond of acetophenones with molecular iodine and DMSO. Further, an efficient reaction protocol was developed with which both symmetrical and some novel unsymmetrical bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes were synthesized. For this purpose, we have exploited the highly reactive and good leaving nature of 1,3-dimethylbarbituric acid.

Introduction

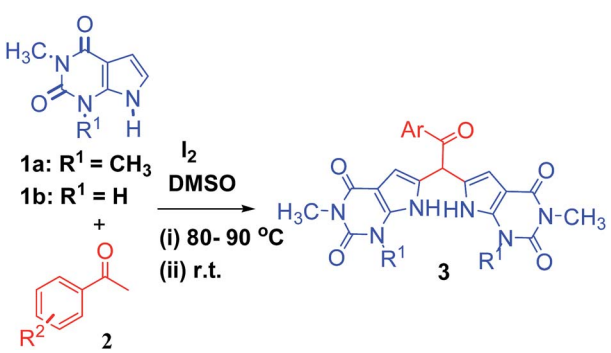
The importance of pyrrolo[2,3-*d*]pyrimidines is well recognized by biological, medicinal and synthetic organic chemists. Compounds with this molecular motif possess diverse biological activities such as anti-microbial,[1] analgesic,[2] anti-inflammatory,[3] anti-viral,[4] anti-cancer,[5] antioxidant and neuroprotective activity.[6] Some of their representatives are protein kinase inhibitors,[7] E1 enzyme inhibitors,[8] insulin-like growth factor 1 receptor inhibitors,[9] STAT6 inhibitors[10] and 2 microtubule targeting agents.[11] Pyrrolo[2,3-*d*]pyrimidine constitutes the basic molecular unit of various nucleosides[12] such as toyocamycine, tubercidin and sangivamycin which exhibit antiviral, antimicrobial, antiparasitic and antineoplastic activity. Some other compounds of this class have significant activity against a variety of RNA, DNA viruses, HSV-1, HSV-2 and HCMV.[13]

Insertion of an aryl group to a sp^3 carbon atom next to a carbonyl group, which frequently involves in the synthesis of many useful compounds including medicines, natural products of biological significance and industrial materials,[14] is a long-standing problem in synthetic organic chemistry.[15] Most common and widely used methods for α-arylation of sp^3 C–H bond of ketones include the coupling of C sp^3–H bond with aryl halide/aryl metal and cross-dehydrogenative coupling.[16] Very recently, Myrboh and his co-workers reported the sp^3 C–H bond diarylation by selenium dioxide in presence of $BF_3 \cdot Et_2O$.[17]

As a part of our continued interest in the synthesis of diverse heterocyclic compounds,[18] particularly annelated pyrimidines of biological importance,[19] in a recent communication, we reported for the first time the synthesis of bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes, a novel class of compounds, from the reaction of pyrrolo[2,3-*d*]pyrimidines and aldehydes/ketones *via* a mild process of carbon–carbon bond formation using iodine as catalyst in aqueous medium.[20] In the present paper, we report the full account of our advanced study of the reaction process and synthesis of some novel bis(pyrrolo[2,3-*d*]pyrimidinyl)methane derivatives **3** from the reaction of pyrrolo[2,3-*d*]-pyrimidine-2,4-diones **1** and acetophenones **2** *via* diheteroarylation of sp^3 CH bond in the presence of molecular iodine and DMSO (Scheme 1), and also an efficient method for the synthesis of both symmetrical and novel unsymmetrical-bis-(pyrrolo[2,3-*d*]pyrimidinyl)methanes (Scheme 3).

Results and discussion

We initiated our study with an objective to synthesize some new bis(pyrrolo[2,3-*d*]pyrimidinyl)methane derivatives *via* diheteroarylation of sp^3 CH bond of acetophenones with pyrrolo[2,3-*d*]pyrimidine-2,4-diones using SeO_2 + $BF_3 \cdot Et_2O$ system in dry toluene.[17] In the reaction strategy, we treated 1,3-dimethyl-pyrrolo[2,3-*d*]pyrimidine-2,4-dione **1a** and acetophenone **2a** in the presence of SeO_2 + $BF_3 \cdot Et_2O$ system in dry toluene, initially at room temperature and then in refluxing conditions. But no satisfactory results were obtained. It was observed that the



Scheme 1 Synthesis of bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes **3**.

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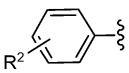
† Electronic supplementary information (ESI) available: Compound characterizations data (^{1}H NMR, 13C NMR spectra and elemental analysis). See DOI: 10.1039/c4ra09729g

solubility of 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione **1a** is very poor in toluene, and at elevated temperature some breakdown products were formed instead of the desired compound. Then, we replaced (SeO_2 + $BF_3 \cdot Et_2O$) system with (DMSO + I_2)[21] system which is considerably mild and easy to handle, and DMSO also acts as solvent. So, first we conducted the reaction using 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione **1a** and acetophenone **2a** in the presence of DMSO + I_2 at room temperature using DMSO as solvent. But the reaction did not occur. Then the reaction was studied under refluxing condition. The reaction occurred to give the desired product, but a number of breakdown products were formed. However, the formation of the desired product was improved when the reaction was carried out at 90 °C. But very interestingly, when we first carried out the reaction using acetophenone **2a** with DMSO + I_2 at 90 °C, and resulting solution was treated with 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione **1a** at room temperature under stirring condition, afforded the desired product bis-(pyrrolo[2,3-*d*]pyrimidinyl)methanes **3a** in almost pure form and in high yield. The structure of the compound was ascertained as **3a** from the spectroscopic data and elemental analysis. The ^{1}H NMR spectra (DMSO-d_6) of the compound showed the presence of an isolated proton at δ 6.36 as singlet, and two symmetric protons of the two pyrrolo[2,3-*d*]pyrimidine-2,4-dione molecular units at δ 6.03 as singlet. A clean peak of the two symmetric >NH protons were observed at δ 11.77 as a singlet. The mass spectra showed a sharp molecular ion peak at 475.6 ($[M + H]^+$). The generality of the reaction was established by synthesizing compounds **3a–p** and characterizing them (Table 1). It was observed that acetophenones **2** with both electron donating and electron withdrawing groups at the aromatic ring are equally reactive and gave good yield of the products. However, 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione **1a** was more reactive (entry 1–8, Table 1) than 3-methylpyrrolo[2,3-*d*]pyrimidine-2,4-dione **1b** (entry 9–16, Table 1) and gave better yield of the products.

The probable mechanism of the reaction is outlined in the Scheme 2. The reaction occurred *via* initial iodination of the acetophenone **2a** by iodine to give the compound [**A**] which was subsequently oxidized by DMSO to the intermediate aldehyde [**B**].[21] The rest of the reaction follow the mechanism as reported in the previous paper.[20] The aldehyde [**B**] suffered a nucleophilic attack by the pyrrolo[2,3-*d*]pyrimidines **1a** in presence of iodine to give the intermediate [**C**] by the elimination of water molecule. The intermediate [**C**] then suffered a nucleophilic attack by the second 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione **1a** molecule to give the final product **3a**. The mechanism was further established by performing the reaction of commercially available phenyl glyoxal [**B**] with 1,3-dimethylpyrrolo[2,3-*d*] pyrimidine-2,4-dione **1a** in the presence of iodine as catalyst using DMSO as solvent which afforded the expected compound **3a** in good yield.

