4. Results and discussion

The work performed to achieve the proposed aims and objectives has been discussed under two main headings:

4.1 Chemical studies

4.2 Biological studies

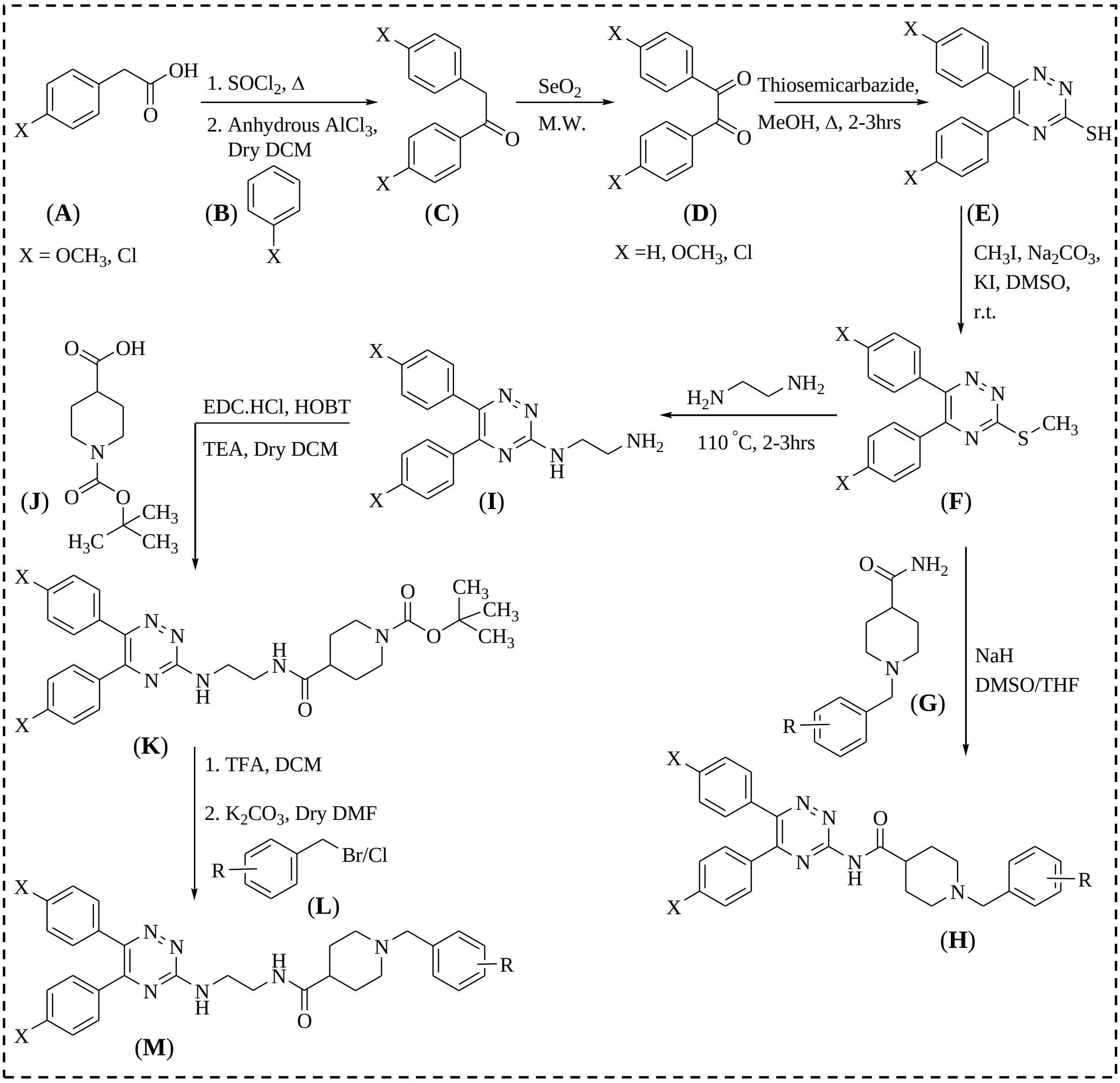
4.1 Chemical studies

The proposed compounds were synthesized using synthetic schemes as depicted in **general schemes 1-3**.

Using **general scheme-1**, two different series of vicinal diaryl-substituted triazines *viz.* *N*-(5,6-diaryl-1,2,4-triazin-3-yl)-1-benzylpiperidine-4-carboxamides (**H**) and *N*-(2-(5,6-diaryl-1,2,4-triazin-3-ylamino)ethyl)-1-benzylpiperidine-4-carboxamides (**M**) were prepared.

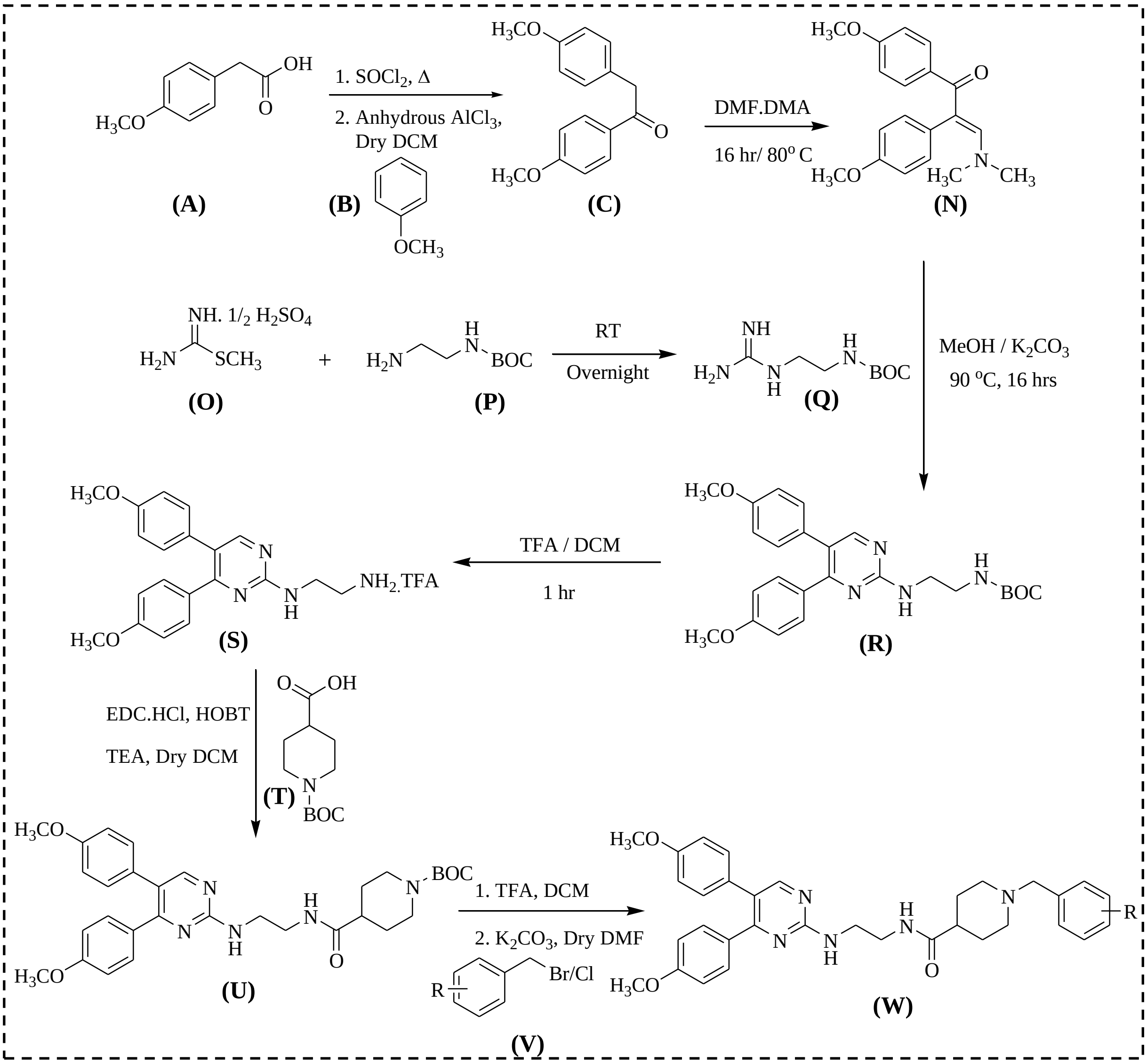
In the first step, the acid chlorides were prepared from substituted phenylacetic acids (**A**) using thionyl chloride. Subsequently, Friedel-Crafts acylation using substituted benzenes (**B**) and the acid chlorides produced 1,2-diarylethanones (**C**). Further oxidation of **C** was carried out using selenium dioxide to get 1,2-diarylethan-1,2-diones (**D**) which on refluxing with thiosemicarbazide undergo cyclization to give 5,6-diaryl-1,2,4-triazine-3-thiols (**E**). In the next step, the thiols (**E)** were methylated by methyl iodide under basic conditions to obtain 3-(methylthio)-5,6-diphenyl-1,2,4-triazines (**F**). Finally, the 3-(methylthio)-5,6-diphenyl-1,2,4-triazines (**F**) were treated with 1-substituted benzylpiperidine-4-carboxamides (**G**) in the presence of sodium hydride-DMSO at room temperature to obtain the desired *N*-(5,6-diaryl-1,2,4-triazin-3-yl)-1-benzylpiperidine-4-carboxamides (**H**).

3-(Methylthio)-5,6-diaryl-1,2,4-triazines (**F**) on refluxing with ethylenediamine at 110 ^{o}C for 2-3 hrs gave *N*-(2-aminoethyl)-5,6-diaryl-1,2,4-triazin-3-amines (**I**) which in the next step were treated with 1-(*t.*butyloxycarbonyl)piperidine-4-carboxylic acid (**J**) in presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC.HCl) and hydroxybenzo triazole (HOBt) under basic condition to prepare *t.*butyl 4-(2-(5,6-diaryl-1,2,4-triazin-3-yl amino)ethylcarbamoyl)piperidine-1-carboxylates (**K**). In the last step, the carbamates (**K)** were deprotected using trifluoroacetic acid (TFA) and refluxed with substituted benzyl bromides (**L**) to obtain the final desired products *N*-(2-(5,6-diaryl-1,2,4-triazin-3-ylamino)ethyl)-1-substituted benzyl piperidine-4-carboxamides (**M**).

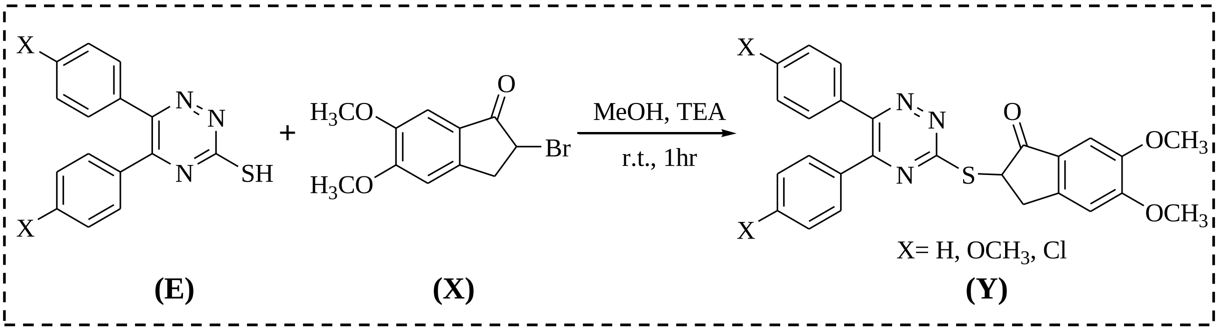


General Scheme 1

General scheme-2 was adopted to synthesize vicinal diaryl-substituted pyrimidine derivatives (**W**) wherein the intermediate (**C**) was treated with *N*,*N*-dimethylformamide dimethylacetal (DMF.DMA) to get 3-(dimethylamino)-1,2-diarylprop-2-en-1-one (**N**). Cyclization of **N** using *t*.butyl 2-guanidinoethylcarbamate (**Q**) offered *t*.butyl 2-(4,5-diaryl pyrimidin-2-ylamino)ethylcarbamate (**R**) which on deprotection and subsequent acid-amine coupling reaction yielded *t*.butyl 4-(2-(4,5-diarylpyrimidin-2-ylamino)ethylcarbamoyl) piperidine-1-carboxylate (**U**). In the final step, (**U**) was deprotected using TFA and refluxed with substituted benzyl bromides (**V**) to afford the final *N*-(2-(4,5-diarylpyrimidin-2-ylamino)ethyl)-1-substituted benzyl-4-carboxamides (**W**).



General Scheme 2



General Scheme 3

In **general scheme-3**, 5,6-diaryl-1,2,4-triazine-3-thiols (**E**) were hybridized with 2-bromo-5,6-dimethoxyindan-2-one (**X**) to produce vicinal diaryltriazine-donepezil hybrids (**Y**).

To synthesize the targeted compounds (**H, M, W** and **Y**), commercially available substituted phenylacetic acids (**A**), substituted benzenes (**B**), benzil, piperidine-4-carboxylic acid, piperidine-4-carboxamide, *S*-methylisothiourea, *t*.butyl 2-aminoethylcarbamate, substituted benzyl bromides/chlorides and 5,6-dimethoxyindan-1-one were used to prepare the intermediates. As per general **scheme 1-3**, the work related to the synthesis of all the intermediates and targeted compounds (**H, M, W** and **Y**) has been described under the following headings:

4.1.1 Synthesis of vicinal diaryl-substituted triazines

- **4.1.1.1** Synthesis of 1,2-diarylethanones (**81** and **82**)
- **4.1.1.2** Synthesis of 1,2-diarylethane-1,2-diones (**83** and **84**)
- **4.1.1.3** Synthesis of 5,6-diaryl-1,2,4-triazine-3-thiols (**86-88**)
- **4.1.1.4** Synthesis of 3-(methylthio)-5,6-diaryl-1,2,4-triazines (**89-91**)
- **4.1.1.5** Synthesis of 1-substituted benzylpiperidine-4-carboxamides (**94-107**)
- **4.1.1.6** Synthesis of *N*-(2-aminoethyl)-5,6-diaryl-1,2,4-triazin-3-amines (**108-110**)
- **4.1.1.7** Synthesis of 1-(*t*.butoxycarbonyl)piperidine-4-carboxylic acid (**112**)
- **4.1.1.8** Synthesis of *t*.butyl 4-(2-(5,6-diaryl-1,2,4-triazin-3-ylamino)ethyl-carbamoyl)piperidine-1-carboxylates (**113-115**)
- **4.1.1.9** Synthesis of *N*-(2-(5,6-diaryl-1,2,4-triazin-3-ylamino)ethyl)-1-benzyl piperidine-4-carboxamides (**119-160**)
- **4.1.1.10** Synthesis of *N*-(5,6-diaryl-1,2,4-triazin-3-yl)-1-benzylpiperidine-4-carboxamides (**161-194**)

4.1.2 Synthesis of vicinal diaryl-substituted pyrimidines

- **4.1.2.1** Synthesis of 3-(dimethylamino)-1,2-bis(4-methoxyphenyl)prop-2-en-1-one (**196**)
- **4.1.2.2** Synthesis of *t*.butyl 2-guanidinylethylcarbamate (**197**)
- **4.1.2.3** Synthesis of *t*.butyl 2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-ylamino)ethyl carbamate (**198**)
- **4.1.2.4** Synthesis of *N*-(2-aminoethyl)-4,5-bis(4-methoxyphenyl)pyrimidin-2-amine (**199**)
- **4.1.2.5** Synthesis of *t*.butyl 4-(2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-ylamino) ethylcarbamoyl)piperidine-1-carboxylate (**200**)
- **4.1.2.6** Synthesis of *N*-(2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-ylamino)ethyl)-1-substituted benzyl-4-carboxamides (**202-215**)

4.1.3 Synthesis of vicinal diaryltriazines-donepezil hybrids

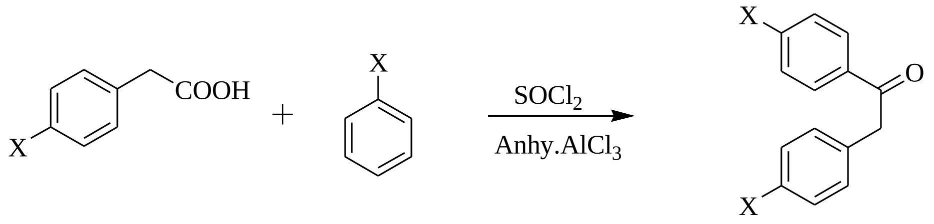
4.1.3.1 Synthesis of 2-bromo-5,6-dimethoxyindan-1-one (**217**)

4.1.3.2 Synthesis of 2-(5,6-diaryl-1,2,4-triazin-3-ylthio)-5,6-dimethoxyindan-1-ones (**218-220**)

4.1.1 Synthesis of vicinal diaryl-substituted triazines (119-160 and 161-194)

4.1.1.1 Synthesis of 1,2-diarylethanones (81 and 82)

As depicted in **scheme-1**, substituted phenylacetic acids (**77** and **78**) were treated with thionyl chloride to prepare 4-substituted phenylacetyl chlorides which on subsequent Friedel-Craft acylation reaction using substituted benzenes (**79** and **80**) in presence of anhydrous aluminium chloride afforded 1,2-diarylethanones (**81** and **82**). IR spectrum of compound (**81**) displayed the characteristic peaks for the C=O stretching at 1674 cm^{-1} along with other peaks at 1261 and 1023 cm^{-1} for the C-O stretching. For compound (**82**) the characteristic peak for the C=O stretching was observed at 1689 cm^{-1} in its IR spectrum.



(77, 78) **(79, 80)** **(81, 82)**

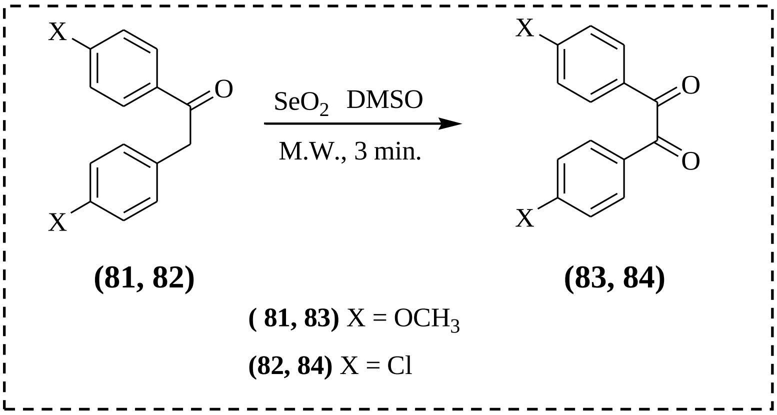
(77, 79, 81) X = OCH_3

(78, 80, 82) X = Cl

Scheme-1

4.1.1.2 Synthesis of 1,2-diarylethane-1,2-diones (83 and 84)

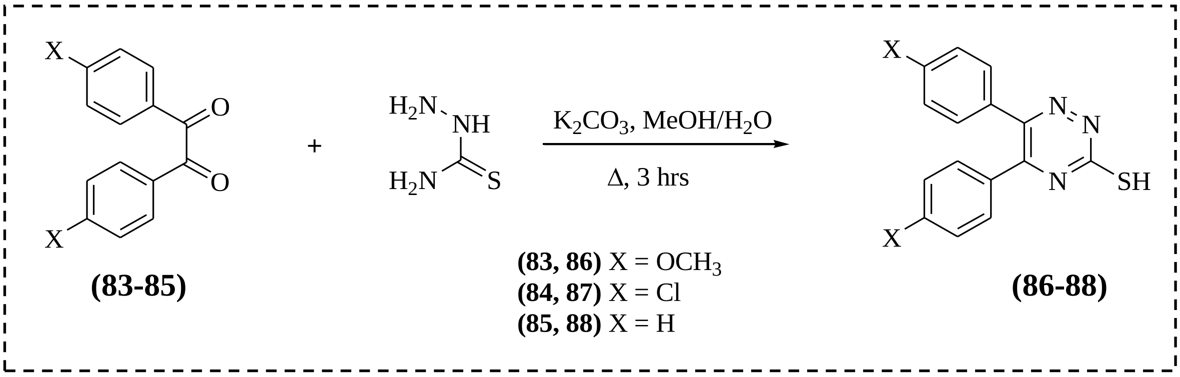
1,2-Diarylethanones (**81** and **82**) on selective α-oxidation (**Scheme-2**) using microwave irradiation in presence of selenium oxide yielded 1,2-diarylethane-1,2-diones (**83** and **84**). IR spectrum of compounds (**83** and **84**) showed the characteristic peaks for C=O stretching at 1655 and 1662 cm^{-1} respectively.