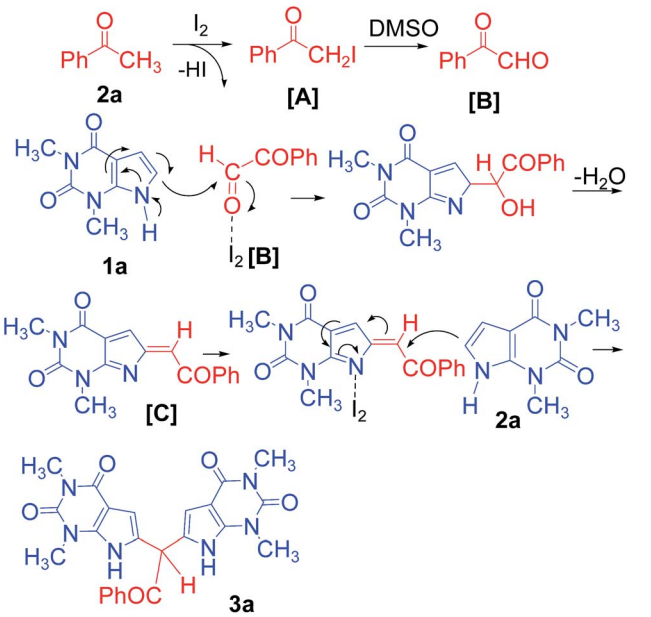
It was observed in our previous[20] and the present study that the intermediate [**C**] (in the present case) is not isolable which suffers a quick nucleophilic attack by the second molecule of pyrrolo[2,3-*d*]pyrimidine-2,4-dione giving symmetrical bis-(pyrrolo[2,3-*d*]pyrimidinyl)methanes in all the cases. Therefore, we have efficiently developed the reaction process which was applicable for the synthesis of both symmetrical and unsymmetrical bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes that contain two similar or dissimilar pyrrolo[2,3-*d*]pyrimidine-2,4-dione molecules respectively (Scheme 3). For this purpose, we have exploited the highly reactive and good leaving nature of 1,3-dimethylbarbituric acid which we demonstrated in our earlier works.[19d,22] In the reaction protocol, 1,3-dimethylbarbituric acid **4** was first reacted with aldehydes **5** following our reported method[23] to afford the Knoevenagel condensed products **6**

Table 1 Synthesis of bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes **3**[a]

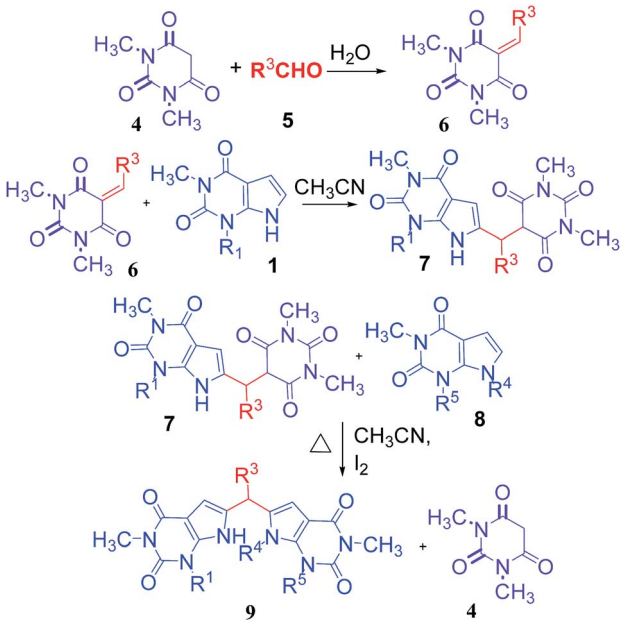


En.	R^1	R^2	Pd.	R.T. (h)	Yield (%)
1	CH_3	C_6H_5	**3a**	3	82
2	CH_3	4-$CH_3C_6H_4$	**3b**	3	80
3	CH_3	4-$CH_3OC_6H_4$	**3c**	3	80
4	CH_3	4-ClC_6H_4	**3d**	3	82
5	CH_3	4-BrC_6H_4	**3e**	3	81
6	CH_3	4-$NO_2C_6H_4$	**3f**	3	81
7	CH_3	2-Thiophenyl	**3g**	3	79
8	CH_3	2-Naphthyl	**3h**	3	82
9	H	C_6H_5	**3i**	4	78
10	H	4-$CH_3C_6H_4$	**3j**	4	77
11	H	4-$CH_3OC_6H_4$	**3k**	4	77
12	H	4-ClC_6H_4	**3l**	4	78
13	H	4-BrC_6H_4	**3m**	4	78
14	H	4-$NO_2C_6H_4$	**3n**	4	78
15	H	2-Thiophenyl	**3o**	4	75
16	H	2-Naphthyl	**3p**	4	78

[a] En. = entry; Pd. = product; R.T. = reaction time.



Scheme 2 Plausible mechanism for the formation of **3a**.



Scheme 3 Synthesis of bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes **9**.

which on stirring with pyrrolo[2,3-*d*]pyrimidine derivatives **1** at room temperature afforded the compounds **7** (Scheme 3). The compound **7**, on treatment with various pyrrolo[2,3-*d*] pyrimidine-2,4-diones **8** in presence of iodine as catalyst under refluxing conditions in acetonitrile afforded bis(pyrrolo [2,3-*d*]pyrimidinyl)methanes **9** in very high yields (Table 2). 1,3-Dimethylbarbituric acid **4** was eliminated in the reaction process which was isolated and recycled in the reaction process. The use of compounds **8**, identical with compounds **1** (Scheme 1) produced symmetrical bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes (entry 1 and 2, Table 2). The structure of the compounds were ascertained from the spectroscopic data, elemental analysis and by comparing with the authentic samples we prepared earlier.[20] On the other hand, utilization of compounds **8**, dissimilar from compounds **1** produced unsymmetrical bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes (entry 3–17). The structure of the novel unsymmetrical bis(pyrrolo[2,3-*d*]pyrimidinyl) methanes (entry 3–17, Table 2) were confirmed from their spectroscopic data and elemental analysis.