Scheme-2

4.1.1.3 Synthesis of 5,6-diaryl-1,2,4-triazine-3-thiols (86-88)

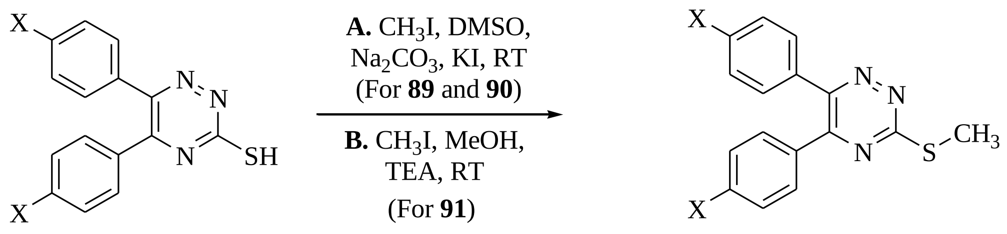
Following the **scheme-3**, reaction of 1,2-diarylethane-1,2-diones (**83-85**) with thiosemicarbazide resulted into cyclization offering 5,6-diaryl-1,2,4-triazine-3-thiols (**86-88**). Cyclization was confirmed by IR spectra of **86-88** wherein the characteristic peaks for C=O stretching disappeared.



Scheme-3

4.1.1.4 Synthesis of 3-(methylthio)-5,6-diaryl-1,2,4-triazines (89-91)

5,6-Diaryl-1,2,4-triazine-3-thiols (**86** and **87**) were methylated as shown in **scheme-4** using methyl iodide in presence of sodium carbonate and potassium iodide to obtain 3-(methylthio)-5,6-diaryl-1,2,4-triazines (**89, 90**). Methylation of 5,6-diphenyl-1,2,4-triazine-3-thiol (**88**) was carried out using methyl iodide and triethylamine to get 3-(methylthio)-5,6-diphenyl-1,2,4-triazine (**91**).



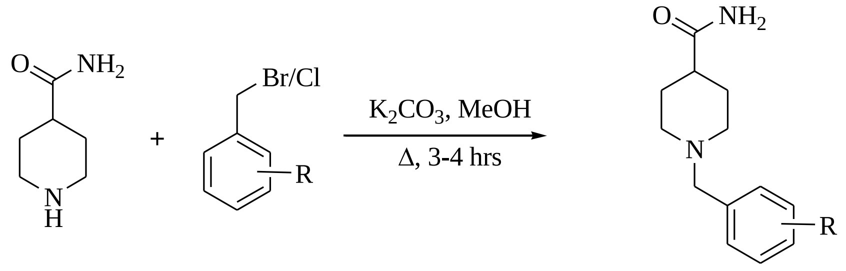
(86-88) **(89-91)**

(86, 89) X = OCH_3
(87, 90) X = Cl
(88, 91) X = H

Scheme-4

4.1.1.5 Synthesis of 1-substituted benzylpiperidine-4-carboxamides (94-107)

Piperidine-4-carboxamide (**92**) was reacted with substituted benzyl bromides/chlorides (**93**) using potassium carbonate to obtain 1-substituted benzylpiperidine-4-carboxamides (**94-107**) (**Scheme-5**). IR spectra of compounds (**94-107**) showed the characteristic peak for NH stretching in the range of 3160-3407 cm^{-1} and for C=O stretching in the range of 1630-1660 cm^{-1} (**Table 1**). The mass spectra of compounds (**94**) and (**103**) displayed quasimolecular ion peak $[M+H]^+$ at 303.34 and 255.27 respectively.



(92) **(93)** **(94-107)**

R =

93a 4-OCF_3; **93b** 2-Cl; **93c** 4-CF_3; **93d** 4-Cl; **93e** 4-CN;
93f 3-OCH_3; **93g** 2-CH_3; **93h** 2-CF_3; **93i** 2-CN; **93j** 2,6-diF
93k 3,5-diF; **93l** 4-CH_3; **93m** 2-F; **93n** 4-F

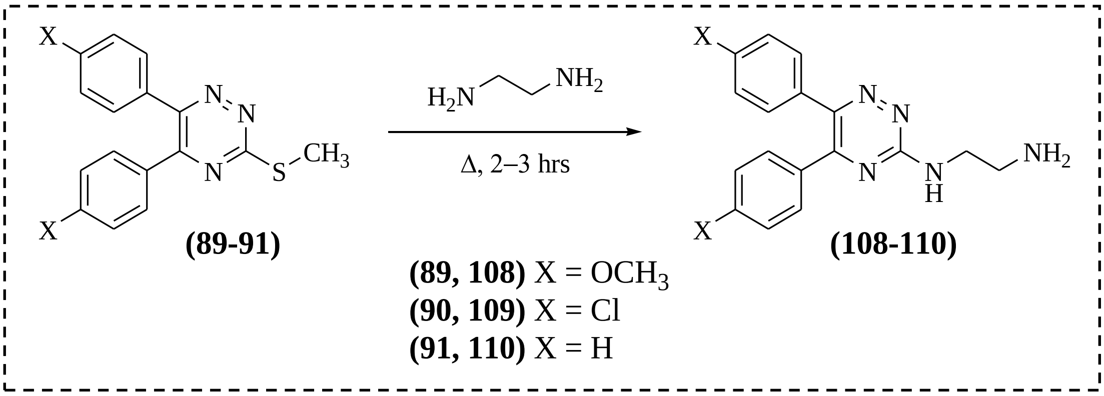
Scheme-5

Table 1: Spectral data of 1-substituted benzylpiperidine-4-carboxamides (**94-107**)

Comp.	**R**	**IR peaks (cm^{-1})**
94	4-OCF_3	3372 and 3184 (N-H stretching), 1650 (C=O stretching of amide)
95	2-Cl	3334 and 3164 (N-H stretching), 1632 (C=O stretching of amide)
96	4-CF_3	3330 and 3160 (N-H stretching), 1635 (C=O stretching of amide)
97	4-Cl	3339 and 3168 (N-H stretching), 1631 (C=O stretching of amide)
98	4-CN	3368 and 3180 (N-H stretching), 1647 (C=O stretching of amide), 2224 (CN stretching)
99	3-OCH_3	3333 and 3163 (N-H stretching), 1632 (C=O stretching of amide), 1261 and 1040 (C-O stretching)
100	2-CH_3	3407 and 3214 (N-H stretching), 1657 (C=O stretching of amide)
101	2-CF_3	3381 and 3194 (N-H stretching), 1649 (C=O stretching of amide)
102	2-CN	3383 and 3184 (N-H stretching), 1646 (C=O stretching of amide), 2220 (CN stretching)
103	2,6-diF	3380 and 3195 (N-H stretching), 1649 (C=O stretching of amide)
104	3,5-diF	3384 and 3196 (N-H stretching), 1660 (C=O stretching of amide)
105	4-CH_3	3339 and 3170 (N-H stretching), 1634 (C=O stretching of amide)
106	2-F	3372 and 3187 (N-H stretching), 1648 (C=O stretching of amide)
107	4-F	3340 and 3177 (N-H stretching), 1634 (C=O stretching of amide)

4.1.1.6 Synthesis of *N*-(2-aminoethyl)-5,6-diaryl-1,2,4-triazin-3-amines (108-110)

As shown in **scheme-6**, *N*-(2-aminoethyl)-5,6-diaryl-1,2,4-triazin-3-amines (**108-110**) were prepared by refluxing 3-(methylthio)-5,6-diaryl-1,2,4-triazines (**89-91**) with ethylene diamine for 2-3 hrs. Structures of the compounds (**108-110**) were confirmed by ^{1}H-NMR and Mass spectra.



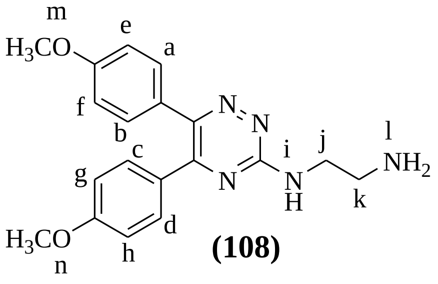
(89-91)

(108-110)

(89, 108) X = OCH_3
(90, 109) X = Cl
(91, 110) X = H

Scheme-6

IR spectrum of compound (**108**) displayed the characteristic peaks for NH stretching at 3239 and 3072 cm^{-1}. Its ^{1}H-NMR spectrum showed doublets at δ 7.48-7.46 (d, 2H$_{a,\,b}$, J = 8.6 Hz) and 7.38-7.36 (d, 2H$_{c,\,d}$, J = 8.5 Hz) for aromatic protons. Other aromatic protons were observed at δ 6.86-6.80 (m, 4H$_{e,\,f,\,g,\,h}$) as a multiplet. A broad singlet appeared at δ 6.22 (bs, NH$_i$) due to proton attached to *sec.*amine. Six protons of two methoxyl groups were observed at δ 3.81 (s, 3H$_m$) and 3.80 (s, 3H$_n$) as singlets. Other aliphatic protons were observed at δ 3.65-3.64 as a doublet (2H$_j$, J = 6.2 Hz) and δ 3.02-2.99 as a triplet (2H$_k$, J = 6.2 Hz).

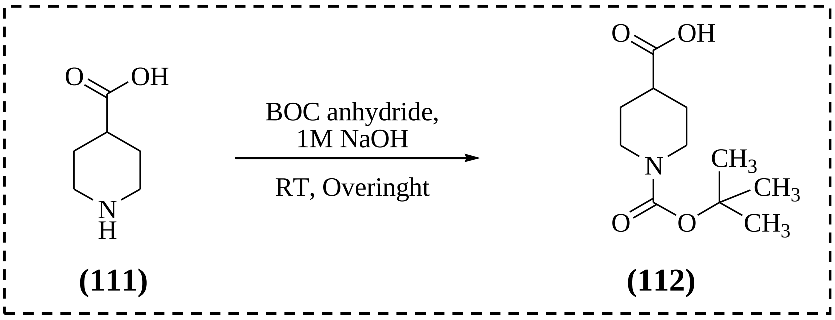


(108)

IR spectrum of compound (**109**) showed the characteristic peaks for NH stretching at 3237 and 3072 cm^{-1}. Its mass spectrum showed the molecular ion peak at 360.74 [M]$^+$. IR spectrum of compound (**110**) showed the characteristic peaks for NH stretching at 3243 and 3074 cm^{-1}. Its mass spectrum showed the quasimolecular ion peak at 292.68 [M+H]$^+$.

4.1.1.7 Synthesis of 1-(*t*.butoxycarbonyl)piperidine-4-carboxylic acid (112)

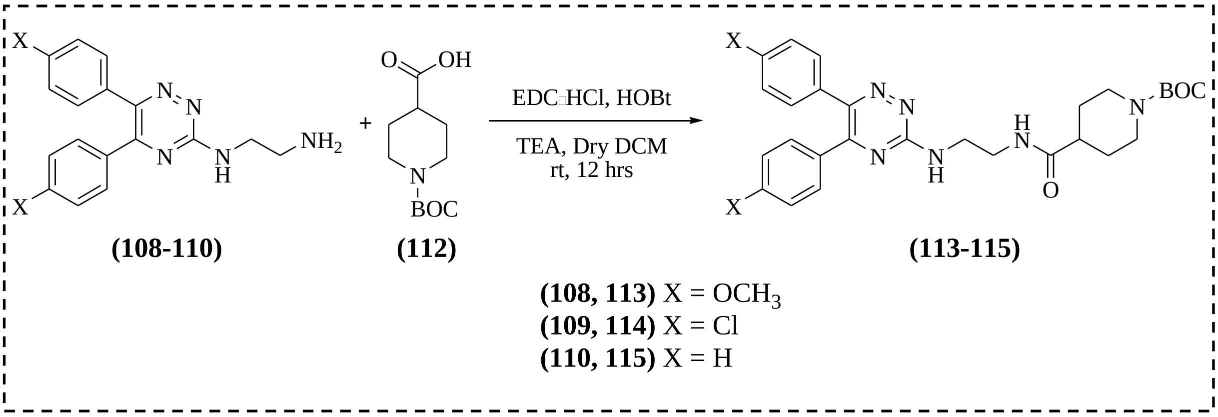
Secondary amine of piperidine-4-carboxylic acid (**111**) was protected using BOC anhydride in presence of 1M sodium hydroxide solution and THF to prepare 1-(*t*.butoxy carbonyl)piperidine-4-carboxylic acid (**112**) (**Scheme-7**). IR spectrum of compound (**112**) displayed the characteristic peaks for OH stretching at 3212 cm^{-1}, C=O stretching of carbamate at 1735 cm^{-1} and C=O stretching of acid at 1661 cm^{-1}.



Scheme-7

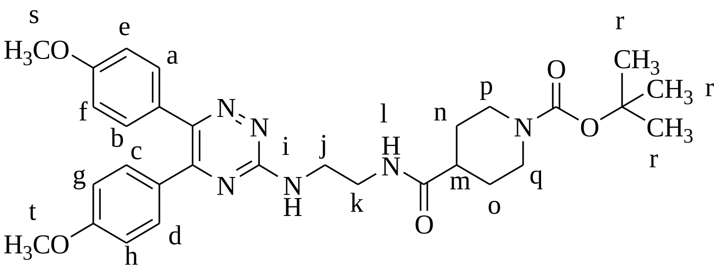
4.1.1.8 Synthesis of *t*.butyl 4-(2-(5,6-diaryl-1,2,4-triazin-3-ylamino)ethylcarbamoyl) piperidine-1-carboxylates (113-115)

As shown in **scheme-8**, *N*-(2-aminoethyl)-5,6-diaryl-1,2,4-triazin-3-amines (**108-110**) were treated with 1-(*t*.butoxycarbonyl)piperidine-4-carboxylic acid (**112**) for acid-amine coupling reaction under basic conditions to obtain *t*.butyl-4-(2-(5,6-diaryl-1,2,4-triazin-3-yl amino)ethylcarbamoyl)piperidine-1-carboxylates (**113-115**).



(108, 113) X = OCH_3
(109, 114) X = Cl
(110, 115) X = H

Scheme-8



(113)

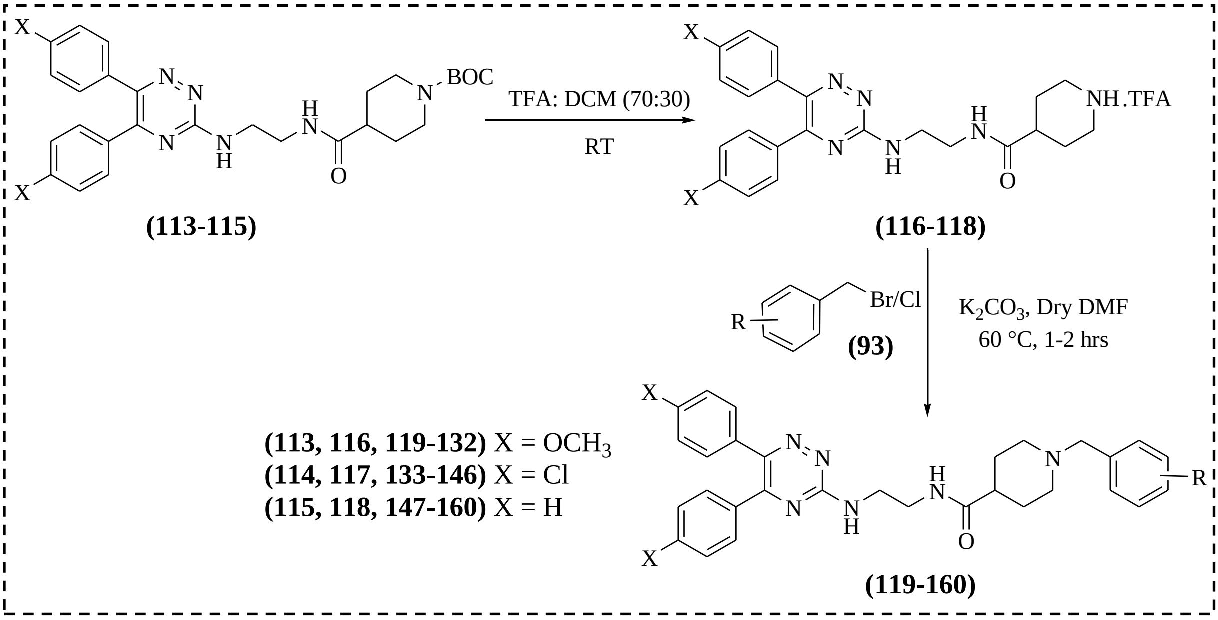
In the IR spectrum of compound (**113**), the C=O stretching for amide and carbamate was observed at 1684 cm^{-1}. Its PMR spectrum showed amidic proton at δ 7.9 (bs, $1H_{l}$) as a broad singlet. Aromatic protons were observed as doublet at δ 7.53-7.51 (d, $2H_{a, b}$) which coupled with other protons at δ 6.84-6.82 (d, $2H_{e, f}$) with a coupling constant of 8.7 Hz. Other aromatic protons appeared as doublets at δ 7.35-7.33 (d, $2H_{c, d}$) which coupled with protons at δ 6.90-6.88 (d, $2H_{g, h}$) with a coupling constant of 8.6 Hz. A broad singlet was obtained at δ 3.91 for two protons (bs, $2H_{1p, 1q}$) while another singlet at δ 3.82 (s, $6H_{s, t}$) was observed for six protons of two methoxyl groups. Four aliphatic protons appeared as two broad singlets at δ 3.72 (bs, $2H_{j}$) and 3.63 (bs, $2H_{k}$). Other aliphatic protons were observed as broad singlets at δ 2.31 (bs, $2H_{1p, 1q}$) and 1.86 (bs, $2H_{m, 1o}$) and as a multiplet at 1.46-1.25 (m, $12H_{9r, 2n, 1o}$).

IR spectrum of Compound (**114**) showed the characteristic peak for NH stretching at 3300 cm^{-1} and C=O stretching of amide and carbamate at 1689 cm^{-1}. Its mass spectrum displayed $[M+2H]^{+}$ peak at 572.31. IR spectrum of compound (**115**) showed characteristic peaks at 3252 cm^{-1} for NH stretching, and at 1695 and 1672 cm^{-1} for C=O stretching of the carbamate and amide groups respectively. In its mass spectrum, $[M+2H]^{+}$ peak was observed at 504.20.

4.1.1.9 Synthesis of *N*-(2-(5,6-diaryl-1,2,4-triazin-3-ylamino)ethyl)-1-benzylpiperidine-4-carboxamides (119-160)

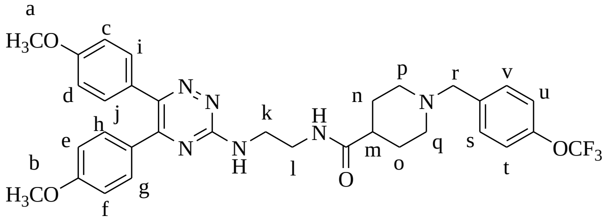
In the final step, *t*.butyl 4-(2-(5,6-diaryl-1,2,4-triazin-3-ylamino)ethylcarbamoyl) piperidine-1-carboxylates (**113-15**) were deprotected as per **scheme-9** in presence of trifluoroacetic acid and DCM to get *N*-(2-(5,6-diaryl-1,2,4-triazin-3-ylamino)ethyl) piperidine -4-carboxamides (**116-118**). In their IR spectra, compounds (**116-118**) showed characteristic peaks for NH stretching at 3319, 3414 and 3307 cm^{-1} respectively whereas the C=O stretching was observed at 1673, 1678 and 1680 cm^{-1} respectively. Mass spectra of compounds (**116-118**) showed molecular ion peaks at 464.10 $[M+2H]^{+}$, 471.98 $[M]^{+}$ and 403.94 $[M+H]^{+}$ respectively.

These deprotected compounds (**116-118**) were further reacted with substituted benzyl bromides/chlorides (**93**) in presence of potassium carbonate and DMF to afford the final targeted compounds, *N*-(2-(5,6-diaryl-1,2,4-triazin-3-ylamino)ethyl)-1-benzylpiperidine-4-carboxamides (**119-160**).

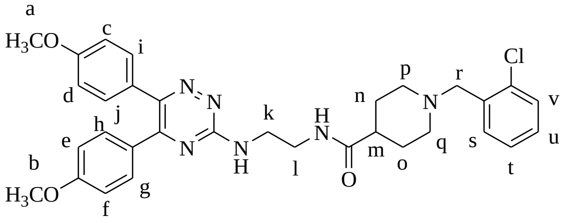


Scheme-9

IR spectrum of compound (**119**) showed the characteristic peaks for the NH stretching and C=O stretching at 3271 and 1666 cm^{-1} respectively. Its PMR spectrum showed two doublets at δ 7.50-7.47 (d, 2H$_{i, j}$, *J* = 7.6 Hz) and 7.36-7.34 (d, 4H$_{g, h}$, *J* = 7.8 Hz) for four aromatic protons while two more doublets were observed for four protons at δ 7.29-7.28 (d, 2H$_{s, v}$, *J* = 6.6 Hz) and 7.13-7.11 (d, 2H$_{t, u}$, *J* = 6.6 Hz). Other aromatic protons appeared as a multiplet at δ 6.87-6.80 (m, 4H$_{c, d, e, f}$). Six protons of two methoxyl groups were observed as singlets at δ 3.82 (s, 3H$_{a}$) and 3.81 (s, 3H$_{b}$). Two multiplet signals were observed for four protons at δ 3.77-3.74 (m, 2H$_{k}$) and 3.61-3.58 (m, 2H$_{l}$). Other aliphatic protons appeared as a singlet at δ 3.40 (s, 2H$_{r}$), a broad singlet at δ 2.76-2.75 (bs, 2H$_{1p, 1q}$) and a multiplet at δ 1.92-1.79 (m, 7H$_{m, n, o, 1p, 1q}$). In its mass spectrum, quasimolecular ion peak was observed at 637.9 [M+H]$^{+}$.



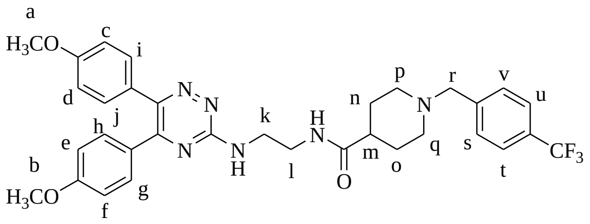
(119)



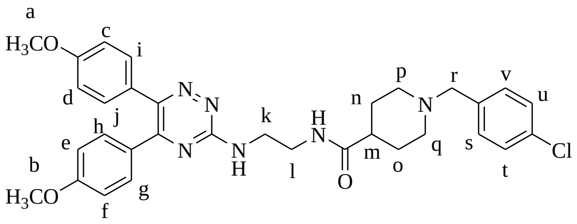
(120)

In the IR spectrum of compound (**120**), peaks for NH and C=O stretching were seen at 3257 and 1669 cm^{-1} respectively. PMR spectrum of compound (**120**) offered four doublets for six aromatic protons at δ 7.51-7.49 (d, $2H_{i, j}$, J = 8.8 Hz), 7.42-7.41 (d, $1H_{v}$, J = 7.2 Hz), 7.36-7.34 (d, $2H_{g, h}$, J = 8.4 Hz) and 7.31-7.29 (dd, $1H_{s}$, J = 1.6, 7.6 Hz). Other aromatic protons were observed as a multiplet at 7.20-7.12 (m, $2H_{t, u}$) and 6.88-6.80 (m, $4H_{c, d, e, f}$). Among aliphatic protons, six protons of two methoxyl groups appeared as singlet at δ 3.81 (s, $6H_{a, b}$) whereas four protons of ethylene linker appeared at δ 3.76-3.72 (m, $2H_{k}$) and 3.63-3.59 (m, $2H_{l}$). Other aliphatic protons were seen as singlet at δ 3.49 (s, $2H_{r}$), broad singlets at δ 2.78 (bs, $1H_{p}$) and 2.75 (bs, $1H_{q}$), and a multiplet at δ 1.72-1.61 (m, $7H_{m, n, o, 1p, 1q}$). Quasimolecular ion peak was observed at 587.9 $[M+H]^{+}$ in its mass spectrum.

IR spectrum of compound (**121**) exhibited NH stretching at 3265 cm^{-1} and C=O stretching at 1664 cm^{-1}. In its PMR spectrum, aromatic protons were observed as triplet at δ 7.52-7.48 (dt, $4H_{i, j, t, u}$, J = 2, 8.4 Hz), as multiplets at δ 7.37-7.32 (m, $4H_{g, h, s, v}$) and 6.87-6.79 (m, $4H_{c, d, e, f}$). Two singlets for six protons of methoxyl groups appeared at 3.81 (s, $3H_{a}$) and 3.80 (s, $3H_{b}$). Peaks for four protons of ethylene linker were observed as multiplets at δ 3.75-3.71 (m, $4H_{k}$) and 3.62-3.58 (m, $4H_{l}$). Other aliphatic protons appeared as a singlet at δ 3.40 (s, $2H_{r}$) and broad singlets at δ 2.69 (bs, $3H_{m, 1p, 1q}$) and 1.66-1.59 (bs, $6H_{n, o, 1p, 1q}$).



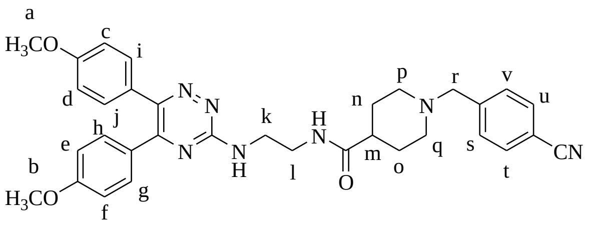
(121)



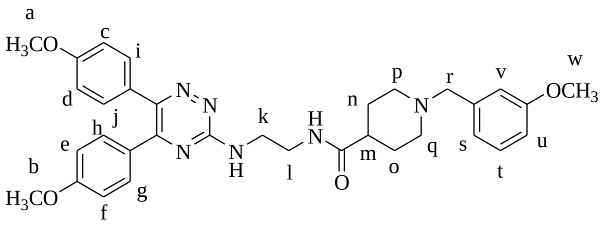
(122)

Compound (**122**) in its IR spectrum showed characteristic peaks for NH stretching at 3338 and 3243 cm^{-1}, and C=O stretching at 1653 cm^{-1}. Its ^{1}H-NMR spectra offered peaks for four aromatic protons as two doublets at δ 7.50-7.48 (d, $2H_{i, j}$, J = 8.4 Hz) and 7.34-7.32 (d, $2H_{g, h}$, J = 8.4 Hz). Other aromatic protons were observed as doublets at δ 7.23-7.21 (d, $2H_{s, t}$, J = 8.0 Hz), 7.17-7.15 (d, $2H_{u, v}$, J = 8.0 Hz) and as a multiplet at δ 6.86-6.80 (m, $4H_{c, d, e, f}$). Two singlets appeared at δ 3.81 (s, $3H_{a}$) and 3.80 (s, $3H_{b}$) representing six protons of two methoxyl groups. Four protons of ethylene linker were represented by two multiplets at δ 3.74-3.71 (m, $2H_{k}$) and 3.62-3.58 (m, $2H_{l}$). Other aliphatic protons were seen as a singlet at δ 3.32 (s, $2H_{r}$), as broad singlets at δ 2.68-2.66 (bs, $2H_{1p, 1q}$) and as a multiplet at δ 1.81-1.58 (m, $7H_{m, n, o, 1p, 1q}$).

In the IR Spectrum of Compound (**123**), signals for NH and C=O stretching were observed at 3267 and 1663 cm^{-1} respectively whereas the characteristic peak of CN stretching appeared at 2229 cm^{-1}. Its PMR spectrum showed two doublet signals for four aromatic protons at δ 7.56-7.54 (d, 2H$_{t, u}$, *J* = 8.4 Hz) and 7.49-7.47 (d, 2H$_{i, j}$, *J* = 8.8 Hz) whereas two multiplets were observed for remaining eight aromatic protons at δ 7.38-7.32 (m, 4H$_{g, h, s, v}$) and 6.87-6.79 (m, 4H$_{c, d, e, f}$). A singlet corresponding to six protons of two methoxyl groups appeared at δ 3.81 (s, 6H$_{a, b}$). Four protons of ethylene linker offered two multiplet signals at δ 3.77-3.73 (m, 2H$_{k}$) and 3.62-3.58 (m, 2H$_{l}$). Other aliphatic protons were observed at δ 3.42 (s, 2H$_{r}$), 2.70-2.68 (bs, 2H$_{1p, 1q}$) and 1.63 (bs, 7H$_{m, n, o, 1p, 1q}$). The quasimolecular ion peak for compound (**123**) was observed at 578.9 [M+H]$^{+}$ in its mass spectrum.



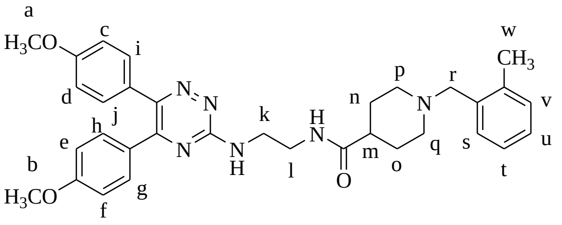
(123)



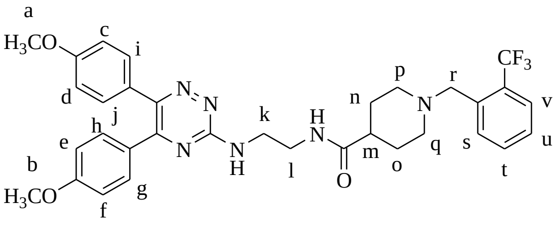
(124)

IR spectrum of compound (**124**) exhibited the characteristic peak for NH and C=O stretching at 3245 and 1662 cm^{-1}. In its PMR spectrum, aromatic protons were observed as doublets at δ 7.50-7.48 (d, 2H$_{i, j}$, *J* = 8.4 Hz), 7.34-7.32 (d, 2H$_{g, h}$, *J* = 8.4 Hz), a triplet at δ 7.18-7.14 (t, 1H$_{t}$, *J* = 7.8 Hz) and a multiplet at δ 6.85-6.74 (m, 7H$_{c, d, e, f, s, u, v}$). Among aliphatic protons, nine protons of methoxyl groups appeared as a singlet at δ 3.80 (s, 6H$_{a, b}$) and 3.76 (s, 3H$_{w}$). Multiplets at δ 3.73-3.70 (m, 2H$_{k}$) and 3.61-3.57 (m, 2H$_{l}$) were observed for four protons of ethylene linker. Other aliphatic protons appeared as a singlet at δ 3.34 (s, 2H$_{r}$), and multiplets at δ 2.94-2.71 (m, 3H$_{m, 1p, 1q}$) and 1.65-1.53 (m, 6H$_{n, o, 1p, 1q}$). Its mass spectrum showed the quasimolecular ion peak at 583.9 [M+H]$^{+}$.

Compound (**125**) displayed peaks for NH stretching and C=O stretching at 3337 and 1656 cm^{-1} in its IR spectrum. In the PMR spectrum of compound (**126**), aromatic protons offered doublets at δ 7.50-7.48 (d, 2H$_{i, j}$, *J* = 8.6 Hz) and 7.35-7.33 (d, 2H$_{g, h}$, *J* = 6.6 Hz), multiplets at δ 7.21-7.05 (m, 4H$_{s, t, u, v}$), and doublets at δ 6.87-6.85 (d, 2H$_{c, d}$, *J* = 8.6 Hz) and 6.82-6.80 (d, 2H$_{e, f}$, *J* = 6.6 Hz). Six protons of methoxyl groups afforded a singlet at δ 3.81 (s, 6H$_{a, b}$). Four protons of ethylene linker appeared as multiplets at δ 3.76-3.72 (m, 2H$_{k}$) and 3.61-3.57 (m, 2H$_{l}$). Other aliphatic protons were observed as a singlet at δ 3.35 (s, 2H$_{r}$), a multiplet at δ 2.95-2.74 (m, $3H_{m, 1p, 1q}$), a singlet at δ 2.29 (s, $3H_w$) and a broad singlet at δ 1.60 (bs, $6H_{n, o, 1p, 1q}$).



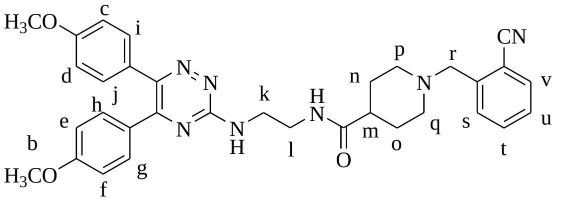
(125)



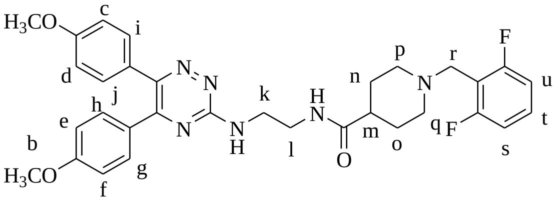
(126)

In the IR spectrum of compound (**126**), signals for NH and C=O stretching were seen at 3273 and 1667 cm^{-1} respectively. Its PMR spectra displayed a doublet signal for a proton at δ 7.75-7.73 (d, $1H_v$) which coupled with adjacent proton at δ 7.58-7.56 (d, $1H_u$) showing ortho coupling with a constant of 8.0 Hz. Other aromatic protons appeared as three multiplets at δ 7.50-7.43 (m, $3H_{i, j, t}$), 7.36-7.26 (m, $3H_{g, h, s}$) and 6.87-6.79 (m, $4H_{c, d, e, f}$). Amongst the aliphatic protons, two singlets were seen at δ 3.80 (s, $6H_{a, b}$) for six protons of two methoxyl groups. Ethylene protons were observed at δ 3.76-3.72 (m, $2H_k$) and 3.62-3.58 (m, $2H_l$). Other aliphatic protons appeared at δ 3.51 (s, $2H_r$), 2.94-2.70 (m, $3H_{m, 1p, 1q}$), 1.78 (bs, $2H_{1p, 1q}$) and 1.66-1.62 (m, $4H_{n, o}$). The $[M+2H]^+$ peak was observed at 622.0 in the mass spectrum of compound (**126**).

Compound (**127**) in its IR spectrum showed the characteristic peaks for NH stretching at 3258 cm^{-1}, CN stretching at 2219 cm^{-1} and C=O stretching at 1669 cm^{-1}. PMR spectrum of compound (**127**) showed doublets for four aromatic protons at δ 7.58-7.56 (d, $1H_v$, J = 7.6 Hz) and 7.50-7.49 (d, $3H_{i, j, t}$), and multiplets for eight protons at δ 7.35-7.25 (m, $4H_{g, h, s, u}$) and 6.88-6.75 (m, $4H_{c, d, e, f}$). Singlets were obtained at δ 3.81 (s, $6H_{a, b}$) for six protons of methoxyl groups. Multiplets were observed at δ 3.74-3.70 (m, $2H_k$) and 3.62-3.60 (m, $2H_l$) due to four protons of ethylene linker. Other aliphatic protons appeared at δ 3.54 (s, $2H_r$), 2.69-2.66 (bs, $2H_{1p, 1q}$) and 1.75-1.59 (m, $7H_{m, n, o, 1p, 1q}$).



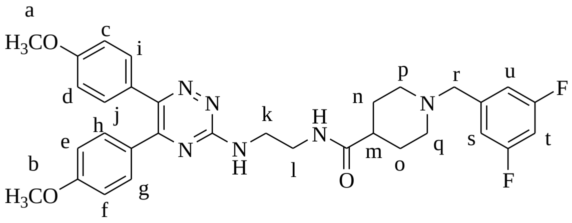
(127)



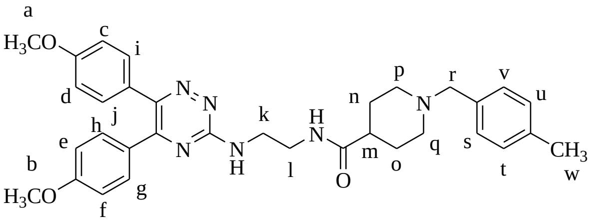
(128)

In the IR spectrum of compound (**128**), characteristic peaks were observed at 3339 cm^{-1} for NH stretching and 1656 cm^{-1} for C=O stretching. Its PMR spectrum offered signals for aromatic protons as doublets at δ 7.49-7.47 (d, 2H$_{i, j}$, *J* = 8.8 Hz) and 7.34-7.32 (d, 2H$_{g, h}$, *J* = 8.8 Hz). Other aromatic protons afforded signals at δ 7.24-7.16 (m, 1H$_{t}$) and 6.87-6.79 (m, 6H$_{c, d, e, f, s, u}$). Two singlets were obtained at δ 3.82 (s, 3H$_{a}$) and 3.81 (s, 3H$_{b}$) for six protons of methoxyl groups. Other aliphatic protons appeared as multiplets at δ 3.74-3.70 (m, 2H$_{k}$) and 3.59-3.55 (m, 4H$_{l, r}$). Protons of piperidine ring were observed at δ 2.81-2.78 (bs, 2H$_{1p, 1q}$) and 1.66-1.59 (m, 7H$_{m, n, o, 1p, 1q}$). Mass spectrum of compound (**128**) exhibited $[M+2H]^+$ peak at 590.