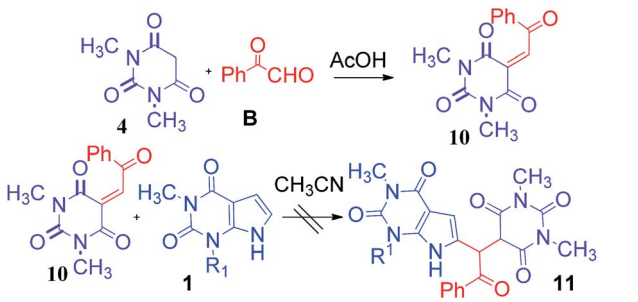
Table 2 Synthesis of bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes **9**[a]

En.	R^1	R^3	R^4	R^5	Pd.	R.T. (h)	Yd. (%)
1	CH_3	Ph	H	CH_3	**9a**	2	95
2	H	Ph	H	H	**9b**	2	92
3	CH_3	Ph	H	H	**9c**	2	84
4	CH_3	4-$OCH_3C_6H_4$	H	H	**9d**	2	82
5	CH_3	4-$NO_2C_6H_4$	H	H	**9e**	2	80
6	CH_3	Ph	CH_3	CH_3	**9f**	2	90
7	CH_3	4-$OCH_3C_6H_4$	CH_3	CH_3	**9g**	2	89
8	CH_3	4-$NO_2C_6H_4$	CH_3	CH_3	**9h**	2	87
9	H	Ph	CH_3	CH_3	**9i**	2	70
10	H	4-$OCH_3C_6H_4$	CH_3	CH_3	**9j**	2	69
11	H	4-$NO_2C_6H_4$	CH_3	CH_3	**9k**	2	68
12	CH_3	Thiophenyl	H	H	**9l**	2	83
13	CH_3	$(CH_3)_2CH$	H	H	**9m**	2	82
14	CH_3	Thiophenyl	CH_3	CH_3	**9n**	2	85
15	CH_3	$(CH_3)_2CH$	CH_3	CH_3	**9o**	2	84
16	H	Thiophenyl	CH_3	CH_3	**9p**	2	70
17	H	$(CH_3)_2CH$	CH_3	CH_3	**9q**	2	68

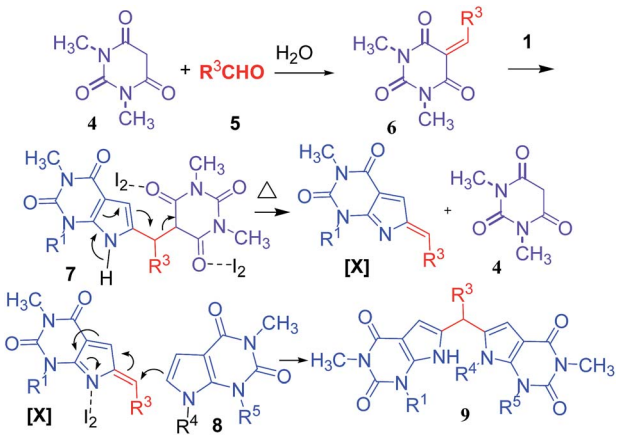
[a] En = entry; Pd. = product; R.T. = reaction time; Yd = yield.

As in the earlier case, both electron donating and electron withdrawing groups at the aromatic ring of aldehydes **5** are equally reactive and gave good yield of the products. Again, *N*-methylated pyrrolo[2,3-*d*]pyrimidine-2,4-diones were more reactive than the partially unsubstituted pyrrolo[2,3-*d*] pyrimidine-2,4-diones. However, although the condensation of glyoxal [**B**] and 1,3-dimethylbarbituric acid **4** took place very easily,[24] the Michael addition of pyrrolo[2,3-*d*]pyrimidine-2,4-diones **1** to the condensed product did not occur under our reaction conditions (Scheme 4). It might be because of the keto group which deactivates the nucleophilic addition.

The mechanism for the formation of the **9** is outlined in the Scheme 5. Michael addition of compound **1** to the Knoevenagel condensed product **6** produced the compound **7**. Then, the intermediate [**X**], formed *in situ* from compound **7** under thermal condition *via* elimination of compound **4**, suffered nucleophilic attack by the compound **8** in presence of iodine to give the product **9**. The mechanism was supported by the



Scheme 4



Scheme 5 Mechanism for the formation of bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes **9**.

isolation and characterization of the eliminated 1,3-dimethylbarbituric acid **4** from the reaction mixture. Notably, such good leaving nature of the compound **4** is well documented.[19d,22]

Conclusions

In conclusion, we have reported the synthesis of some novel bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes **3**, *via* diheteroarylation of sp^3 CH bond of acetophenones in the presence of molecular iodine and DMSO. The reactants were consumed completely in the reaction process and single product was isolated in each case. The very small amount of impurity observed in the TLC study, was removed by column chromatography. Thus, products were obtained in very high yield. Furthermore, we have developed the reaction protocol in an efficient way which produced both symmetrical and unsymmetrical bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes as per requirements. The products were obtained in solid form after simple work up procedure and were purified by crystallization.

Experimental

General considerations

Melting points were measured with a Buchi-540 melting point apparatus. IR spectra were recorded on a SHIMADZU FTIR-8400. ^{1}H NMR and ^{13}C NMR Spectra were recorded on Bruker Avance-DPX 300 MHz and 75 MHz FT NMR in DMSO-d_6 using TMS as an internal standard. Chemical shifts (δ units) are given from TMS (0 ppm) and coupling constants are expressed in Hertz (Hz). Chemical shifts for DMSO-d_6 were reported at around 3.36 and 2.50 ppm respectively (δ units). Mass spectra were recorded on ESQUIRE 3000 Mass spectrometer. All experiments were monitored by Thin Layer Chromatography (TLC). TLC was performed on pre-coated silica gel plates (Merck).

General procedure for the synthesis of bis(pyrrolo[2,3-*d*] pyrimidinyl)methanes 3

In a typical experimental procedure, acetophenone **2a** (0.120 g, 1 mmol), I_2 (0.3795 g, 1.5 mmol) and DMSO (5 mL) were first treated at 90 °C for 2 h. The resulting mixture was then cooled to room temperature and reacted with 1,3-dimethylpyrrolo[2,3-*d*] pyrimidine-2,4-dione **1a** (0.362 g, 2 mmol) at room temperature for 1 h. After completion (monitored by TLC) of the reaction, 5% aqueous sodium thiosulphate solution (5 mL) was added to the reaction mixture and extracted with ethyl acetate (5 mL × 3 mL). The combined solvent was evaporated under reduced pressure and the product was purified by column chromatography on silica gel using 2 : 8 ratio of hexane : ethylacetate as eluent. The structure of the compound was ascertained as bis(pyrrolo[2,3-*d*]pyrimidinyl)methane derivative **3a** from the spectroscopic data and elemental analysis. Similarly compounds **3b–p** were synthesized and characterized.

3a. Purple solid. Yield: 388 mg (82%); mp. 279–280 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.18 (s, 6H), 3.42 (s, 6H), 6.03 (s, 2H), 6.14 (s, 1H), 7.26–8.04 (m, 5H), 11.77 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 31.0 (2C), 45.8, 98.7 (2C), 104.1 (2C), 126.9 (2C), 129.0 (2C), 129.3 (2C), 133.9, 135.9, 139.7 (2C), 151.1 (2C), 158.6 (2C), 194.4; IR (KBr) ν_{max} 3570.2, 3204.8, 1694.9, 1558.9 cm$^{-1;}$ MS (ESI) 475.6 ([M + H]$^+$); anal. cald for $C_{24}H_{22}N_6O_5$ C, 60.75; H, 4.67; N, 17.71% found: C, 60.80; H, 4.71; N, 17.75%.