IR spectrum compound (**129**) displayed characteristic peaks for NH stretching at 3268 cm^{-1} and C=O stretching at 1673 cm^{-1}. In its PMR spectrum, aromatic protons offered two doublets at δ 7.51-7.49 (d, 2H$_{i, j}$, *J* = 9.2 Hz) and 7.35-7.32 (d, 2H$_{g, h}$, *J* = 8.8 Hz). A multiplet comprising of six aromatic protons was observed at δ 6.87-6.77 (m, 6H$_{c, d, e, f, s, u}$). The remaining aromatic proton appeared as multiplet at δ 6.67-6.61 (m, 1H). Six protons of methoxyl groups were observed as singlets at 3.81 (s, 6H$_{a, b}$). Two multiplets were obtained at δ 3.75-3.71 (m, 2H$_{k}$) and 3.63-3.59 (m, 2H$_{l}$) for four protons of the ethylene linker. Signals for other aliphatic protons were observed at 3.32 (s, 2H$_{r}$), 2.68-2.66 (bs, 2H$_{1p, 1q}$) and 1.69-1.58 (m, 7H$_{m, n, o, 1p, 1q}$).



(129)

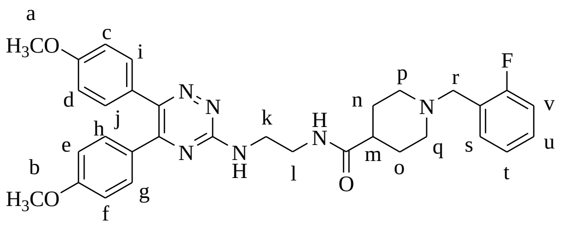


(130)

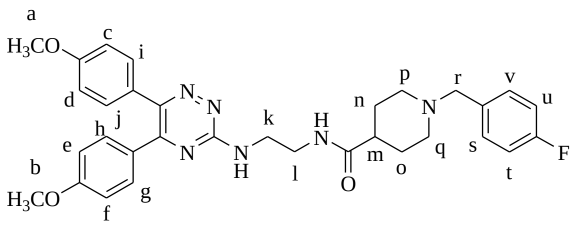
In the IR Spectrum of compound (**130**), characteristic peaks for NH stretching and C=O stretching were observed at 3337 and 1656 cm^{-1} respectively. PMR spectrum of compound (**130**) showed signals for aromatic protons as doublets at 7.49-7.48 (d, 2H$_{i, j}$, *J* = 6.8 Hz), 7.35-7.34 (d, 2H$_{g, h}$, *J* = 7.0 Hz), 7.17-7.15 (d, 2H$_{s, v}$, *J* = 6.2 Hz), 7.10-7.08 (d, 2H$_{t, u}$, *J* = 6.2 Hz), 6.87-6.85 (d, 2H$_{c, d}$, *J* = 6.8 Hz) and 6.82-6.80 (d, 2H$_{e, f}$, *J* = 7.0 Hz). Two singlets for six protons were obtained at δ 3.82 (s, 3H$_{a}$) and 3.81 (s, 3H$_{b}$). Four protons of the ethylene linker offered two multiplets at 3.75-3.72 (m, 2H$_{k}$) and 3.60-3.57 (m, 2H$_{l}$). Signals for other aliphatic protons appeared at 3.43 (s, 2H$_{r}$), 2.81 (bs, 3H$_{m, 1p, 1q}$), 2.31 (s, 3H$_{w}$) and

1.77-1.67 (m, $6H_{n, o, 1p, 1q}$). Its mass spectrum displayed the quasimolecular ion peak at 567.9 $[M+H]^+$.

Compound (**131**) offered signals at 3255 cm^{-1} for NH stretching and 1671cm^{-1} for C=O stretching in its IR spectrum. In the PMR spectrum of compound (**131**), aromatic protons were observed as a doublet at δ 7.50-7.48 (d, $2H_{i, j}$, J = 8.8 Hz), and as multiplets at δ 7.35-7.32 (m, $3H_{g, h, u}$), 7.23-7.17 (m, $1H_s$), 7.08-6.96 (m, $2H_{t, v}$) and 6.87-6.79 (m, $4H_{c, d, e, f}$). A singlet representing six protons of methoxyl groups was obtained at δ 3.82 (s, $6H_{a, b}$). Signals for four ethylene protons appeared as two multiplets at δ 3.76-3.72 (m, $2H_k$) and 3.61-3.57 (m, $2H_l$). Other aliphatic protons were seen at δ 3.48 (s, $2H_r$), 2.79 (bs, $1H_{1p}$), 2.76 (bs, $1H_{1q}$) and 1.81-1.70 (bs, $7H_{m, n, o, 1p, 1q}$).



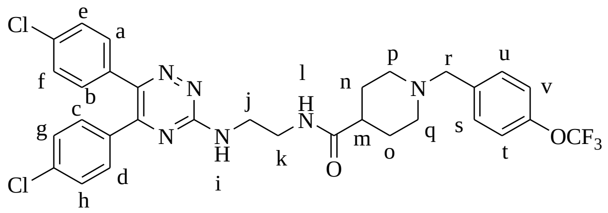
(131)



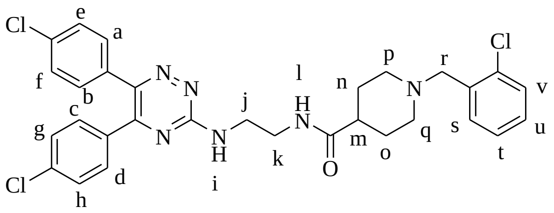
(132)

IR spectrum of compound (**132**) showed characteristic peaks for NH stretching at 3327 cm^{-1} and C=O stretching at 1653 cm^{-1}. Its PMR spectrum afforded signals for aromatic protons as a doublet at δ 7.50-7.48 (d, $2H_{i, j}$, J = 8.8 Hz) and as multiplets at δ 7.36-7.32 (m, $2H_{g, h}$), 7.22-7.18 (m, $2H_{s, v}$), 6.98-6.92 (m, $2H_{t, u}$) and 6.87-6.79 (m, $4H_{c, d, e, f}$). Among aliphatic protons, signals were observed as a singlet at δ 3.81 (s, $6H_{a, b}$) for six protons, multiplets at δ 3.76-3.72 (m, $2H_k$) and 3.61-3.57 (m, $2H_l$) for four protons of ethylene linker. Other aliphatic protons afforded peaks at δ 3.35 (s, $2H_r$), 2.74 (bs, $1H_{1p}$), 2.71 (bs, $1H_{1q}$) and 1.75-1.60 (bs, $7H_{m, n, o, 1p, 1q}$).

Compound (**133**) exhibited characteristic peaks at 3248 cm^{-1} for NH stretching and 1661 cm^{-1} for C=O stretching in the IR spectrum. Its PMR spectra displayed peaks for aromatic protons as a doublet at δ 7.43-7.41 (d, $2H_{a, b}$, J = 8.4 Hz), and as multiplets at δ 7.35-7.28 (m, $8H_{c, d, e, f, g, h, s, u}$) and 7.15-7.11 (m, $2H_{t, v}$). Two broad singlets were observed at δ 6.75 (bs, NH_l) and 6.20 (bs, NH_i) due to protons attached amidic and amine nitrogens respectively. Signals for the protons of ethylene linker appeared at δ 3.75-3.73 (m, $2H_j$) and 3.62-3.58 (m, $2H_k$) whereas signals due to other aliphatic protons were observed at δ 3.44 (s, $2H_r$), 2.81 (bs, $1H_p$), 2.79 (bs, $1H_q$) and 1.87-1.68 (m, $7H_{m, n, o, 1p, 1q}$). The mass spectrum of compound (**133**) displayed quasimolecular ion peak at 646.03 $[M+2H]^+$.



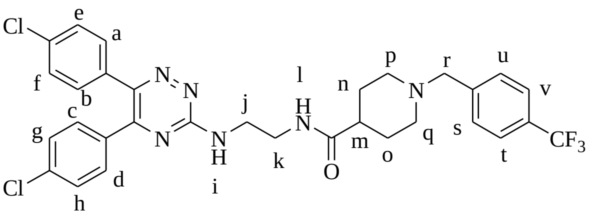
(133)



(134)

In the IR spectrum of Compound (**134**), characteristic peaks were observed at 3274 cm^{-1} for NH stretching and 1648 cm^{-1} for C=O stretching. In its PMR spectrum, a broad singlet was observed at δ 7.63 (bs, $1H_{l}$) due to amidic proton whereas signals for other aromatic protons appeared as a doublet for two protons at δ 7.42-7.40 (d, $2H_{a, b}$, J = 8.4 Hz) and a multiplet for ten protons at δ 7.35-7.21 (m, $10H_{c,d,e,f,g,h,s,t,u,v}$). Another broad singlet was seen at δ 6.91 (bs, $1H_{i}$) corresponding to the proton attached to amine nitrogen. Among the aliphatic protons, signals for two protons of ethylene linker and two benzylic protons merged together offering a multiplet at δ 3.79-3.74 (m, $4H_{j, r}$) while other two protons of ethylene linker afforded a multiplet at δ 3.61-3.57 (m, $2H_{k}$). Protons of piperidine ring were observed as a broad singlet at δ 3.05-3.02 (bs, $2H_{1p, 1q}$) and 2.17 (bs, $3H_{m, 1p, 1q}$), and a multiplet at δ 1.86-1.81 (m, $4H_{n, o}$).

IR spectrum of compound (**135**) showed characteristic peaks for NH stretching at 3292 cm^{-1} and C=O stretching at 1650 cm^{-1}. Compound (**135**) in its PMR spectrum showed peaks for aromatic protons at δ 7.54-7.52 (d, $2H_{v, t}$, J = 8.4 Hz), 7.44-7.42 (d, $2H_{a, b}$, J = 8.4 Hz), 7.39-7.36 (m, $2H_{c, d}$) and 7.33-7.29 (m, $6H_{e, f, g, h, s, u}$),. Signals were observed at δ 3.75 (bs, $2H_{j}$) and 3.64-3.61 (m, $2H_{k}$) for aliphatic protons of ethylene linker. Other aliphatic protons offered peaks at δ 3.44 (s, $2H_{r}$), 2.74 (bs, $2H_{1p, 1q}$) and 1.71-1.60 (m, $7H_{m, n, o, 1p, 1q}$).



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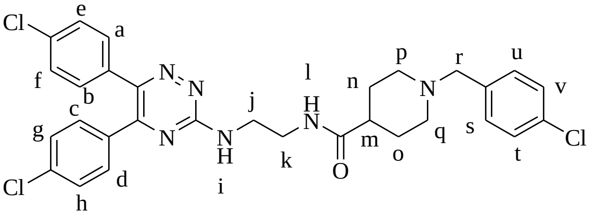
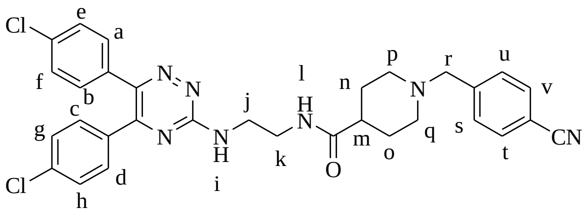


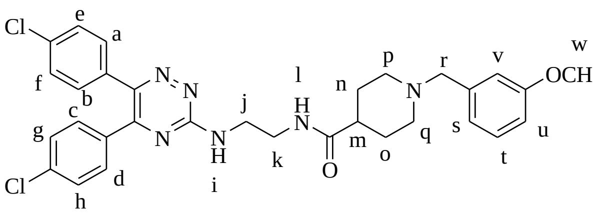
(136)

Compound (**136**) in its IR spectrum showed signals for NH stretching at 3372 cm^{-1} and C=O stretching at 1668 cm^{-1}. PMR spectrum of compound (**136**) offered aromatic protons as a doublet at δ 7.42-7.40 (d, $2H_{a, b}$, J = 8.4 Hz) and a multiplet at δ 7.34-7.29 (m, $10H_{c, d, e, f, g, h, s, t, u, v}$). Aliphatic protons were observed at δ 3.77-3.73 (m, $2H_{k}$) and 3.61-3.57

(m, $4H_{j, r}$) as multiplets. Protons of piperidine ring afforded signals as broad singlets at δ 2.95 (bs, $1H_{p}$), 2.93 (bs, $1H_{q}$) and 1.80-1.78 (bs, $7H_{m, n, o, 1p, 1q}$). Its mass spectrum displayed the molecular ion peak at 594.09 $[M]^{+}$ and 596.21 $[M+2]^{+}$.

In the IR spectrum of compound (**137**), characteristic peaks were obtained at 3353 cm^{-1} for NH stretching, 2230 cm^{-1} for CN stretching and 1659 cm^{-1} for C=O stretching. Compound (**137**) in its PMR spectrum showed a doublet at δ 7.60-7.58 (d, $2H_{t, v}$, J = 8.0 Hz) for two aromatic protons which coupled with protons observed at δ 7.41-7.39 (d, $2H_{s, u}$, J = 8.0 Hz). Other aromatic protons offered signals at δ 7.46-7.44 (d, $2H_{a, b}$, J = 7.6 Hz) and 7.35-7.32 (m, $6H_{c, d, e, f, g, h}$). Protons of ethylene linker provided signals as multiplet at δ 3.78-3.74 (m, $2H_{j}$) and 3.65-3.61 (m, $2H_{k}$) while a singlet at δ 3.46 (s, $2H_{r}$) was observed for two benzylic protons. Two broad singlets representing nine protons of piperidine ring appeared each at δ 2.74 (bs, $2H_{1p, 1q}$) and 1.78 (bs, $7H_{m, n, o, 1p, 1q}$). The mass spectrum of compound (**137**) exhibited quasimolecular ion peak at 586.96 $[M+H]^{+}$.

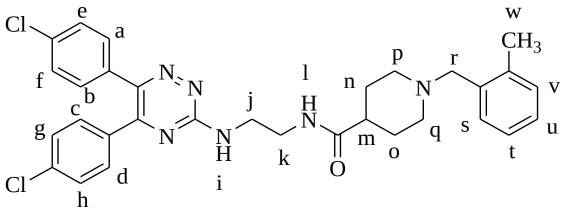




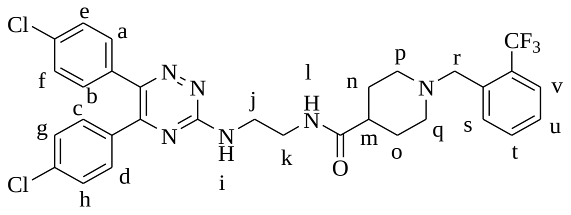
(137) **(138)**

IR spectrum of compound (**138**) offered peaks for NH stretching at 3278 cm^{-1} and C=O stretching at 1649 cm^{-1}. Its PMR spectra showed signals for aromatic protons as a doublet at δ 7.48-7.46 (d, $2H_{a, b}$, J = 6.8 Hz). A multiplet signal was observed at δ 7.39-7.36 (m, $3H_{c, d, i}$) for two aromatic protons and one proton attached to amine nitrogen ($1NH_{i}$) merged with each other. Other aromatic protons appeared as a multiplet at δ 7.32-7.28 (m, $4H_{e, f, g, h}$). Protons of phenyl ring of benzyl group gave peaks at δ 7.22-7.19 (t, $1H_{t}$, J = 7.8 Hz), 6.99 (bs, $1H_{v}$), 6.90-6.88 (d, $1H_{s}$, J = 7.8 Hz) and 6.83-6.81 (dd, $1H_{u}$, J = 2.4, 7.8 Hz). Among aliphatic protons, signal for three protons of methoxyl group merged with that of two protons of ethylene linker offering a multiplet at δ 3.79-3.74 (m, $5H_{j, w}$). Signals for other aliphatic protons were observed at δ 3.61-3.57 (m, $4H_{k, r}$), 2.95 (bs, $1H_{p}$), 2.92 (bs, $1H_{q}$), 1.79 (bs, $7H_{m, n, o, 1p, 1q}$). The mass spectrum of compound (**138**) exhibited the molecular ion peak at 590.2 $[M]^{+}$ and 592.22 $[M+2]^{+}$.

In the IR spectrum of compound (**139**), characteristic peaks were observed at 3416 cm^{-1} for NH stretching and 1642 cm^{-1} for C=O stretching. PMR spectrum of compound (**139**) showed a broad singlet at δ 8.04 (bs, NH_{l}) due to proton attached to amide nitrogen and a doublet at δ 7.46-7.44 (d, $2H_{a, b}$, J = 8.0 Hz) for two aromatic protons. Other aromatic protons offered multiplets at δ 7.36-7.30 (m, $7H_{c, d, e, f, g, h, i}$) and 7.20-7.11 (m, $4H_{s, t, u, v}$). A broad singlet appeared at δ 3.76 (bs, $2H_{j}$) for two protons of ethylene linker while other two protons afforded a multiplet at δ 3.65-3.61 (m, $2H_{k}$). Benzylic protons were observed as a singlet at δ 3.35 (s, $2H_{r}$) whereas other remaining aliphatic protons offered signals at δ 2.77 (bs, $2H_{1p, 1q}$), 2.31 (s, $3H_{w}$), 1.93 (bs, $4H_{n, o}$) and 1.62-1.56 (m, $3H_{m, 1p, 1q}$).



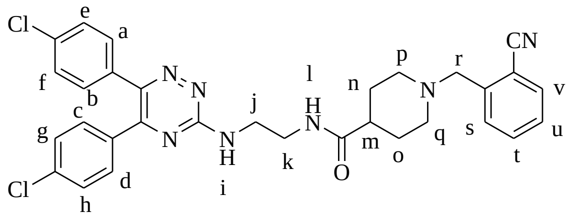
(139)



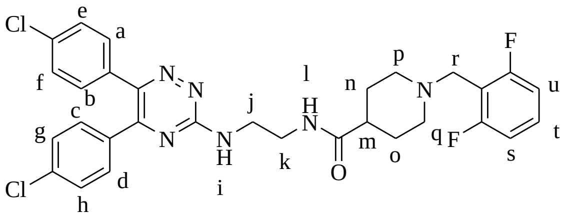
(140)

Compound (**140**) in its IR spectrum exhibited signals for NH stretching at 3292 cm^{-1} and C=O stretching at 1669 cm^{-1}. Its PMR spectra showed a doublet for an aromatic proton at δ 7.74-7.72 (d, $1H_{v}$, J = 7.7 Hz) which coupled with another proton at δ 7.59-7.57 (dd, $1H_{t}$, J = 1.5, 7.7 Hz). Other aromatic protons were observed at δ 7.48-7.42 (m, $3H_{a, b, c}$) and 7.35-7.27 (m, $7H_{d, e, f, g, h, s, u}$). Signals for four protons of ethylene linker were observed at δ 3.75-3.73 (m, $2H_{j}$) and 3.64-3.60 (m, $2H_{k}$). Other aliphatic protons afforded signals at δ 3.54 (s, $2H_{r}$), 2.76 (bs, $1H_{p}$), 2.73 (bs, $1H_{q}$) and 1.70-1.64 (bs, $7H_{m, n, o, 1p, 1q}$). Compound (**140**) displayed the quasimolecular ion peak at 629.94 $[M+H]^{+}$ in the mass spectrum.

IR spectrum of compound (**141**) displayed characteristic peaks at 3277 cm^{-1} for NH stretching and 1648 cm^{-1} for C=O stretching. In the PMR spectrum of compound (**141**), aromatic protons were observed at δ 7.61-7.60 (d, $1H_{v}$, J = 7.6 Hz), 7.53-7.51 (m, $2H_{t, u}$), 7.44-7.42 (d, $2H_{a, b}$, J = 8.0 Hz) and 7.36-7.30 (m, $7H_{c, d, e, f, g, h, s}$) whereas aliphatic protons offered peaks at δ 3.76-3.72 (m, $2H_{j}$) and 3.63-3.60 (m, $4H_{k, r}$). Protons of piperidine ring gave broad singlets at δ 2.78-2.75 (bs, $2H_{1p, 1q}$), 1.85 (bs, $3H_{1m, 1p, 1q}$) and 1.63 (bs, $4H_{n, o}$).



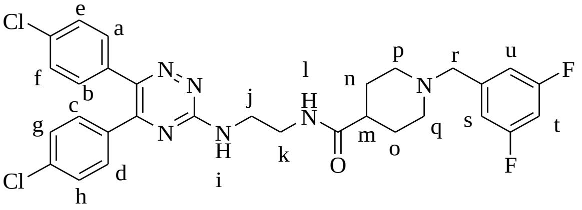
(141)



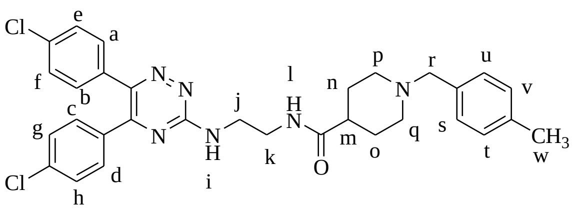
(142)

Characteristic peaks were observed at 3289 cm^{-1} for NH stretching and 1658 cm^{-1} for C=O stretching in the IR spectrum of compound (**142**). Its PMR spectrum offered signals as a doublet at δ 7.44-7.42 (d, 2H$_{a, b}$, J = 8.0 Hz) and multiplets at δ 7.34-7.27 (m, 6H$_{c, d, e, f, g, h}$), 7.25-7.20 (m, 1H$_{t}$) and 6.89-6.82 (m, 2H$_{s, u}$). Among aliphatic protons, peaks appeared at δ 3.72 (bs, 2H$_{j}$) and 3.61-3.59 (m, 4H$_{k, r}$) for protons of ethylene linker and benzylic protons. Peaks for protons of piperidine ring were observed at δ 2.81 (bs, 2H$_{1p, 1q}$), 2.09-2.04 (m, 1H$_{m}$) and 1.62-1.52 (m, 6H$_{n, o, 1p, 1q}$). Mass spectrum of compound (**142**) showed quasimolecular ion peak at 599.96 [M+3H]$^{+}$.

In the IR spectrum of compound (**143**), characteristic peaks were observed at 3290 cm^{-1} for NH stretching and 1647 cm^{-1} for C=O stretching. PMR spectrum of compound (**143**) displayed peaks for aromatic protons at δ 7.44-7.42 (d, 2H$_{a, b}$, J = 8.4 Hz) as a doublet, and 7.36-7.30 (m, 6H$_{c, d, e, f, g, h}$), 6.83-6.78 (m, 2H$_{s, u}$) and 6.69-6.64 (m, 1H$_{t}$) as multiplets. Aliphatic protons of ethylene linker appeared as a broad singlet at δ 3.75 (bs, 2H*j*) and a multiplet at δ 3.63-3.59 (m, 2H$_{k}$). A singlet was seen at δ 3.37 (s, 2H$_{r}$) representing two benzylic protons. Protons of piperidine ring were observed as two broad singlets at δ 2.77-2.74 (bs, 2H$_{1p, 1q}$) and 1.79-1.65 (bs, 7H$_{m, n, o, 1p, 1q}$).



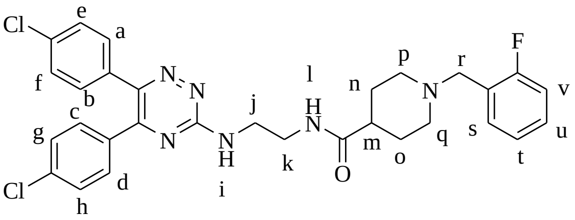
(143)



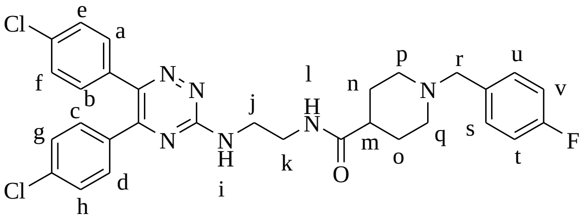
(144)

IR spectrum of compound (**144**) exhibited characteristic peaks for NH stretching at 3275 cm^{-1} and C=O stretching at 1667 cm^{-1}. In its PMR spectrum, aromatic protons offered signals at δ 7.43-7.40 (d, 2H$_{a, b}$, J = 8.4 Hz) and 7.35-7.29 (m, 6H$_{c, d, e, f, g, h}$). Four aromatic protons at δ 7.16-7.13 (d, 2H$_{s, u}$, J = 8.2 Hz) and 7.11-7.09 (d, 2H$_{t, v}$, J = 8.2 Hz) showed *ortho* coupling with a coupling constant of 8.2. Two signals were seen for aliphatic protons of ethylene linker at δ 3.75 (bs, 2H$_{j}$) and 3.62-3.57 (m, 2H$_{k}$). Other aliphatic protons gave signal at δ 3.41 (s, 2H$_{w}$) for benzylic protons, 2.83-2.80 (bs, 2H$_{1p, 1q}$) for piperidine protons, 2.32 (s, 3H$_{w}$) for methyl protons and 1.81 (bs, 7H$_{m, n, o, 1p, 1q}$) for piperidine protons. Mass spectrum of compound (**144**) displayed quasimolecular ion peak at 575.98 [M+H]$^{+}$.

Compound (**145**) in its IR spectrum gave characteristic peaks at 3280 cm^{-1} for NH stretching and 1646 cm^{-1} for C=O stretching. PMR spectrum of compound (**145**) gave signals for aromatic protons of vicinal diaryl groups as a doublet at δ 7.43-7.41 (d, $2H_{a, b}$, J = 8.0 Hz) and a multiplet at δ 7.35-7.28 (m, $6H_{c, d, e, f, g, h}$). Other aromatic protons appeared as multiplets at δ 7.25-7.20 (m, $2H_{s, u}$), 7.10-7.06 (m, $1H_t$) and 7.03-6.98 (m, $1H_v$). Among aliphatic protons, signals were observed at δ 3.75 (bs, $2H_j$) and 3.62-3.58 (m, $2H_k$) representing four protons of ethylene linker whereas two benzylic protons offered a singlet at δ 3.51 (s, $2H_r$). Other aliphatic protons of piperidine ring displayed broad singlets at δ 2.84-2.81 (bs, $2H_{1p, 1q}$) and 1.71 (bs, $7H_{m, n, o, 1p, 1q}$). Its mass spectrum showed quasimolecular ion peak at 579.91 $[M+2H]^+$.



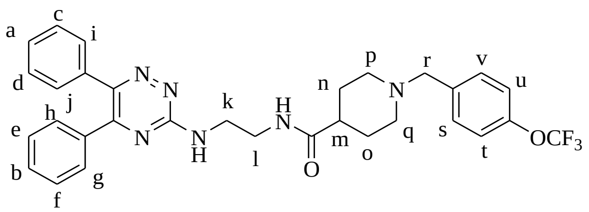
(145)

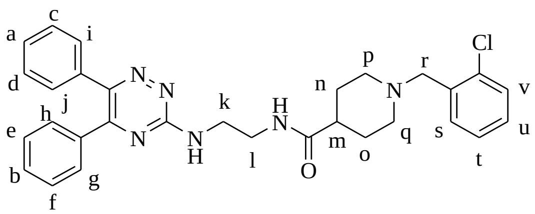


(146)

Compound (**146**) in its IR spectrum displayed characteristic peaks for NH stretching at 3263 cm^{-1} and C=O stretching at 1668 cm^{-1}. Its PMR spectra offered signals for aromatic protons as a doublet at δ 7.42-7.40 (d, $2H_{a, b}$, J = 8.0 Hz), and multiplets at δ 7.34-7.28 (m, $8H_{c, d, e, f, g, h, s, u}$) and 7.02-6.95 (m, $2H_{t, v}$). Among aliphatic protons, signals for protons of ethylene linker appeared as a multiplet at δ 3.76-3.72 (m, $2H_j$) for two protons while signals for other two protons of ethylene linker merged with signals of two benzylic protons offering a multiplet at δ 3.63-3.56 (m, $4H_{k, r}$). Signals for other aliphatic protons were obtained at δ 3.00-2.95 (m, $2H_{1p, 1q}$), 2.21-2.17 (bs, $3H_{m, 1p, 1q}$) and 1.85-1.80 (bs, $4H_{n, o}$).

IR spectrum of compound (**147**) showed NH and C=O stretchings at 3314 and 1663 cm^{-1} respectively. Its PMR spectrum showed signals for aromatic protons as a doublet at δ 7.49-7.47 (d, $2H_{i, j}$, J = 7.7 Hz), multiplets at δ 7.41-7.37 (m, $3H_{g, h, s}$) and 7.33-7.25 (m, $7H_{a, b, c, d, e, f, v}$) and a doublet at δ 7.12-7.10 (d, $2H_{t, u}$, J = 8.0 Hz). Two multiplet signals appeared at δ 3.78-3.74 (m, $2H_k$) and 3.64-3.60 (m, $2H_l$) comprising four protons of ethylene linker. Other aliphatic protons were observed at δ 3.37 (s, $2H_r$), 2.72 (bs, $1H_p$), 2.69 (bs, $1H_q$) and 1.87-1.77 (bs, $7H_{m, n, o, 1p, 1q}$). The molecular ion peak was observed at 576.16 $[M]^+$ in its mass spectrum.

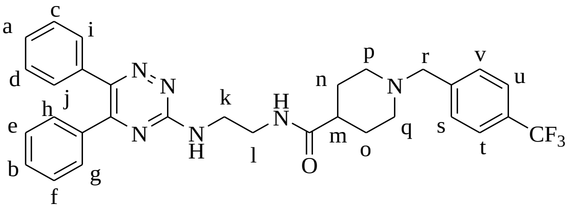


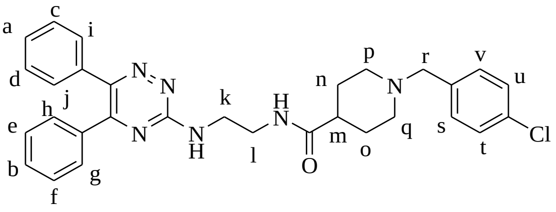


(147) **(148)**

In the IR spectrum of compound (**148**), characteristic peaks were obtained at 3318 cm^{-1} for NH stretching and 1659 cm^{-1} for C=O stretching. Compound (**148**) in its PMR spectrum afforded a doublet at δ 7.50-7.48 (d, $2H_{i, j}$, J = 6.8 Hz). Other aromatic protons were observed as multiplets at δ 7.41-7.37 (m, $4H_{g, h, s, v}$), 7.33-7.27 (m, $6H_{a, b, c, d, e, f}$) and 7.20-7.12 (m, $2H_{t, u}$). Four protons of ethylene linker afforded multiplets at δ 3.78-3.74 (m, $2H_{k}$) and 3.64-3.60 (m, $2H_{l}$). Signals for other aliphatic protons appeared at δ 3.48 (s, $2H_{r}$), 2.75 (bs, $1H_{p}$), 2.72 (bs, $1H_{q}$), 1.87 (bs, $3H_{m, 1p, 1q}$) and 1.66-1.58 (m, $4H_{n. o}$).

Compound (**149**) displayed characteristic peaks for NH stretching at 3317 cm^{-1} and C=O stretching at 1671 cm^{-1} in its IR spectrum. Its PMR spectrum offered signals for aromatic protons as doublets at δ 7.53-7.51 (d, $2H_{t, u}$, J = 8.0 Hz) and 7.48-7.46 (d, $2H_{i, j}$, J = 6.8 Hz). Other aromatic protons gave multiplets at δ 7.40-7.35 (m, $4H_{g, h, s, v}$) and 7.34-7.25 (m, $6H_{a, b, c, d, e, f}$). Among aliphatic protons, four protons of ethylene linker showed multiplets at δ 3.80-3.76 (m, $2H_{k}$) and 3.63-3.59 (m, $2H_{l}$). Remaining aliphatic protons showed signals at δ 3.44 (s, $2H_{r}$), 2.74 (bs, $1H_{p}$), 2.71 (bs, $1H_{q}$) and 1.62 (bs, $7H_{m, n, o, 1p, 1q}$). The mass spectrum of compound (**149**) exhibited $[M]^+$ peak at 560.18.

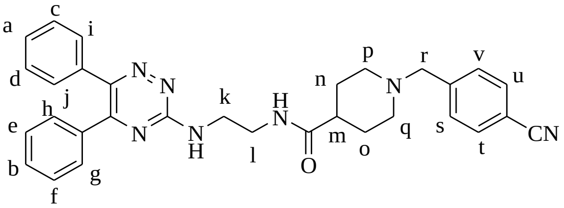




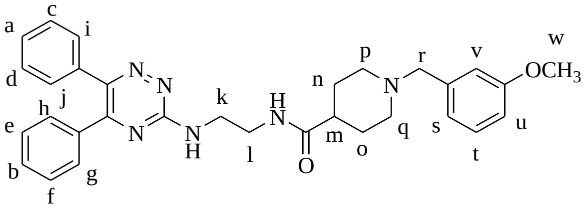
(149) **(150)**

IR spectrum of the compound (**150**) exhibited signals for NH stretching at 3414 cm^{-1} and C=O stretching at 1659 cm^{-1}. Its ^{1}H-NMR spectrum gave doublet for two protons at δ 7.49-7.47 (d, $2H_{i, j}$, J = 7.2 Hz), multiplets at δ 7.41-7.37 (m, $3H_{g, h, f}$) and 7.34-7.27 (m, $5H_{a, b, c, d, e}$). A doublet was observed at δ 7.24-7.22 (d, $2H_{t, u}$, J = 7.4 Hz) for two protons which coupled with protons at δ 7.18-7.16 (d, $2H_{s, v}$, J = 7.4 Hz). Aliphatic protons appeared as multiplets at δ 3.78-3.74 (m, $2H_{k}$) and 3.63-3.59 (m, $2H_{l}$). Other aliphatic protons offered signals at δ 3.33 (s, 2H$_{r}$), 2.70 (bs, 1H$_{p}$), 2.67 (bs, 1H$_{q}$) and 1.86-1.74 (bs, 7H$_{m, n, o, 1p, 1q}$). The mass spectrum of compound (**150**) showed [M]$^{+}$ peak at 526.05 and [M+2H]$^{+}$ peak at 528.14.

Compound (**151**) showed characteristic peaks for NH stretching at 3280 cm^{-1} and C=O stretching at 1652 cm^{-1} in its IR spectrum. PMR spectrum of compound (**151**) afforded doublets for four aromatic protons at 7.57-7.55 (d, 2H$_{t, u}$, J = 7.6 Hz) and 7.48-7.46 (d, 2H$_{i, j}$, J = 7.2 Hz). Other aromatic protons were obtained as multiplets at δ 7.42-7.36 (m, 4H$_{g, h, s, v}$) and 7.34-7.27 (m, 6H$_{a, b, c, d, e, f}$). Among aliphatic protons, four protons of ethylene linker gave multiplets at δ 3.78-3.74 (m, 2H$_{k}$) and 3.63-3.59 (m, 2H$_{l}$). Remaining aliphatic protons appeared as broad singlets at δ 3.52 (s, 2H$_{r}$), 2.77 (bs, 2H$_{1p, 1q}$) and 1.95-1.68 (bs, 7H$_{m, n, o, 1p, 1q}$).



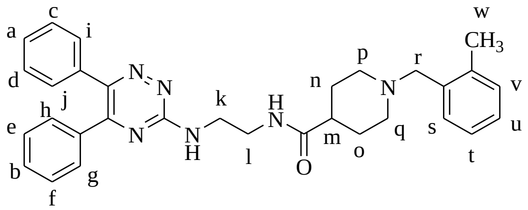
(151)



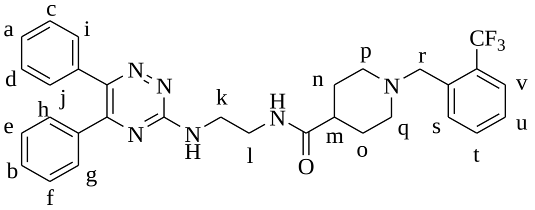
(152)

In the IR spectrum of compound (**152**), peaks for NH stretching and C=O stretching appeared at 3248 and 1651 cm^{-1} respectively. Its PMR spectrum gave signals for aromatic protons as a doublet at δ 7.49-7.46 (d, 2H$_{i, j}$, J = 8.0 Hz), and multiplets at δ 7.40-7.37 (m, 3H$_{g, h, f}$), 7.32-7.27 (m, 5H$_{a, b, c, d, e}$). Other aromatic protons provided signals at δ 7.20-7.16 (t, 1H$_{t}$, J = 8.0 Hz) and 6.83-6.75 (m, 3H$_{s, u, v}$). In aliphatic protons, signals for three protons of methoxyl group merged with that of two protons of ethylene linker offering a multiplet at δ 3.79-3.74 (m, 5H$_{k, w}$). Other aliphatic protons afforded a multiplet at δ 3.63-3.59 (m, 2H$_{l}$), a singlet at δ 3.37 (s, 2H$_{r}$), and broad singlets at δ 2.76 (bs, 1H$_{p}$), 2.73 (bs, 1H$_{q}$) and 1.73-1.61 (bs, 7H$_{m, n, o, 1p, 1q}$). It showed a molecular ion peak at 522.17 [M]$^{+}$ in its mass spectrum.

IR spectrum of compound (**153**) showed characteristic peaks for NH stretching at 3302 cm^{-1} and C=O stretching at 1661 cm^{-1}. Its PMR spectrum offered signals for aromatic protons as a doublet at δ 7.47-7.45 (d, 2H$_{i, j}$, J = 7.2 Hz), and multiplets at δ 7.39-7.36 (m, 2H$_{g, h}$), 7.33-7.26 (m, 6H$_{a, b, c, d, e, f}$) and 7.22-7.12 (m, 4H$_{s, t, u, v}$). Signals for aliphatic protons were observed as multiplets at δ 3.78-3.74 (m, 4H$_{k, r}$) and 3.60-3.56 (m, 2H$_{l}$) whereas other aliphatic protons appeared at δ 3.04 (bs, 2H$_{1p, 1q}$), 2.34 (s, 3H$_{w}$) and 1.83-1.72 (bs, 7H$_{m, n, o, 1p, 1q}$).