3b. Purple solid. Yield: 394 mg (80%); mp. 276–280 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 2.35 (s, 3H), 3.18 (s, 6H), 3.42 (s, 6H), 6.03 (s, 2H), 6.13 (s, 1H), 7.32 (d, J = 7.92 Hz, 2H), 7.91 (d, J = 7.98 Hz, 2H), 11.75 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 21.5, 28.0 (2C), 31.0 (2C), 45.7, 98.7 (2C), 104.1 (2C), 127.0 (2C), 129.1 (2C), 129.8 (2C), 133.4, 139.7 (2C), 144.4, 151.1 (2C), 158.6 (2C), 194.0; IR (KBr) ν_{max} 3374.5, 3277.5, 1686.2, 1555.6 cm^{-1}; MS (ESI) 489.3 ([M + H]$^+$); anal. cald for $C_{25}H_{24}N_6O_5$ C, 61.47; H, 4.95; N, 17.20% found: C, 61.49; H, 4.97; N, 17.26%.

3c. Pink solid. Yield: 403 mg (80%); mp. 275–277 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.18 (s, 6H), 3.42 (s, 6H), 3.66 (s, 3H), 6.02 (s, 2H), 6.15 (s, 1H), 7.31 (d, J = 10.38 Hz, 2H), 7.90 (d, J = 10.95 Hz, 2H), 11.76 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 31.0 (2C), 42.3, 56.0, 98.4 (2C), 102.9 (2C), 114.2 (2C), 128.5, 129.7 (2C), 132.5 (2C), 132.9, 139.6 (2C), 151.1 (2C), 158.7 (2C), 194.0; IR (KBr) ν_{max} 3375.5, 3278.5, 1687.2, 1554.6 cm^{-1}; MS (ESI) 505.3 ([M + H]$^+$); anal. cald for $C_{25}H_{24}N_6O_6$ C, 59.52; H, 4.80; N, 16.66% found: C, 59.57; H, 4.87; N, 16.69%.

3d. Pink solid. Yield: 416 mg (82%); mp. 274–279 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.18 (s, 6H), 3.42 (s, 6H), 6.04 (s, 2H), 6.14 (s, 1H), 7.61 (d, J = 8.46 Hz, 2H), 8.01 (d, J = 8.49 Hz, 2H), 11.74 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 31.0 (2C), 45.7, 98.7 (2C), 104.3 (2C), 126.5 (2C), 129.5, 130.8 (2C), 134.6, 138.8 (2C), 139.8 (2C), 151.1 (2C), 158.6 (2C), 194.0; IR (KBr) ν_{max} 3378.9, 3275.2, 1687.2, 1558.2 cm^{-1}; MS (ESI) 509.1 ([M + H]$^+$); anal. cald for $C_{24}H_{21}ClN_6O_5$ C, 56.64; H, 4.16; N, 16.51% found: C, 56.70; H, 4.19; N, 16.55%.

3e. Pink solid. Yield: 447 mg (81%); mp. 275–279 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.18 (s, 6H), 3.43 (s, 6H), 6.02 (s, 2H), 6.22 (s, 1H), 7.73 (d, J = 8.49 Hz, 2H), 7.96 (d, J = 8.43 Hz, 2H), 11.97 (s, 2H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 31.1 (2C), 46.7, 98.7 (2C), 104.3 (2C), 126.5 (2C), 129.5, 130.8 (2C), 134.6, 138.8 (2C), 139.8 (2C), 151.1 (2C), 158.6 (2C), 194.0; IR (KBr) ν_{max} 3388.7, 3279.2, 1689.1, 1555.4 cm^{-1}; MS (ESI) 554.3 ([M + H]$^+$); anal. cald for $C_{24}H_{21}BrN_6O_5$ C, 52.09; H, 3.83; N, 15.19% found: C, 52.16; H, 3.89; N, 15.25%.

3f. Pinkish orange solid. Yield: 420 mg (81%); mp. 273–277 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.18 (s, 6H), 3.43 (s, 6H), 6.07 (s, 2H), 6.22 (s, 1H), 8.09–8.37 (m, 4H), 11.77 (s, 2H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 31.0 (2C), 46.5, 98.8 (2C), 104.5 (2C), 124.5 (2C), 126.0 (2C), 129.0 (2C), 130.3, 133.3, 139.9 (2C), 151.1 (2C), 158.6 (2C), 194.1; IR (KBr) ν_{max} 3387.2, 3281.2, 1679.1, 1565.4 cm^{-1}; MS (ESI) 520.2 ([M + H]$^+$); anal. cald for $C_{24}H_{21}N_7O_7$ C, 55.49; H, 4.07; N, 18.87% found: C, 55.56; H, 4.19; N, 18.95%.

3g. Pink solid. Yield: 379 mg (79%); mp. 275–279 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.19 (s, 6H), 3.41 (s, 6H), 6.08 (s, 2H), 6.20 (s, 1H), 6.90–7.48 (m, 3H), 11.80 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 31.0 (2C), 38.3, 98.3 (2C), 102.6 (2C), 125.6, 126.2, 127.2, 131.7 (2C), 139.4 (2C), 144.7,

151.0 (2C), 158.6 (2C), 194.0; IR (KBr) ν_{max} 3378.9, 3277.1, 1677.5, 1556.2 cm^{-1}; MS (ESI) 481.6 ($[M + H]^+$); anal. cald for $C_{22}H_{20}N_6O_5S$ C, 54.99; H, 4.20; N, 17.49% found: C, 55.06; H, 4.25; N, 17.58%.

3h. Pink solid. Yield: 430 mg (82%); mp. 277–280 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.18 (s, 6H), 3.44 (s, 6H), 6.10 (s, 2H), 6.35 (s, 1H), 7.61–8.74 (m, 7H), 11.80 (s, 2H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 31.0 (2C), 45.9, 98.8 (2C), 104.2 (2C), 124.6, 126.9 (2C), 127.6, 128.1, 128.9, 129.3, 130.0, 130.6, 132.5, 133.2, 135.4, 139.8 (2C), 151.1 (2C), 158.6 (2C), 194.5; IR (KBr) ν_{max} 3386.4, 3284.9, 1669.5, 1562.1 cm^{-1}; MS (ESI) 525.3 ($[M + H]^+$); anal. cald for $C_{28}H_{24}N_6O_5$ C, 64.11; H, 4.61; N, 16.02% found: C, 64.21; H, 4.69; N, 16.15%.

3i. Brown solid. Yield: 348 mg (78%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.18 (s, 6H), 6.03 (s, 2H), 6.17 (s, 1H), 7.40–7.68 (m, 5H), 10.73 (s, 2H, NH), 11.58 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 45.8, 98.7 (2C), 104.1 (2C), 126.9 (2C), 129.0 (2C), 129.3 (2C), 133.9, 135.93, 139.7 (2C), 151.1 (2C), 158.6 (2C), 194.4; IR (KBr) ν_{max}; 3370.1, 3278.5, 1656.3, 1617.1 cm^{-1}; MS (ESI) 447.4 ($[M + H]^+$); anal. cald for $C_{22}H_{18}N_6O_5$ C, 59.19; H, 4.06; N, 18.83% found: C, 59.26; H, 4.14; N, 18.89%.