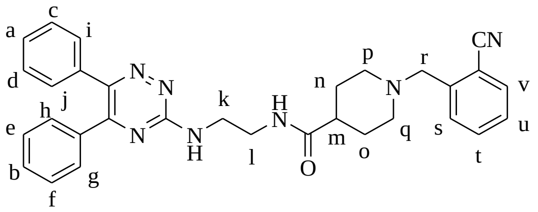
(153)



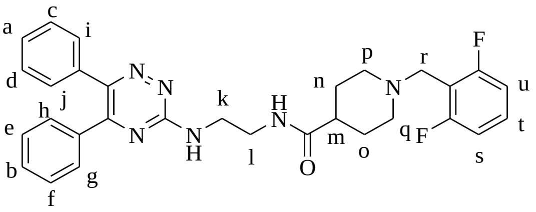
(154)

Compound (**154**) in its IR spectra displayed characteristic peaks for the NH stretching at 3296 cm^{-1} and C=O stretching at 1663 cm^{-1}. Its PMR spectrum showed signals for aromatic protons as doublets at δ 7.74-7.72 (d, 1H$_{v}$, J = 7.6 Hz) and 7.59-7.57 (d, 1H$_{t}$, J = 8.0 Hz). Other aromatic protons offered multiplets at δ 7.50-7.37 (m, 6H$_{g, h, i, j, s, u}$) and 7.34-7.26 (m, 6H$_{a, b, c, d, e, f}$). Four aliphatic protons of ethylene linker were observed as multiplets at δ 3.79-3.75 (m, 2H$_{k}$) and 3.65-3.61 (m, 2H$_{l}$). Other aliphatic protons were observed as singlet at δ 3.51 (s, 2H$_{r}$), broad singlets at δ 2.71 (bs, 1H$_{p}$) and 2.68 (bs, 1H$_{q}$), and a multiplet at δ 1.78-1.58 (m, 7H$_{m, n, o, 1p, 1q}$).

In the IR spectrum of compound (**155**), peaks were obtained at 3248 cm^{-1} for NH stretching, 2223 cm^{-1} for CN stretching and 1667 cm^{-1} for C=O stretching. PMR spectrum of **155** afforded a doublet at δ 7.60-7.58 (d, 1H$_{v}$, J = 7.6 Hz) for one aromatic proton whereas other aromatic protons appeared as multiplets at δ 7.51-7.47 (m, 4H$_{g, h, i, j}$), 7.42-7.38 (m, 3H$_{s, t, u}$) and 7.34-7.28 (m, 6H$_{a, b, c, d, e, f}$). Signals for four aliphatic protons of ethylenic spacer were observed at δ 3.78-3.74 (m, 2H$_{k}$) and 3.64-3.60 (m, 2H$_{l}$). Peaks at δ 3.56 (s, 2H$_{r}$), 2.72 (bs, 1H$_{p}$), 2.69 (bs, 1H$_{q}$), and 1.81-1.63 (m, 7H$_{m, n, o, 1p, 1q}$) represented the remaining aliphatic protons. In the mass spectrum of compound (**155**), molecular ion peak was obtained at 517.05 [M]$^{+}$.



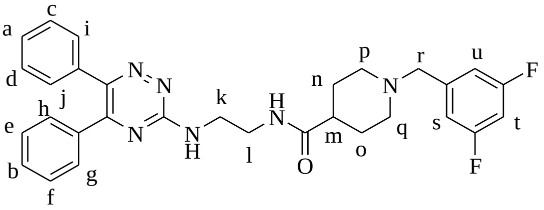
(155)



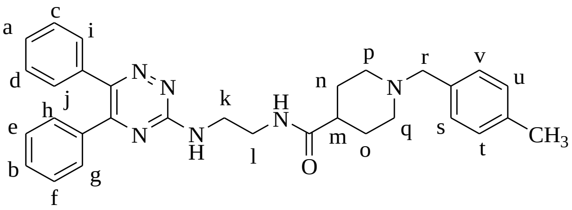
(156)

IR spectrum of compound (**156**) offered peaks for NH stretching at 3269 cm^{-1} and for C=O stretching at 1670 cm^{-1}. Its PMR spectra showed signals for aromatic protons as doublets at δ 7.49-7.47 (d, 2H$_{i, j}$, J = 7.2 Hz) and 7.38-7.36 (d, 2H$_{g, h}$, J = 7.0 Hz). Other aromatic protons were observed as multiplets at δ 7.32-7.24 (m, 6H$_{a, b, c, d, e, f}$), 7.23-7.17 (m, 1H$_{t}$) and 6.88-6.81 (m, 2H$_{s, u}$). Among aliphatic protons, signals for protons of ethylene spacer and benzyl group appeared as multiplets at δ 3.76-3.72 (m, 2H$_k$) and 3.61-3.58 (m, 4H$_{l, r}$). Other peaks were obtained at δ 2.77 (bs, 1H), 2.75 (bs, 1H) and 1.74-1.56 (m, 7H) for remaining aliphatic protons.

Characteristic peaks were observed for NH stretching at 3266 cm^{-1} and C=O stretching at cm^{-1} in the IR spectrum of compound (**157**) whereas its PMR spectra offered two doublets at δ 7.49-7.47 (d, 2H$_{i, j}$, *J* = 7.2 Hz) and 7.40-7.38 (d, 2H$_{g, h}$, *J* = 7.2 Hz) for aromatic four protons. Three multiplet signals were obtained for remaining aromatic protons at δ 7.34-7.28 (m, 6H$_{a, b, c, e, f}$), 6.80-6.78 (m, 2H$_{s, u}$) and 6.68-6.62 (m, 1H). Aliphatic protons afforded multiplets at δ 3.79-3.75 (m, 2H$_k$) and 3.64-3.60 (m, 2H$_l$). Other aliphatic protons appeared as a singlet at δ 3.34 (s, 2H$_r$), and broad singlets at δ 2.70 (bs, 1H$_p$), 2.68 (bs, 1H$_q$) and 1.71-1.61 (bs, 7H$_{m, n, o, 1p, 1q}$). In the mass spectrum of compound (**157**), molecular ion peak was observed at 528.03 [M]$^+$.



(157)

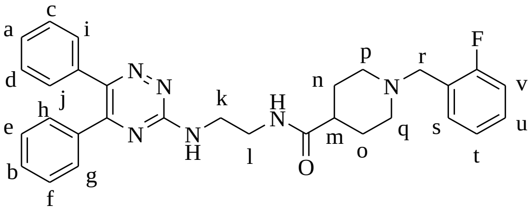


(158)

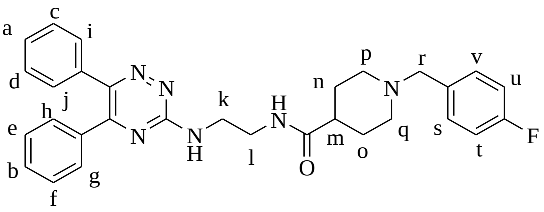
Compound (**158**) in its IR spectrum showed peaks for NH stretching at 3275 cm^{-1} and C=O stretching at 1668 cm^{-1}. ^{1}H-NMR spectrum of compound (**158**) gave signals for aromatic protons as a doublet at δ 7.48-7.46 (d, 2H$_{i, j}$, *J* = 7.0 Hz), and multiplets at δ 7.39-7.36 (m, 2H$_{g, h}$) and 7.33-7.26 (m, 6H$_{a, b, c, d, e, f}$). Four protons of substituted benzyl group appeared as two doublets at δ 7.18-7.16 (d, 2H$_{s, v}$, *J* = 7.6 Hz) and 7.10-7.08 (d, 2H$_{t, u}$, *J* = 7.6 Hz) showing *ortho* coupling with a coupling constant of 7.6 Hz. Two multiplets at δ 3.77-3.73 (m, 2H$_k$) and 3.62-3.57 (m, 2H$_l$) were observed due to four aliphatic protons of ethylene spacer whereas other aliphatic protons afforded signals at δ 3.48 (s, 2H$_r$), 2.85 (bs, 1H), 2.82 (bs, 1H), 2.31 (s, 3H) and 1.68 (bs, 7H).

In the IR spectrum of compound (**159**), characteristic peaks were observed at 3314 cm^{-1} for NH stretching and 1662 cm^{-1} for C=O stretching. Its PMR spectra showed doublets for five aromatic protons at δ 7.49-7.47 (d, 2H$_{i, j}$, *J* = 7.6 Hz) and 7.39-7.37 (d, 3H$_{g, h, s}$, *J* = 7.4 Hz). A multiplet was seen for six aromatic protons at δ 7.33-7.27 (m, 6H$_{a, b, c, d, e, f}$) while three protons of substituted benzyl group offered multiplets at δ 7.23-7.17 (m, 1H$_u$), 7.08-7.04 (m, 1H$_v$) and 7.01-6.96 (m, 1H$_t$). Protons of ethylene linker showed multiplets at δ 3.77-

3.73 (m, $2H_k$) and 3.63-3.59 (m, $2H_l$). Benzylic protons afforded a singlet peak at δ 3.46 (s, $2H_r$) whereas piperidine protons provided broad singlets at δ 2.75 (bs, $1H_p$), 2.72 (bs, $1H_q$), 1.74-1.58 (bs, $7H_{m, n, o, 1p, 1q}$).



(159)

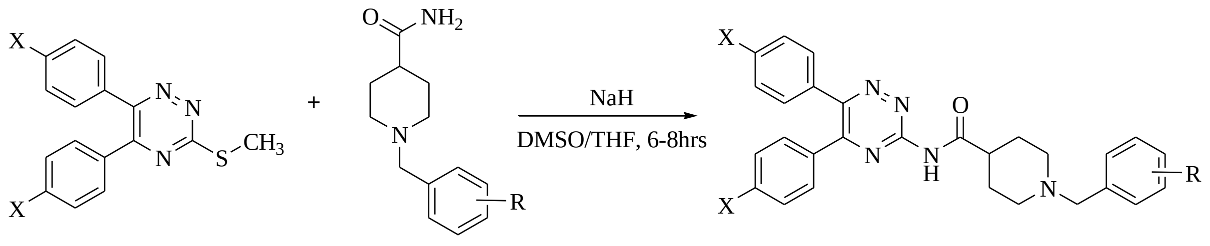


(160)

IR spectrum of compound (**160**) displayed characteristic peaks at 3259 cm^{-1} for NH stretching and 1665 cm^{-1} for C=O stretching. In its PMR spectrum, peaks for aromatic protons were obtained as a doublet at 7.49-7.47 (d, $2H_{i, j}$, J = 7.2 Hz) and a multiplet at δ 7.41-7.37 (m, $3H_{f, g, h}$). Multiplets for other aromatic protons appeared at δ 7.34-7.27 (m, $5H_{a, b, c, d, e}$), 7.22-7.17 (m, $2H_{s, v}$) and 6.98-6.93 (m, $2H_{t, u}$). Four protons of ethylene linker afforded signals at δ 3.78-3.74 (m, $2H_k$) and 3.63-3.59 (m, $2H_l$). A singlet was obtained for methylene protons of benzyl group at δ 3.35 (s, $2H_r$) whereas protons of piperidine ring offered broad singlets at δ 2.73 (bs, $1H_p$) and 2.70 (bs, $1H_q$), and a multiplet at δ 1.77-1.60 (m, $7H_{m, n, o, 1p, 1q}$). Compound (**160**) exhibited molecular ion peak at 510.18 $[M]^+$.

4.1.1.10 Synthesis of *N*-(5,6-diaryl-1,2,4-triazin-3-yl)-1-benzylpiperidine-4-carboxamides (161-194)

As shown in **scheme-10**, 3-(methylthio)-5,6-diaryl-1,2,4-triazines (**89-91**) were treated with 1-substituted benzylpiperidine-4-carboxamides (**94-107**) in presence of sodium hydride and DMSO/THF to obtain the final compounds, *N*-(5,6-diaryl-1,2,4-triazin-3-yl)-1-benzylpiperidine-4-carboxamides (**161-194**).

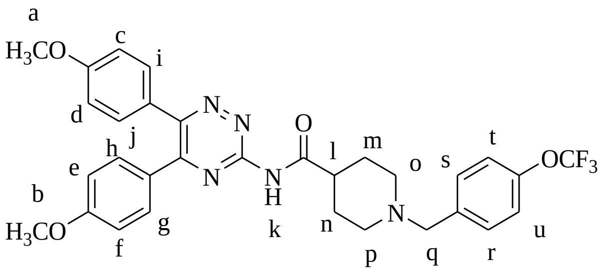


(89-91) **(94-107)** **(161-194)**

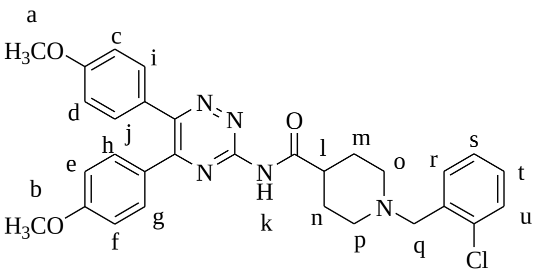
(89, 161-174) X = OCH_3
(90, 175-180) X = Cl
(91, 181-194) X = H

Scheme- 10

Compound (**161**) in its IR spectrum showed characteristic peaks for NH stretching at 3210 cm^{-1} and for C=O stretching at 1725 cm^{-1}. Its PMR spectrum gave a signal at δ 9.26 (s, NH$_{k}$) for the amidic proton. A doublet was obtained at δ 7.65-7.62 (d, 2H$_{i,\ j}$, *J* = 9.4 Hz) for two aromatic protons which coupled with other protons at δ 6.84-6.82 (d, 2H$_{c,\ d}$, *J* = 9.4 Hz). Another set of aromatic protons showing *ortho* coupling offered signals at δ 7.50-7.47 (d, 2H$_{g,\ h}$, *J* = 9.2 Hz) and 6.94-6.91 (d, 2H$_{e,\ f}$, *J* = 9.2 Hz) which coupled with each other. Signals for aromatic protons of benzyl group were observed as doublets at δ 7.35-7.32 (d, 2H, *J* = 7.7 Hz) and 7.16-7.14 (d, 2H, *J* = 7.7 Hz). Among the aliphatic protons, six protons of two methoxyl groups afforded singlets at δ 3.85 (s, 3H$_{a}$) and 3.83 (s, 3H$_{b}$). Other aliphatic protons appeared as a singlet at δ 3.44 (s, 2H$_{q}$), a broad singlet at δ 3.03 (bs, 1H$_{l}$), and multiplets at δ 2.92-2.88 (m, 2H$_{1o,\ 1p}$) and 2.04-1.97 (m, 6H$_{m,\ n,\ 1o,\ 1p}$). Mass spectrum of compound (**161**) displayed quasimolecular ion peak at 594.1 [M+H]$^{+}$.



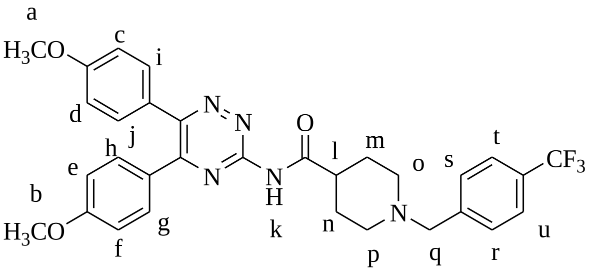
(161)



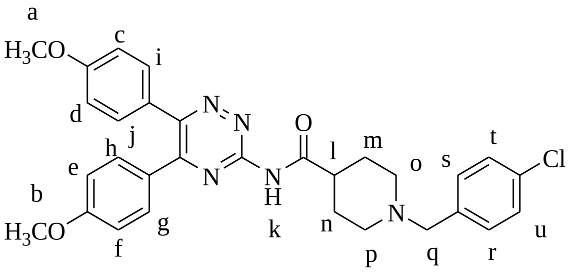
(162)

In the IR spectrum of compound (**162**), characteristic peaks were observed at 3203 cm^{-1} for NH stretching and 1722 cm^{-1} for C=O stretching. PMR spectrum of compound (**162**) showed a broad singlet at δ 9.94 (s, NH$_{k}$) due to proton attached to amide nitrogen. Aromatic protons were observed to couple with each other giving several doublets at δ 7.67-7.65 (d, 2H$_{i,\ j}$, *J* = 6.8 Hz), 7.51-7.49 (d, 2H$_{g,\ h}$, *J* = 6.8 Hz), 6.94-6.92 (d, 2H$_{e,\ f}$, *J* = 6.8 Hz) and 6.84-6.82 (d, 2H$_{c,\ d}$, *J* = 6.8 Hz). One of the aromatic protons of phenyl ring of benzyl group offered a signal at δ 7.33-7.31 (dd, 1H$_{u}$, *J* = 1.4, 7.6 Hz) while other protons appeared as a multiplet at δ 7.25-7.14 (m, 3H$_{r,\ s,\ t}$). Signals for aliphatic protons of methoxyl groups were obtained at δ 3.84 (s, 3H$_{a}$) and 3.82 (s, 3H$_{b}$). A singlet was observed at δ 3.56 (s, 2H$_{q}$) due to benzylic protons whereas protons of piperidine ring afforded signals at δ 2.96-2.91 (m, 3H$_{l,\ 1p,\ 1q}$) and 1.99-1.94 (m, 6H$_{m,\ n,\ 1o,\ 1p}$). Compound (**162**) displayed quasimolecular ion peak at 544.4 [M+H]$^{+}$ and [M+2]$^{+}$ at 545.4.

Characteristic peaks for NH stretching at 3215 cm^{-1} and C=O stretching at 1720 cm^{-1} were observed in the IR spectrum of compound (**163**). Its PMR spectra offered a broad singlet at δ 8.59 (s, NH_k) for amidic proton. Signals for aromatic protons were observed as multiplets at δ 7.63-7.56 (m, $4H_{i, j, t, u}$) and 7.50-7.44 (m, $4H_{g, h, r, s}$). Two doublets were obtained at δ 6.93-6.91 (d, $2H_{e, f}$, J = 6.6 Hz) and 6.85-6.83 (d, $2H_{c, d}$, J = 7.0 Hz) for other aromatic protons. Six aliphatic protons of methoxyl groups appeared as singlets at δ 3.85 (s, $3H_a$) and 3.83 (s, $3H_b$). A singlet was seen at δ 3.55 (s, $2H_q$) due to methylene protons while protons of piperidine ring exhibited signals at δ 3.03 (bs, $1H_l$), 2.94 (bs, $1H_o$), 2.92 (bs, $1H_p$), 2.13-2.07 (m, $2H_{1o, 1p}$) and 1.99-1.94 (m, $4H_{m, n}$). Mass spectrum of compound (**163**) showed quasimolecular ion peak at 578.2 $[M+H]^+$.



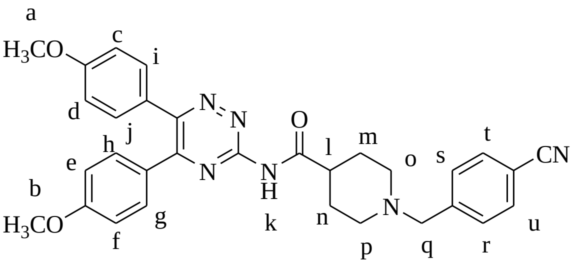
(163)



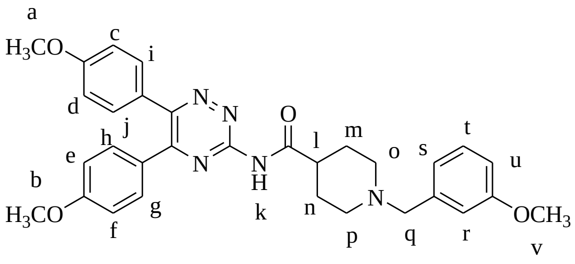
(164)

IR spectrum of compound (**164**) displayed the characteristic peaks for NH stretching at 3181 cm^{-1} and for C=O stretching at 1698 cm^{-1}. In its PMR spectra, a broad singlet was observed at δ 8.88 (s, NH_k) for proton attached to amide nitrogen. Aromatic protons at δ 7.63-7.61 (d, $2H_{i, j}$, J = 8.8 Hz) coupled with protons at δ 6.84-6.82 (d, $2H_{c, d}$, J = 8.8 Hz) whereas other aromatic protons at δ 7.49-7.47 (d, $2H_{g, h}$, J = 8.8 Hz) and 6.93-6.91 (d, $2H_{e, f}$, J = 8.8 Hz) showed ortho coupling. Aromatic protons of benzyl group appeared at δ 7.29-7.27 (m, $4H_{r, s, t, u}$). Among aliphatic protons, six protons afforded two singlets at δ 3.85 (s, $3H_a$) and 3.83 (s, $3H_b$). Methylene protons of benzyl group appeared as singlet at δ 3.46 (s, $2H_q$) while protons of piperidine ring gave signals at δ 3.01 (bs, $1H_l$), 2.94-2.91 (bs, $2H_{o, p}$), 2.07-2.04 (bs, $2H_{o, p}$) and 1.971.95 (m, $4H_{m, n}$).

Compound (**165**) showed characteristic peaks at 3198 cm^{-1} for NH stretching, 2225 cm^{-1} for CN stretching and 1721 cm^{-1} for C=O stretching in its IR spectrum. Its PMR spectra offered signal for amidic proton at δ 8.95 (s, 1H) as a broad singlet while aromatic protons were observed as multiplets at δ 7.64-7.59 (m, $4H_{i, j, t, u}$) and 7.49-7.43 (m, $4H_{g, h, r, s}$). Signals were obtained at δ 6.93-6.91 (d, $2H_{e, f}$, J = 8.8 Hz) and 6.85-6.83 (d, $2H_{c, d}$, J = 8.8 Hz) for four aromatic protons. Signals appeared at δ 3.85 (s, $3H_a$) and 3.83 (s, $3H_b$) due to protons of methoxyl groups. Other aliphatic protons afforded signals at δ 3.51 (s, $2H_q$), 3.05 (bs, $1H_l$), 2.90-2.87 (m, 2H*o, p*) and 2.03-1.93 (m, 6H*m, n, 1o, 1p*). Mass spectrum of compound (**165**) displayed the quasimolecular ion peak at 535.2 $[M+H]^+$.

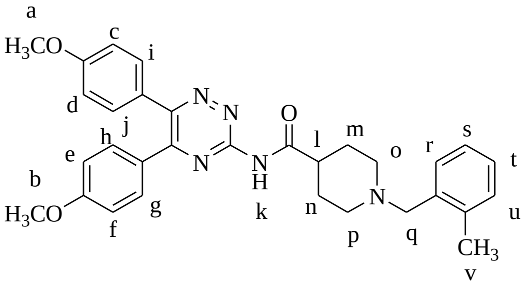


(165)



(166)

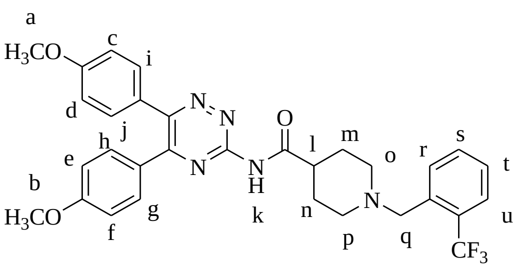
In the IR spectrum of compound (**166**), peaks were observed for NH stretching at 3194 cm-1 and C=O stretching at 1691 cm-1. PMR spectra of compound (**166**) showed a broad singlet at 8.97 (bs, NH*k*) due to amidic proton. Aromatic protons were observed as doublets at δ 7.68-7.66 (d, 2H*i, j*, *J* = 9.4 Hz) and 7.54-7.52 (d, 2H*g, h*, *J* = 9.4 Hz). A triplet appeared at δ 7.29-7.25 (t, 1H*t*, *J* = 7.8 Hz) for one aromatic proton whereas other aromatic protons afforded multiplets at δ 6.99-6.94 (m, 4H*e, f, r, u*) and 6.90-6.83 (m, 3H*c, d, s*). Nine protons of three methoxyl groups offered singlets at δ 3.90 (s, 3H*a*), 3.88 (s, 3H*b*) and 3.86 (s, 3H*v*). Signals for other aliphatic protons were obtained at δ 3.53 (s, 2H*q*) as a singlet, 3.03-3.00 (bs, 3H*l, 1o, 1p*) as a broad singlet and 2.13-1.99 (m, 6H*m, n, 1o, 1p*) as a multiplet. Compound (**166**) in its mass spectrum exhibited quasimolecular ion peak at 540.2 $[M+H]^+$.



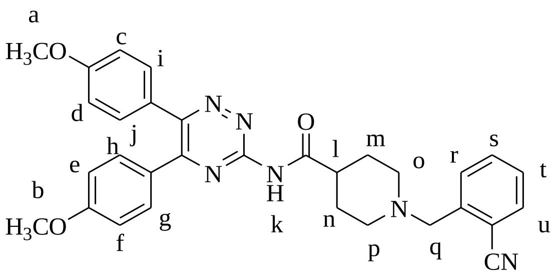
(167)

IR spectrum of compound (**167**) offered signals for NH stretching at 3204 cm^{-1} and for C=O stretching at 1713 cm^{-1}. PMR spectra of compound (**167**) gave a broad singlet at δ 8.54 (s, NH*k*) for amidic proton. An *ortho* coupling was observed between aromatic protons wherein protons at δ 7.62-7.60 (d, 2H*i, j*, *J* = 6.8 Hz) coupled with protons at δ 6.85-6.83 (d, 2H*c, d*, *J* = 6.8 Hz) whereas other aromatic protons at δ 7.49-7.47 (d, 2H*g, h*, *J* = 7.0 Hz) coupled with protons at δ 6.92-6.91 (d, 2H*e, f*, *J* = 7.0 Hz). A multiplet was obtained at δ 7.27-7.16 (m, 4H*r, s, t, u*) corresponding to protons of phenyl ring of benzyl group. Signals for aliphatic protons appeared at δ 3.85 (s, 3H$_{a}$) and 3.83 (s, 3H$_{b}$) representing six protons of methoxyl groups whereas other aliphatic protons afforded signals at δ 3.47 (s, 2H$_{q}$), 2.97 (bs, 3H$_{l, 1o, 1p}$), 2.37 (s, 3H$_{v}$), 2.09-1.97 (m, 6H$_{m, n, 1o, 1p}$).

Peaks were observed at 3198 cm-1 for NH stretching and 1719 cm-1 for C=O stretching in the IR spectrum of compound (**168**). Its PMR spectrum offered a broad singlet at δ 9.07 (s, NH$_{k}$) due to proton attached to amide nitrogen. A doublet was observed at δ 7.85-7.84 (d, 1H$_{u}$, J = 7.6 Hz) for one aromatic protons which coupled with other aromatic proton showing a triplet at δ 7.34-7.30 (t, 1H$_{t}$, J = 7.6 Hz). Six aromatic protons afforded two multiplets at δ 7.65-7.60 (m, 3H$_{i, j, s}$) and 7.54-7.47 (m, 3H$_{g, h, r}$) whereas other aromatic protons appeared as doublets at δ 6.93-6.91 (d, 2H$_{e, f}$, J = 8.8 Hz) and 6.85-6.83 (d, 2H$_{c, d}$, J = 9.2 Hz). In aliphatic protons, signals for six protons of methoxyl groups were obtained as singlets at δ 3.85 (s, 3H$_{a}$) and 3.83 (s, 3H$_{b}$). Methylene protons offered a singlet at δ 3.64 (s, 2H$_{q}$), while signals at δ 3.07 (bs, 1H$_{l}$), 2.94-2.90 (m, 2H$_{1o, 1p}$), 2.18-2.11 (m, 2H$_{1o, 1p}$) and 2.00-1.95 (m, 4H$_{m, n}$) represented protons of piperidine ring.



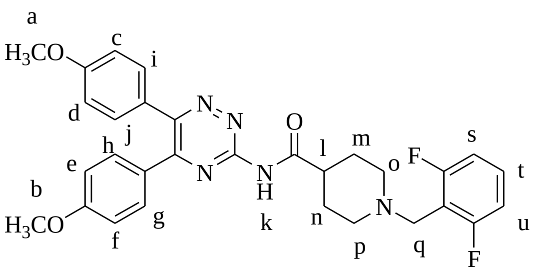
(168)



(169)

Compound (**169**) in its IR spectrum displayed characteristic peaks for NH stretching at 3197 cm^{-1}, CN stretching at 2221 cm^{-1} and C=O stretching at 1717 cm^{-1}. PMR spectrum of compound (**169**) presented a broad singlet at δ 8.79 (s, NH$_{k}$) corresponding to amidic proton. Aromatic protons offered multiplets at δ 7.64-7.55 (m, 5H$_{i, j, s, t, u}$), 7.50-7.46 (m, 2H$_{g, h}$) and 7.39-7.33 (m, 1H). Other aromatic protons showed signals as doublets at δ 6.93-6.91 (d, 2H$_{e, f}$, J = 7.7 Hz) and 6.86-6.84 (d, 2H$_{c, d}$, J = 7.7 Hz). Aliphatic protons provided signals as singlets at δ 3.85 (s, 3H$_{a}$) and 3.84 (s, 3H$_{b}$). A singlet was observed at δ 3.71 (s, 2H$_{q}$) due to methylene protons whereas protons of piperidine ring offered signals as broad singlets at δ 3.07 (bs, 1H$_{l}$) and 2.97-2.94 (bs, 2H$_{1o, 1p}$), and as multiplets at δ 2.23-2.17 (m, 2H$_{1o, 1p}$) and 1.99-1.93 (m, 4H$_{m, n}$). The quasimolecular ion peak was obtained at 535.3 $[M+H]^+$ in the mass spectrum of compound (**169**).

In the IR spectrum of compound (**170**), characteristic peaks were detected at 3204 cm^{-1} for NH stretching and 1724 cm^{-1} for C=O stretching. In its PMR spectrum, a broad singlet at δ 9.05 (s, NH_k) was interpreted for amidic proton. Peaks for aromatic protons were observed as a doublet at δ 7.61-7.59 (d, $2H_{i, j}$, J = 7.2 Hz) and 7.48-7.46 (d, $2H_{g, h}$, J = 7.2 Hz). Other aromatic protons afforded as multiplets at δ 7.27-7.21 (m, $1H_t$), 6.92-6.88 (m, $4H_{e, f, s, u}$) and 6.82-6.80 (m, $2H_{c, d}$). Among aliphatic protons, six protons of methoxyl groups offered singlets at δ 3.84 (s, $3H_a$) and 3.83 (s, $3H_b$), while two benzylic protons appeared as a singlet at δ 3.70 (s, $2H_q$). Signals for protons of piperidine ring were obtained at δ 3.03-2.99 (m, $3H_{l, 1o, 1p}$) and 1.97-1.89 (m, $6H_{m, n, 1o, 1p}$).



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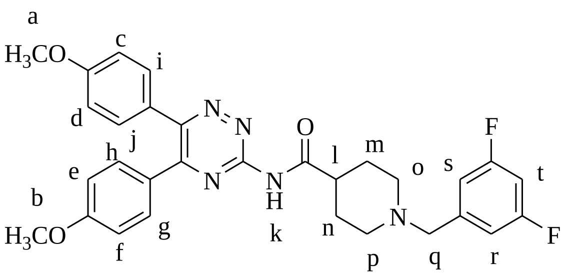
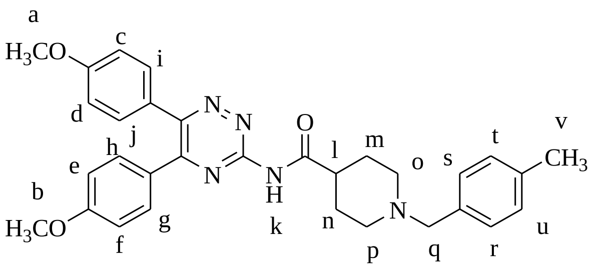


(171)

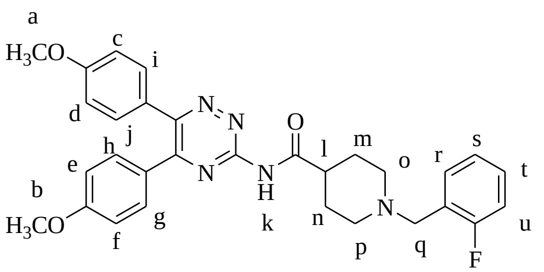
IR spectrum of compound (**171**) showed signals for NH stretching at 3211 cm^{-1} and C=O stretching at 1724 cm^{-1}. Its PMR spectra offered a broad singlet at δ 8.95 (s, NH_k) corresponding to amidic proton. Signals for aromatic protons were obtained as doublets at δ 7.65-7.63 (d, $2H_{i, j}$), 7.51-7.49 (d, $2H_{g, h}$) and 6.95-6.93 (d, $2H_{e, f}$). Other aromatic protons gave multiplet signals at δ 6.89-6.84 (m, $4H_{c, d, s, r}$) and 6.73-6.67 (m, $1H_t$). Six protons of methoxyl groups offered singlet peaks at δ 3.87 (s, 3H) and 3.85 (s, 3H) whereas two protons of methylene appeared as a singlet at δ 3.45 (s, 2H). Piperidine ring protons afforded signals at δ 3.03 (bs, 1H), 2.97-2.91 (bs, 2H) and 2.10-1.92 (m, 6H).



(172)

Compound (**172**) exhibited peaks at 3211 cm^{-1} for NH stretching and 1719 cm^{-1} for C=O stretching. PMR spectrum of compound (**172**) displayed a broad singlet at δ 8.56 (s, NH$_k$) for proton attached to amide nitrogen. Aromatic protons offered a doublet at δ 7.64-7.62 (d, 2H$_{i, j}$, J = 8.8 Hz) which coupled with protons at δ 6.87-6.85 (d, 2H$_{c, d}$, J = 8.8 Hz) whereas aromatic protons at δ 7.51-7.49 (d, 2H$_{g, h}$, J = 8.8 Hz) coupled with other protons at δ 6.95-6.93 (d, 2H$_{e, f}$, J = 7.2 Hz). Four protons of phenyl ring of benzyl group were observed to couple with each other giving doublets at δ 7.25-7.23 (d, 2H$_{s, r}$, J = 7.6 Hz) and 7.16-7.15 (d, 2H$_{t, u}$, J = 7.6 Hz). Among aliphatic protons, three singlet peaks were seen at δ 3.87 (s, 3H$_a$), 3.86 (s, 3H$_b$) for six protons of methoxyl groups, and 3.53 (s, 2H) for two methylene protons. Signals for other aliphatic protons appeared at δ 3.01-2.99 (bs, 3H), 2.36 (s, 3H) and 2.01-1.99 (bs, 6H). In the mass spectrum of compound (**172**), molecular ion peak was obtained at 523.9 $[M]^+$.

In the IR spectrum of compound (**173**), peaks appeared at 3205 cm^{-1} for NH stretching and 1724 cm^{-1} for C=O stretching. Its PMR spectrum gave a broad singlet at δ 8.93 (bs, NH$_k$) due to amidic proton. An *ortho* coupling was observed between aromatic protons at δ 7.67-7.65 (d, 2H$_{i, j}$, J = 8.8 Hz) and 6.89-6.87 (d, 2H$_{c, d}$, J = 8.8 Hz). Protons showing signal at δ 7.54-7.52 (d, 2H$_{g, h}$, J = 8.6 Hz) coupled with protons at δ 6.98-6.96 (d, 2H$_{e, f}$, J = 8.6 Hz). Peaks appeared as multiplet at δ 7.48-7.42 (m, 1H$_t$), 7.29-7.26 (m, 1H$_r$), 7.18-7.14 (m, 1H$_s$) and 7.10-7.05 (m, 1H$_u$) corresponding to aromatic protons of benzyl group. Among aliphatic protons, signals were observed at δ 3.90 (s, 3H$_a$) and 3.88 (s, 3H$_b$) as singlets for six protons of methoxyl group, 3.64 (s, 2H$_q$) as a singlet for benzylic protons, and 3.05-3.01 (m, 3H) and 2.05-1.99 (m, 6H) as multiplets for protons of piperidine ring.



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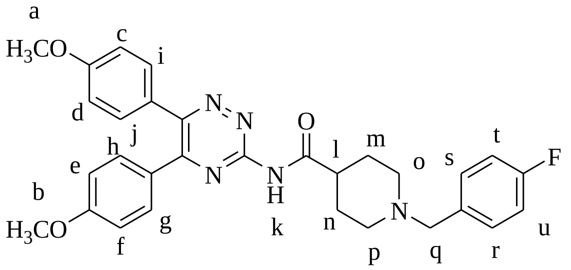
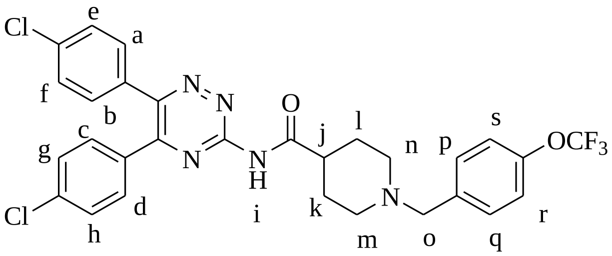


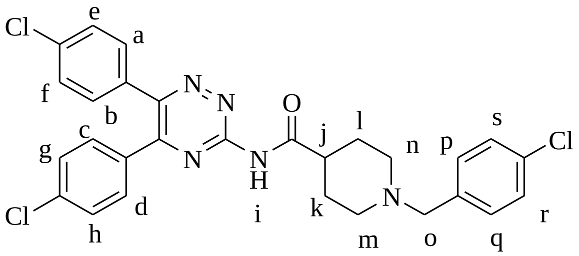
(174)

IR spectrum of compound (**174**) showed characteristic peaks for NH stretching at 3215 cm^{-1} and C=O stretching at 1725 cm^{-1}. Compound (**174**) in its PMR spectrum displayed a broad singlet at δ 9.18 (bs, 1H) due to proton attached to amide proton. Aromatic protons at δ 7.69-7.67 (d, 2H$_{i, j}$, J = 9.0 Hz) exhibited *ortho* coupling with protons at δ 6.89-6.87 (d, 2H$_{c, d}$, J = 9.0 Hz). Aromatic protons gave another doublet at δ 7.54-7.52 (d, 2H$_{g, h}$, J = 8.8 Hz) which coupled with δ 6.98-6.96 (d, 2H$_{e, f}$, J = 8.8 Hz). Other aromatic protons appeared as multiplets at δ 7.33-7.29 (m, $2H_{s, r}$) and 7.06-7.02 (m, $2H_{t, u}$). Singlets were observed at δ 3.90 (s, $3H_{a}$) and 3.88 (s, $3H_{b}$) due to six protons for methoxyl groups whereas another singlet appeared at δ 3.47 (s, $2H_{q}$) for methylene protons. Other aliphatic protons provided signals at δ 3.06 (bs, 1H), 2.97-2.93 (m, 2H) and 2.05-1.95 (m, 6H).