3j. Brown solid. Yield: 354 mg (77%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 2.31 (s, 3H), 3.19 (s, 6H), 6.04 (s, 2H), 6.22 (s, 1H), 7.10–7.21 (m, 4H), 10.75 (s, 2H, NH), 11.71 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 21.5, 28.0 (2C), 45.7, 98.7 (2C), 104.1 (2C), 127.0 (2C), 129.1 (2C), 129.8 (2C), 133.4, 139.7 (2C), 144.4, 151.1 (2C), 158.6 (2C), 194.0 IR (KBr) ν_{max} 3372.1, 3267.9, 1680.2, 1557.6 cm^{-1}; MS (ESI) 461.4 ($[M + H]^+$); anal. cald for $C_{23}H_{20}N_6O_5$ C, 60.02; H, 4.38; N, 18.25% found: C, 60.09; H, 4.47; N, 18.34%.

3k. Brown solid. Yield: 366 (77%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.17 (s, 6H), 3.67 (s, 3H), 6.01 (s, 2H), 6.12 (s, 1H), 6.71–7.26 (m, 4H), 10.71 (s, 2H, NH), 11.55 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 42.4, 55.5, 98.4 (2C), 102.9 (2C), 114.2 (2C), 128.5, 129.7 (2C), 132.5 (2C), 132.9, 139.6 (2C), 151.1 (2C), 158.7 (2C), 194.0; IR (KBr) ν_{max} 3386.2, 3275.4, 1665.5, 1626.6 cm^{-1}; MS (ESI) 477.5 ($[M + H]^+$); anal. cald for $C_{23}H_{20}N_6O_6$ C, 57.98; H, 4.23; N, 17.64% found: C, 58.02; H, 4.31; N, 17.70%.

3l. Brown solid. Yield: 374 mg (78%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.25 (s, 6H), 6.06 (s, 2H), 6.19 (s, 1H), 7.10–7.70 (m, 4H), 10.77 (s, 2H, NH), 11.58 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 45.7, 98.7 (2C), 104.3 (2C), 126.5 (2C), 129.5, 130.8 (2C), 134.6, 138.8 (2C), 139.8 (2C), 151.1 (2C), 158.6 (2C), 194.0; IR (KBr) ν_{max} 3383.5, 3275.4, 1658.1, 1615.5 cm^{-1}; MS (ESI) 481.3 ($[M + H]^+$); anal. cald for $C_{22}H_{17}ClN_6O_5$ C, 54.95; H, 3.56; N, 17.48% found: C, 55.15; H, 3.61; N, 17.51%.

3m. Brown solid. Yield: 408 (78%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.32 (s, 6H), 6.07 (s, 2H), 6.25 (s, 1H), 7.21–7.43 (m, 4H), 10.75 (s, 2H, NH), 11.58 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 46.7, 98.7 (2C), 104.3 (2C), 126.5 (2C), 129.5, 130.8 (2C), 134.6, 138.8 (2C), 139.8 (2C), 151.1 (2C), 158.6 (2C), 194.0; IR (KBr) ν_{max} 3398.2, 3271.2, 1657.2, 1613.5 cm^{-1}; MS (ESI) 525.4 ($[M + H]^+$); anal. cald for $C_{22}H_{17}BrN_6O_5$ C, 50.30; H, 3.26; N, 15.21% found: C, 50.42; H, 3.32; N, 15.29%.

3n. Brown solid. Yield: 382 mg (78%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.32 (s, 6H), 6.08 (s, 2H), 6.22 (s, 1H), 7.18–7.35 (m, 4H), 10.75 (s, 2H, NH), 11.59 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 46.5, 98.8 (2C), 104.5 (2C), 124.5 (2C), 126.0 (2C), 129.0 (2C), 130.3, 133.3, 139.9 (2C), 151.1 (2C), 158.6 (2C), 194.1; IR (KBr) ν_{max} 3387.5, 3272.6, 1657.8, 1610.5 cm^{-1}; MS (ESI) 492.5 ($[M + H]^+$); anal. cald for $C_{22}H_{17}N_7O_7$ C, 53.77; H, 3.49; N, 19.95% found: C, 53.82; H, 3.57; N, 20.06%.

3o. Brown solid. Yield: 339 mg (75%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.19 (s, 6H), 6.07 (s, 2H), 6.15 (s, 1H), 6.92–7.47 (m, 3H), 10.42 (s, 2H, NH), 11.80 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.1 (2C), 38.3, 98.3 (2C), 102.6 (2C), 125.6, 126.2, 127.2, 131.7 (2C), 139.4 (2C), 144.7, 151.0 (2C), 158.6 (2C), 194.0; IR (KBr) ν_{max} 3369.5, 3270.2, 1688.5, 1553.2 cm^{-1}; MS (ESI) 453.5 ($[M + H]^+$); anal. cald for $C_{20}H_{16}N_6O_5S$ C, 53.09; H, 3.56; N, 18.57% found: C, 53.15; H, 3.61; N, 18.64%.

3p. Brown solid. Yield: 386 mg (78%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 3.18 (s, 6H), 6.11 (s, 2H), 6.37 (s, 1H), 7.60–8.75 (m, 7H), 10.76 (s, 2H), 11.58 (s, 2H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0 (2C), 45.9, 98.8 (2C), 104.2 (2C), 124.6, 126.9 (2C), 127.6, 128.1, 128.9, 129.3, 130.0, 130.6, 132.5, 133.2, 135.4, 139.8 (2C), 151.1 (2C), 158.6 (2C), 194.5; IR (KBr) ν_{max} 3387.2, 3274.8, 1679.2, 1560.1 cm^{-1}; MS (ESI) 497.5 ($[M + H]^+$); anal. cald for $C_{26}H_{20}N_6O_5$ C, 62.90; H, 4.06; N, 16.93% found: C, 63.11; H, 4.09; N, 17.15%.

General procedure for the synthesis of compound 7

In a typical experimental procedure, 1,3-dimethylpyrrolo[2,3-*d*] pyrimidine-2,4-dione **1a** (0.181 g, 1 mmol), 5-benzylidene-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione **6** (0.244 g, 1 mmol), I_2 (0.006 g, 5 mol%) and acetonitrile (5 mL) were stirred at room temperature for 2 h. After completion (monitored by TLC) of the reaction, the solid product obtained was filtered and recrystallized from ethanol. The structure of the compound was ascertained as **7a** from the spectroscopic data and elemental analysis. Similarly compounds **7b–e** were synthesized and characterized.

7a. White solid. Yield: 372 mg (88%); mp. 186.5–187.1 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 2.90 (s, 3H), 3.07 (s, 3H), 3.20 (s, 3H), 3.37 (s, 3H), 4.37 (d, $J = 4.17$ Hz, 1H), 5.20 (d, $J = 3.9$ Hz, 1H), 6.26 (s, 1H), 6.73–7.05 (m, 5H), 11.65 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0, 28.2, 28.5, 31.0, 40.9, 52.7, 98.6, 103.4, 115.0, 119.0, 124.9, 128.6, 130.0, 130.4, 139.2, 151.1, 151.8, 154.8, 158.6, 167.8, 168.4; IR (KBr) ν_{max} 3555.7, 3471.2, 1741.2, 1665.1 cm^{-1}; MS (ESI) 424.5 ($[M + H]^+$); anal. cald for $C_{21}H_{21}N_5O_5$ C, 59.57; H, 5.00; N, 16.54% found: C, 59.71; H, 5.19; N, 16.65%.

7b. White solid. Yield: 398 mg (88%); mp. 185.4–186.5 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 2.90 (s, 3H), 3.07 (s, 3H), 3.20 (s, 3H), 3.37 (s, 3H), 3.68 (s, 3H), 4.38 (d, $J = 3.18$ Hz, 1H), 5.21 (d, $J = 0.60$ Hz, 1H), 6.26 (s, 1H), 6.64–6.82 (m, 5H), 11.66 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.1, 28.2, 28.5, 31.0, 50.7, 58.8, 98.6, 103.4, 115.1, 119.0, 124.9, 128.6, 130.0, 130.3, 139.3, 151.1, 151.8, 154.8, 158.6, 167.8, 168.4; IR (KBr) ν_{max} 3547.3,

3470.9, 1745.3, 1662 cm^{-1}; MS (ESI) 454.6 ($[M + H]^+$); anal. cald for $C_{22}H_{23}N_5O_6$ C, 58.27; H, 5.11; N, 15.44% found: C, 58.39; H, 5.29; N, 15.55%.

7c. White solid. Yield: 406 mg (87%); mp. 187.3–188.2 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 2.90 (s, 3H), 3.07 (s, 3H), 3.20 (s, 3H), 3.37 (s, 3H), 4.38 (d, $J = 3.24$ Hz, 1H), 5.20 (d, $J = 3.00$ Hz, 1H), 6.27 (s, 1H), 6.64–7.06 (m, 4H), 11.65 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0, 28.2, 28.5, 31.0, 40.9, 52.7, 98.6, 103.4, 115.0, 119.0, 124.9, 128.6, 130.0, 130.4, 139.2, 151.1, 151.8, 154.8, 158.6, 167.8, 168.3; IR (KBr) ν_{max} 3545.3, 3470.1, 1740.1, 1669.4 cm^{-1}; MS (ESI) 469.1 ($[M + H]^+$); anal. cald for $C_{21}H_{20}N_6O_7$ C, 53.85; H, 4.30; N, 17.94% found: C, 53.99; H, 4.49; N, 18.15%.

7d. White solid. Yield: 377 mg (88%); mp. 185.4–187.3 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 2.90 (s, 3H), 3.06 (s, 3H), 3.20 (s, 3H), 3.37 (s, 3H), 4.37 (d, $J = 4.14$ Hz, 1H), 5.21 (d, $J = 2.94$ Hz, 1H), 6.25 (s, 1H), 6.62–7.03 (m, 3H), 11.64 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 28.0, 28.1, 28.5, 31.0, 40.8, 52.5, 98.5, 103.6, 125.1, 126.2, 127.2, 130.4, 140.1, 145.3, 151.7, 154.5, 158.3, 167.7, 168.2; IR (KBr) ν_{max} 3543.2, 3475.4, 1745.2, 1665.3 cm^{-1}; MS (ESI) 430.5 ($[M + H]^+$); anal. cald for $C_{19}H_{19}N_5O_5S$ C, 53.14; H, 4.46; N, 16.31% found: C, 53.17; H, 4.49; N, 16.35%.

7e. White solid. Yield: 338 mg (87%); mp. 183.2–185.1 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ (ppm) 0.87 (m, 6H), 2.33 (m, 1H), 2.90 (s, 3H), 3.05 (s, 3H), 3.20 (s, 3H), 3.37 (s, 3H), 4.37 (d, $J =$ 3.51 Hz, 1H), 5.20 (d, $J = 2.94$ Hz, 1H), 6.23 (s, 1H), 11.66 (s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ (ppm) 21.4 (2C), 28.0, 28.2, 28.5 (2C), 31.2, 33.0, 40.7, 98.5, 103.5, 135.2, 139.3, 151.7, 154.5, 158.8, 166.2, 168.7; IR (KBr) ν_{max} 3532.1, 3473.6, 1730.5, 1665.2 cm^{-1}; MS (ESI) 390.3 ($[M + H]^+$); anal. cald for $C_{18}H_{23}N_5O_5$ C, 55.52; H, 5.95; N, 17.98% found: C, 55.53; H, 5.96; N, 17.99%.

General procedure for the synthesis of bis(pyrrolo[2,3-*d*]pyrimidinyl)methanes 9

In a typical experimental procedure, 5-((1,3-dimethyl-2,4-dioxo-2,3,4,7-tetrahydro-1*H*-pyrrolo[2,3-*d*]pyrimidin-6-yl)(phenyl)-methyl)-1,3-dimethylpyrimidine-2,4,6-(1*H*,3*H*,5*H*)-trione **7a** (0.423 g, 1 mmol), 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione **1a** (0.181 g, 1 mmol), I_2 (0.006 g, 5 mol%) and acetonitrile (5 mL) were mixed and allowed to run under reflux condition for 3 h. After completion (monitored by TLC) of the reaction, the solid product obtained was filtered and recrystallized from ethanol. The structure of the compound was ascertained as bis(pyrrolo[2,3-*d*]pyrimidinyl)methane derivative **9a** from the spectroscopic data and elemental analysis.

9a. Pink solid; yield: 423 mg (95%); mp. 288–290 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.19 (s, 6H), 3.39 (s, 6H), 5.40 (s, 1H), 5.76 (s, 2H), 7.22–7.39 (m, 5H), 11.74 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0 (2C), 31.1 (2C), 43.2, 98.4 (2C), 103.1 (2C), 127.5, 128.7 (2C), 128.8 (2C), 132.1 (2C), 139.6 (2C), 141.0, 151.1 (2C), 158.7 (2C); IR (KBr) ν_{max} 3373.5, 3278.5, 1687.2, 1557.6 cm^{-1}; MS (ESI) 447.5 ($[M + H]^+$); anal. cald for $C_{23}H_{22}N_6O_4$ C, 61.87; H, 4.92; N, 18.82% found: C, 61.88; H, 4.93; N, 18.83%.

9b. Pinkish violet solid; Yield: 384 mg (92%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.17 (s, 3H), 3.26 (s, 3H), 5.38 (s, 1H), 5.45 (s, 1H), 5.72 (s, 1H), 7.09–7.59 (m, 5H), 10.32 (s, 2H, NH), 11.68 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.6 (2C), 42.2, 99.1 (2C), 103.0 (2C), 125.2, 127.0 (2C), 128.8 (2C), 132.1 (2C), 140.1, 141.1 (2C), 151.0 (2C), 159.2 (2C); IR (KBr) ν_{max} 3372.5, 3279.4, 1658.7, 1615.7 cm^{-1}; MS (ESI) 419.4 ($[M + H]^+$); anal. cald for $C_{21}H_{18}N_6O_4$ C, 60.27; H, 4.30; N, 20.08% found: C, 60.28; H, 4.34; N, 20.09%.

9c. Brown solid; yield: 360 mg (84%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.32 (s, 6H), 3.40 (s, 3H), 5.59 (s, 1H), 5.63 (s, 1H), 5.67 (s, 1H), 6.74–7.14 (m, 5H), 10.71 (br, 1H, NH), 11.68 (br, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0, 28.6, 29.8, 36.3, 98.3, 99.0, 102.9, 104.2, 117.2, 119.3, 127.3, 128.8, 132.3, 139.5, 140.8, 140.9, 151.0, 151.2, 154.9, 158.6, 159.2, 159.5; IR (KBr) ν_{max} 3375.4, 3278.2, 1657.3, 1613.2 cm^{-1}; MS (ESI) 433.4 ($[M + H]^+$); anal. cald for $C_{22}H_{20}N_6O_4$ C, 61.10; H, 4.66; N, 19.43% found: C, 61.22; H, 4.67; N, 19.56%.

9d. Brown solid; yield: 377 mg (82%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.32 (s, 6H), 3.40 (s, 3H), 3.70 (s, 3H), 5.59 (s, 1H), 5.63 (s, 1H), 5.67 (s, 1H), 6.74–6.88 (m, 4H), 10.70 (br, 1H, NH), 11.69 (br, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0, 28.6, 29.8, 36.4, 58.5, 98.3, 99.0, 102.9, 104.2, 117.2, 119.3, 127.3, 128.8, 132.3, 139.5, 140.8, 140.97, 151.0, 151.2, 154.9, 158.6, 159.2, 159.5; IR (KBr) ν_{max} 3369.4, 3272.5, 1656.7, 1619.2 cm^{-1}; MS (ESI) 463.2 ($[M + H]^+$); anal. cald for $C_{23}H_{22}N_6O_5$ C, 59.73; H, 4.79; N, 18.17% found: C, 59.82; H, 4.87; N, 18.26%.

9e. Brown solid; yield: 380 mg (80%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.32 (s, 6H), 3.38 (s, 3H), 5.52 (s, 1H), 5.61 (s, 1H), 5.69 (s, 1H), 6.31–7.14 (m, 4H), 10.71 (br, 1H, NH), 11.68 (br, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0, 28.6, 29.8, 36.4, 98.3, 99.0, 102.9, 104.2, 117.2, 119.3, 127.3, 128.8, 132.3, 139.5, 140.8, 140.9, 151.0, 151.2, 154.9, 158.6, 159.2, 159.5; IR (KBr) ν_{max} 3360.5, 3273.2, 1659.1, 1629.3 cm^{-1}; MS (ESI) 478.5 ($[M + H]^+$); anal. cald for $C_{22}H_{19}N_7O_6$ C, 55.35; H, 4.01; N, 20.54% found: C, 55.42; H, 4.17; N, 20.62%.

9f. Brown solid; yield: 414 mg (90%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.32 (s, 6H), 3.38 (s, 6H), 3.60 (s, 3H), 5.53 (s, 1H), 5.64 (s, 1H), 5.71 (s, 1H), 6.69–7.19 (m, 5H), 11.68 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0, 28.6, 29.8, 30.0, 31.0, 36.4, 98.3, 99.0, 102.9, 104.2, 117.2, 119.3, 127.3, 128.8, 132.3, 139.5, 140.8, 140.9, 151.0, 151.2, 154.9, 158.6, 159.2, 159.5; IR (KBr) ν_{max} 3362.4, 3276.4, 1657.5, 1622.4 cm^{-1}; MS (ESI) 461.6 ($[M + H]^+$); anal. cald for $C_{24}H_{24}N_6O_4$ C, 62.60; H, 5.25; N, 18.25% found: C, 62.72; H, 5.27; N, 18.32%.

9g. Brown solid; yield: 436 mg (89%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.32 (s, 6H), 3.38 (s, 6H), 3.60 (s, 3H), 3.70 (s, 3H), 5.50 (s, 1H), 5.61 (s, 1H), 5.72 (s, 1H), 6.49–7.09 (m, 4H), 11.68 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0, 28.6, 29.8, 30.0, 31.0, 36.4, 58.5, 98.3, 99.1, 102.8, 104.2, 117.2, 119.3, 127.3, 128.8, 132.4, 139.5, 140.8, 140.9, 151.0, 151.2, 154.9, 158.6, 159.2, 159.5; IR (KBr) ν_{max} 3361.5, 3174.4, 1667.5, 1620.4 cm^{-1}; MS (ESI) 491.4 ($[M + H]^+$); anal. cald for $C_{25}H_{26}N_6O_5$ C, 61.22; H, 5.34; N, 17.13% found: C, 61.32; H, 5.37; N, 17.22%.

9h. Brown solid; yield: 439 mg (87%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.32 (s, 6H), 3.39 (s, 6H), 3.59 (s, 3H), 5.54 (s, 1H), 5.63 (s, 1H), 5.75 (s, 1H), 6.35–7.14 (m, 4H), 11.65 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0, 28.6, 29.8, 30.0, 31.0, 36.4, 98.3, 99.1, 102.8, 104.2, 117.2, 119.3, 127.3, 128.8, 132.4, 139.5, 140.8, 140.9, 151.0, 151.2, 154.9, 158.6, 159.2, 159.5; IR

(KBr) ν_{max} 3365.6, 3170.5, 1669.4, 1625.3 cm^{-1}; MS (ESI): 506.5 ($[M + H]^+$); anal. cald for $C_{24}H_{23}N_7O_6$ C, 57.04; H, 4.59; N, 19.40% found: C, 57.12; H, 4.67; N, 19.50%.

9i. Brown solid; yield: 310 mg (70%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.32 (s, 6H), 3.39 (s, 3H), 3.59 (s, 3H), 5.53 (s, 1H), 5.65 (s, 1H), 5.77 (s, 1H), 6.73–7.14 (m, 5H), 10.70 (s, 1H, NH), 11.70 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0, 28.5, 29.7, 31.0, 36.4, 98.3, 99.2, 102.8, 104.2, 117.2, 119.3, 127.3, 128.8, 132.4, 139.5, 140.8, 140.9, 151.1, 151.2, 154.9, 158.6, 159.3, 159.5; IR (KBr) ν_{max}: 3362.4, 3179.3, 1675.4, 1631.4 cm^{-1}; MS (ESI): 447.8 ($[M + H]^+$). Anal. Cald for $C_{23}H_{22}N_6O_4$: C, 61.87; H, 4.97; N, 18.82%; found: C, 61.92; H, 5.07; N, 18.94%.

9j. Brown solid; yield: 327 mg (69%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.32 (s, 6H), 3.39 (s, 3H), 3.58 (s, 3H), 3.70 (s, 3H), 5.50 (s, 1H), 5.63 (s, 1H), 5.74 (s, 1H), 6.71–7.12 (m, 4H), 10.71 (s, 1H, NH), 11.64 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0, 28.5, 29.7, 31.0, 36.4, 58.6, 98.3, 99.2, 102.8, 104.2, 117.2, 119.3, 127.3, 128.8, 132.4, 139.5, 140.8, 140.9, 151.1, 151.2, 154.9, 158.6, 159.3, 159.5; IR (KBr) ν_{max} 3362.4, 3179.3, 1675.4, 1631.4 cm^{-1}; MS (ESI) 477.1 ($[M + H]^+$); anal. cald for $C_{24}H_{24}N_6O_5$ C, 60.50; H, 5.08; N, 17.64% found: C, 60.62; H, 5.17; N, 17.74%.

9k. Brown solid; yield: 333 mg (68%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.33 (s, 6H), 3.38 (s, 3H), 3.56 (s, 3H), 5.54 (s, 1H), 5.67 (s, 1H), 5.76 (s, 1H), 6.72–7.15 (m, 4H), 10.73 (s, 1H, NH), 11.67 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 28.0, 28.5, 29.7, 31.0, 36.4, 98.3, 99.2, 102.8, 104.2, 117.2, 119.3, 127.3, 128.8, 132.4, 139.5, 140.8, 140.9, 151.1, 151.2, 154.9, 158.6, 159.3, 159.5; IR (KBr) ν_{max} 3364.7, 3175.2, 1676.3, 1635.6 cm^{-1}; MS (ESI) 492.4 ($[M + H]^+$); anal. cald for $C_{23}H_{21}N_7O_6$ C, 56.21; H, 4.31; N, 19.95% found: C, 56.32; H, 4.37; N, 20.08%.

9l. Brown solid; yield: 363 mg (83%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.19 (s, 6H), 3.40 (s, 3H), 5.66 (s, 1H), 5.93 (s, 2H), 6.91–7.46 (m, 3H), 10.30 (s, 1H, NH), 11.67 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 27.9, 31.0 (2C), 38.3, 98.3 (2C), 102.6 (2C), 125.6, 126.2, 127.2, 131.7 (2C), 140.0 (2C), 145.7, 150.9 (2C), 157.6 (2C); IR (KBr) ν_{max}: 3376.3, 3275.3, 1659.2, 1610.2 cm^{-1}; MS (ESI): 439.2 ($[M + H]^+$). Anal. cald for $C_{20}H_{18}N_6O_4S$: C, 54.79; H, 4.14; N, 19.17%; found: C, 54.80; H, 4.16; N, 19.18%.

9m. Brown solid; yield: 326 mg (82%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 0.86 (m, 6H), 2.37 (m, 1H), 3.18 (s, 6H), 3.43 (s, 3H), 3.60 (d, 1H), 6.25 (s, 2H), 10.52 (s, 1H, NH), 11.65 (s, 2H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.4 (2C), 28.0 (2C) 31.2, 31.6, 45.3, 98.5 (2C), 101.7 (2C), 133.3 (2C), 139.1 (2C), 153.0 (2C), 159.8 (2C); IR (KBr) ν_{max}: 3375.2, 3265.2, 1655.4, 1615.7 cm^{-1}; MS (ESI): 399.4 ($[M + H]^+$). Anal. cald for $C_{19}H_{22}N_6O_4$: C, 57.28; H, 5.57; N, 21.09%; found: C, 57.30; H, 5.59; N, 21.11%.

9n. Brown solid; yield: 396 mg (85%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.18 (s, 6H), 3.35 (s, 6H), 3.40 (s, 3H), 5.65 (s, 1H), 5.93 (s, 2H), 6.93–7.47 (m, 3H), 11.68 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.8 (2C), 27.9 (2C), 30.2, 39.0, 98.2 (2C), 102.5 (2C), 125.6, 126.2, 127.3, 131.7 (2C), 140.2 (2C), 145.6, 151.0 (2C), 158.1 (2C); IR (KBr) ν_{max}: 3381.2, 3270.5, 1650.9, 1619.5 cm^{-1}; MS (ESI): 467.5 ($[M + H]^+$). Anal. cald for $C_{22}H_{22}N_6O_4S$: C, 56.64; H, 4.75; N, 18.01%; found: C, 56.66; H, 4.76; N, 18.03%.

9o. Brown solid; yield: 357 mg (84%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 0.88 (m, 6H), 2.35 (m, 1H), 3.19 (s, 6H), 3.40 (s, 6H), 3.53 (s, 3H), 3.61 (d, 1H), 6.26 (s, 2H), 11.67 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.4 (2C), 28.2 (2C), 30.3 (3C), 31.5, 45.2, 98.5 (2C), 101.7 (2C), 134.0 (2C), 140.2 (2C), 153.1 (2C), 157.2 (2C); IR (KBr) ν_{max}: 3381.4, 3262.7, 1651.8, 1619.2 cm^{-1}; MS (ESI): 427.8 ($[M + H]^+$). Anal. cald for $C_{21}H_{26}N_6O_4$: C, 59.14; H, 6.14; N, 19.71%; found: C, 59.16; H, 6.15; N, 19.72%.

9p. Brown solid; yield: 316 mg (70%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.19 (s, 6H), 3.35 (s, 3H), 3.45 (s, 3H), 5.62 (s, 1H), 5.95 (s, 2H), 6.89–7.48 (m, 3H), 10.59 (s, 1H, NH), 11.68 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 26.8 (2C), 29.0, 30.2, 39.1, 98.2 (2C), 102.5 (2C), 125.5, 126.3, 127.2, 132.8 (2C), 140.3 (2C), 145.5, 151.1 (2C), 158.3 (2C); IR (KBr) ν_{max}: 3371.5, 3269.2, 1650.4, 1619.3 cm^{-1}; MS (ESI): 453.2 ($[M + H]^+$). Anal. cald for $C_{21}H_{20}N_6O_4S$: C, 55.74; H, 4.46; N, 18.57%; found: C, 56.76; H, 4.47; N, 18.58%.

9q. Brown solid; yield: 280 mg (68%); mp. > 300 °C; ^1H NMR (DMSO-d_6, 300 MHz) δ 0.87 (m, 6H), 2.36 (m, 1H), 3.19 (s, 6H), 3.41 (s, 3H), 3.54 (s, 3H), 3.61 (d, 1H), 6.25 (s, 2H), 10.70 (s, 1H, NH), 11.67 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 21.4 (2C), 29.1 (2C), 30.3 (2C), 31.5, 45.2, 98.5 (2C), 101.7 (2C), 134.1 (2C), 140.2 (2C), 153.1 (2C), 157.2 (2C); IR (KBr) ν_{max}: 3383.7, 3252.3, 1655.6, 1615.7 cm^{-1}; MS (ESI): 413.4 ($[M + H]^+$). Anal. cald for $C_{20}H_{24}N_6O_4$: C, 58.24; H, 5.87; N, 20.38%; found: C, 58.27; H, 5.88; N, 20.39%.

Acknowledgements

We thank the CSIR, New Delhi for financial assistance (CAAF-NE project). MS thanks the DST, New Delhi for the INSPIRE Fellowship.

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