Compound (**175**) in its IR spectrum showed characteristic peaks for NH stretching at 3207 cm^{-1} and C=O stretching at 1728 cm^{-1}. PMR spectrum of compound (**175**) gave a broad singlet at δ 8.81 (s, NH_{i}) for amidic proton. Signals for aromatic protons were obtained as a doublet at δ 7.55-7.53 (d, $2H_{a, b}$, *J* = 6.8 Hz) and multiplets at δ 7.48-7.44 (m, $2H_{c, d}$) and 7.40-7.37 (m, $2H_{g, h}$). Other aromatic protons appeared as a doublet at 7.35-7.32 (d, $2H_{e, f}$, *J* = 6.8 Hz), a as multiplet at δ 7.25-7.22 (m, $2H_{p, q}$) and a doublet at δ 7.18-7.16 (d, $2H_{r, s}$, *J* = 7.0 Hz). Among aliphatic protons, a singlet was observed at δ 3.52 (s, $2H_{o}$) due to benzylic protons. Protons of piperidine ring afforded broad singlets at δ 2.96 (bs, $3H_{j, 1m, 1n}$) and 1.99 (bs, $6H_{k, l, 1m, 1n}$). Compound (**175**) in its mass spectrum exhibited quasimolecular ion peak at 602.2 [M+H]$^{+}$.



(175)

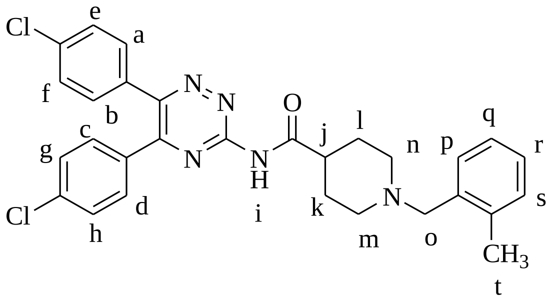


(176)

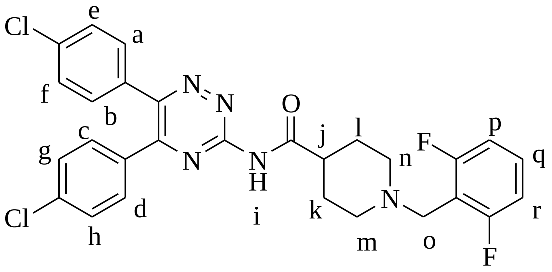
Compound (**176**) in its IR spectrum displayed characteristic peaks for NH stretching at 3215 cm^{-1} and C=O stretching at 1727 cm^{-1}. Its PMR spectrum offered a broad singlet at δ 9.00 (s, NH_{i}) due to proton attached to amide nitrogen. Aromatic protons were observed as doublets at δ 7.61-7.59 (d, $2H_{r, s}$, *J* = 8.8 Hz), 7.52-7.50 (d, $2H_{a, b}$, *J* = 8.4 Hz), 7.45-7.43 (d, $2H_{c, d}$, *J* = 8.4 Hz) and 7.40-7.38 (d, $2H_{g, h}$, *J* = 8.4 Hz), and a multiplet at δ 7.35-7.29 (m, $4H_{e, f, p, q}$). Peaks for aliphatic protons appeared at δ 3.50 (s, $2H_{o}$), 3.00-2.96 (m, $3H_{j, 1m, 1n}$) and 2.07-1.99 (m, $6H_{k, l, 1m, 1n}$).

In the IR spectrum of compound (**177**), characteristic peaks were obtained at 3200 cm^{-1} for NH stretching and 1723 cm^{-1} for C=O stretching. In its PMR spectrum, an amidic proton afforded a broad singlet at δ 9.37 (s, NH_{i}) while aromatic protons offered doublets at δ 7.58-7.56 (d, $2H_{a, b}$, *J* = 8.8 Hz) and 7.48-7.46 (d, $2H_{c, d}$, *J* = 8.8 Hz). Signals for other aromatic protons were observed as multiplets at δ 7.41-7.38 (m, $2H_{g, h}$), 7.35-7.32 (m, $2H_{e, f}$) and 7.18-7.11 (m, $4H_{p, q, r, s}$). Among aliphatic protons, benzylic protons showed a singlet at δ

3.41 (s, $2H_o$) whereas protons of piperidine ring gave multiplets at δ 2.94-2.91 (m, $3H_{j, 1m, 1n}$) and 2.02-1.92 (m, $6H_{k, l, 1m, 1n}$). A singlet was observed at δ 2.36 (s, 3H) due to protons of methyl group.



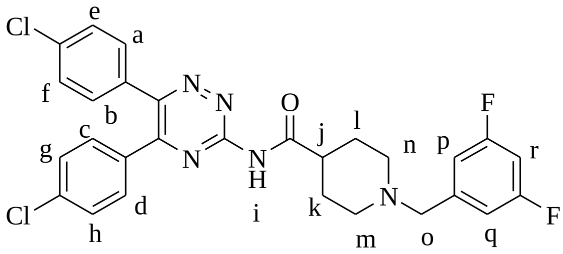
(177)



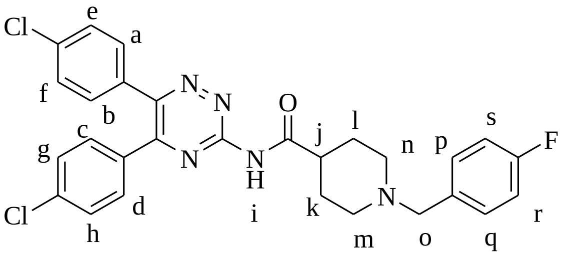
(178)

Compound (**178**) in its IR spectrum exhibited peaks for NH stretching at 3204 cm^{-1} and C=O stretching at 1706 cm^{-1}. PMR spectrum of compound (**178**) offered a broad singlet at δ 8.75 (s, NH_i) due to an amidic proton. Signals for aromatic protons appeared as multiplets at δ 7.58-7.48 (m, $4H_{a, b, c, d}$), 7.44-7.40 (m, $3H_{g, h, q}$), 7.37-7.34 (m, $2H_{e, f}$) and 6.99-6.92 (m, $2H_{p, r}$). Among aliphatic protons, a singlet was observed at δ 3.82 (s, $2H_o$) for two benzylic protons whereas protons of piperidine ring gave multiplets at δ 3.13-3.08 (m, $3H_{j, 1m, 1n}$) and 2.08-1.96 (m, $6H_{k, l, 1m, 1n}$).

In the IR spectrum of compound (**179**), characteristic peaks were obtained at 3202 cm^{-1} for NH stretching and 1724 cm^{-1} for C=O stretching. In its PMR spectrum, a broad singlet appeared at δ 9.59 (s, NH_i) due to amidic proton. Aromatic protons offered doublets at δ 7.59-7.57 (d, $2H_{a, b}$, J = 8.4 Hz) which coupled with protons at δ7.34-7.32 (d, $2H_{e, f}$, J = 8.4 Hz). One more ortho coupling was observed between aromatic protons at δ 7.48-7.46 (d, $2H_{c, d}$, J = 8.8 Hz) and 7.41-7.39 (d, $2H_{g, h}$, J = 8.8 Hz). Other aromatic protons afforded peaks at δ 6.88-6.85 (m, $2H_{p, q}$) and 6.71-6.65 (m, $1H_r$). Aliphatic protons appeared as a singlet at δ 3.41 (s, $2H_o$), as a broad singlet at δ 2.98 (bs, $1H_j$), and as multiplet at δ 2.91-2.88 (m, $2H_{1m, 1n}$), 2.05-1.93 (m, $6H_{k, l, 1m, 1n}$). Mass spectrum of compound (**179**) showed the quasimolecular ion peak at 554.1 $[M+H]^+$.



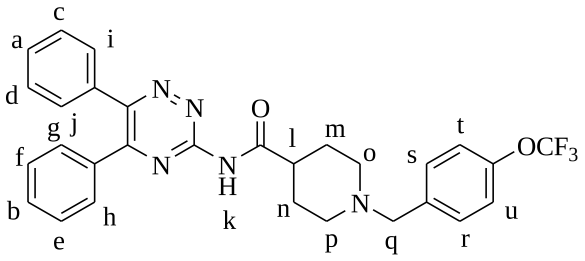
(179)



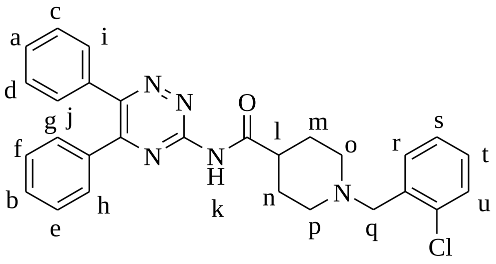
(180)

IR spectrum of compound (**180**) displayed characteristic peaks for NH stretching at 3206 cm^{-1} and C=O stretching at 1719 cm^{-1}. Its PMR spectra offered a broad singlet at δ 9.01 (bs, NH$_{i}$) for an amidic proton. Signals for aromatic protons were obtained as a doublet at δ 7.61-7.59 (d, 2H$_{a, b}$, J = 8.4 Hz) and as multiplets at δ 7.53-7.49 (m, 2H$_{p, q}$), 7.46-7.42 (m, 2H$_{c, d}$) and 7.40-7.37 (m, 2H$_{g, h}$). Two multiplets for four aromatic protons appeared at δ 7.36-7.31 (m, 2H$_{e, f}$) and 7.08-7.02 (m, 2H$_{r, s}$). Peaks for two benzylic protons were observed as a singlet at δ 3.52 (s, 2H$_{o}$) whereas the protons of piperidine ring afforded multiplets at δ 3.01-2.97 (m, 3H$_{j, 1m, 1n}$) and 2.03-1.94 (m, 6H$_{k, l, 1m, 1n}$).

Compound (**181**) in its IR spectrum exhibited characteristic peaks for NH stretching at 3195 cm^{-1} and C=O stretching at 1724 cm^{-1}. PMR spectrum of compound (**181**) gave a broad singlet at δ 9.57 (bs, NH$_{k}$) due to proton attached to amide nitrogen. Aromatic protons were observed as doublets at δ 7.63-7.61 (d, 2H$_{i, j}$, J = 8.8 Hz) and 7.53-7.51 (d, 2H$_{g, h}$, J = 8.4 Hz) while remaining aromatic protons afforded a multiplet at δ 7.46-7.30 (m, 10H$_{a, b, c, d, e, f, r, s, t, u}$). Amongst aliphatic protons, a singlet appeared at δ 3.43 (s, 2H$_{q}$) for benzylic protons whereas protons of piperidine ring showed a broad singlet at δ 3.05 (bs, 1H$_{l}$), and two multiplets at δ 2.92-2.87 (m, 2H$_{1o, 1p}$) and 2.05-1.95 (m, 6H$_{m, n, 1o, 1p}$). The mass spectrum of compound (**181**) displayed quasimolecular ion peak at 534.3 [M+H]$^{+}$.



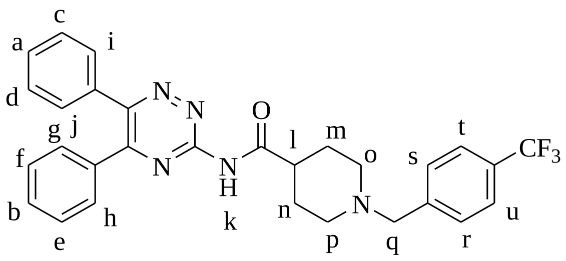
(181)



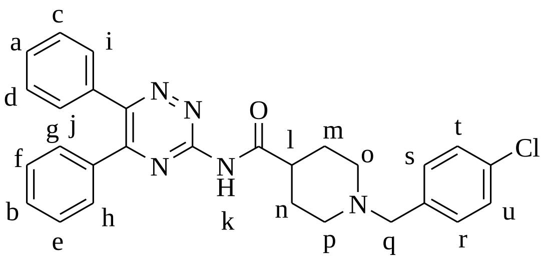
(182)

In the IR spectrum of compound (**182**), characteristic peaks were obtained at 3215 cm^{-1} for NH stretching and 1725 cm^{-1} for C=O stretching. Its ^{1}H-NMR spectrum provided a signal at δ 8.84 (bs, 1H) as a broad singlet for amidic proton. Aromatic protons were observed as doublets at δ 7.61-7.59 (d, 2H$_{i, j}$, J = 7.6 Hz) and 7.53-7.51 (d, 2H$_{g, h}$, J = 7.6 Hz). A multiplet appeared at δ 7.44-7.38 (m, 4H$_{r, s, t, u}$) due to four aromatic protons. Other aromatic protons afforded signals at δ 7.35-7.33 (d, 2H$_{a, b}$) and 7.27-7.17 (m, 4H$_{c, d, e, f}$). Benzylic protons offered a singlet at δ 3.63 (s, 2H$_{q}$) whereas protons of piperidine ring gave broad singlets at δ 3.01 (bs, 3H$_{l, 1o, 1p}$) and 2.01 (bs, 6H$_{m, n, 1o, 1p}$).

IR spectrum of compound (**183**) showed characteristic peaks for NH stretching at 3199 cm^{-1} and C=O stretching at 1724 cm^{-1}. Its PMR spectrum displayed a broad singlet at δ 9.49 (bs, NH_k) for amidic protons. A doublet was observed at δ 7.67-7.65 (d, $2H_{t, u}$, J = 7.2 Hz) due to two aromatic protons. Signals for four aromatic protons appeared as a multiplet at δ 7.62-7.56 (m, $4H_{i, j, g, h}$) while remaining aromatic protons gave a multiplet at δ 7.48-7.35 (m, $8H_{a, b, c, d, e, f, r, s}$). Among aliphatic protons, benzylic protons displayed a singlet at δ 3.53 (s, $2H_q$) while protons of piperidine ring offered multiplets at δ 3.13-3.09 (m, $1H_l$), 2.96-2.92 (m, $2H_{1o, 1p}$) and 2.10-2.01 (m, $6H_{m, n, 1o, 1p}$).



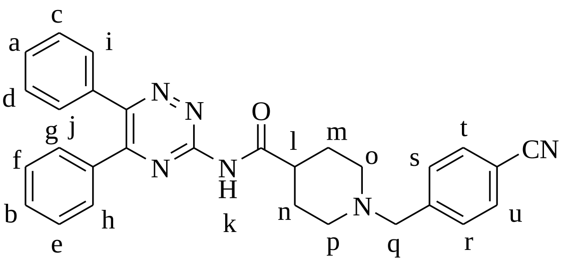
(183)



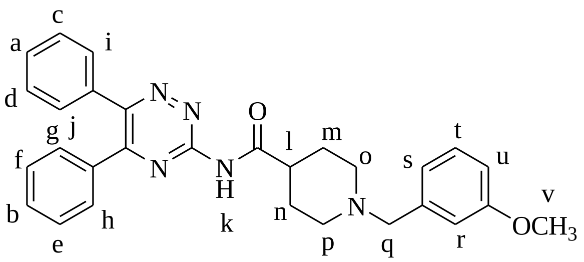
(184)

Compound (**184**) in its IR spectrum gave characteristic peaks at 3189 cm^{-1} for NH stretching and 1722 cm^{-1} for C=O stretching. PMR spectrum of compound (**184**) offered a signal for amidic proton at δ 9.12 (bs, 1H) as a broad singlet. Signals for aromatic protons appeared as a doublet at δ 7.61-7.59 (d, $2H_{i, j}$, J = 8.0 Hz) and as multiplets at δ 7.53-7.51 (m, $2H_{g, h}$), 7.45-7.37 (m, $5H_{a, c, d, t, u}$) and 7.34-7.28 (m, $5H_{b, e, f, r, s}$). Two benzylic protons afforded a singlet at δ 3.46 (s, $2H_q$) whereas other aliphatic protons of piperidine ring offered signals as multiplets at δ 3.05-2.92 (m, $3H_{l, 1o, 1p}$) and 2.08-1.95 (m, $6H_{m, n, 1o\ 1p}$). Its mass spectrum exhibited quasimolecular ion peak at 484.5 $[M+H]^+$.

In its IR spectrum, compound (**185**) displayed characteristic peaks for NH stretching at 3197 cm^{-1}, CN stretching at 2227 cm^{-1} and C=O stretching at 1722 cm^{-1}. Its PMR spectrum provided a broad singlet at δ 9.35 (bs, 1H) for a proton attached to amide nitrogen. Among aromatic protons, two protons exhibited doublets of doublet at δ 7.61-7.59 (dd, $2H_{i, j}$, J = 1.6, 6.8 Hz) and two protons showed a doublet at δ 7.53-7.51 (d, $2H_{g, h}$, J = 5.4 Hz). Other aromatic protons appeared as multiplets at δ 7.45-7.37 (m, $7H_{a, c, d, e, f, t, u}$) and 7.34-7.31 (m, $3H_{b, r, s}$). Benzylic protons afforded a singlet at δ 3.49 (s, $2H_q$) while protons of piperidine ring were observed as a broad singlet at δ 3.05 (bs, $1H_l$), and as multiplets at δ 2.89-2.87 (m, $2H_{1o, 1p}$), 2.09-2.05 (m, $2H_{1o, 1p}$) and 1.97-1.92 (m, $4H_{m, n}$).



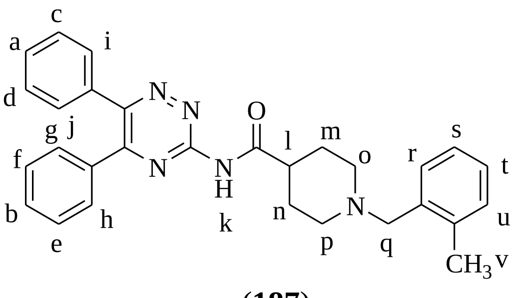
(185)



(186)

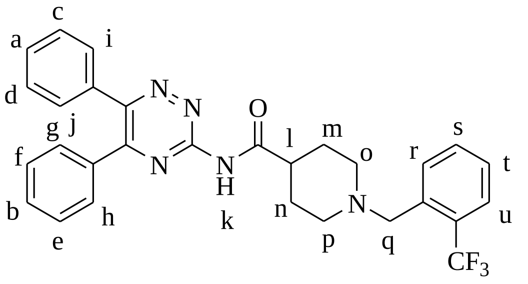
IR spectrum of **186** showed characteristic peaks for NH stretching at 3192 cm^{-1} and C=O stretching at 1722 cm^{-1}. PMR spectrum of compound (**186**) offered a broad singlet at δ 9.33 (bs, 1H) due to an amidic proton. Signals for aromatic protons were obtained as doublets at δ 7.62-7.60 (d, $2H_{i,\ j}$, J = 7.8 Hz) and 7.53-7.51 (d, $2H_{g,\ h}$, J = 8.0 Hz). Two multiplets appeared at δ 7.43-7.38 (m, $4H_{c,\ d,\ e,\ f}$) and 7.34-7.31 (m, $2H_{a,\ b}$) representing six aromatic protons whereas aromatic protons of benzyl group afforded signals as a triplet at δ 7.24-7.20 (t, $1H_t$, J = 6.2 Hz) and multiplets at δ 6.93-6.88 (m, $2H_{r,\ u}$) and 6.81- 6.79 (m, $1H_s$). Three protons of methoxyl group gave a singlet at δ 3.81 (s, $3H_v$). Aliphatic protons of benzyl group displayed a singlet at δ 3.48 (s, $2H_q$). Signals of piperidine protons appeared at δ 3.05 (bs, $1H_l$), 2.98-2.95 (m, $2H_{1o,\ 1p}$) and 2.09-1.97 (m, $6H_{m,\ n,\ 1o,\ 1p}$). Its mass spectrum showed quasimolecular ion peak at 480.3 $[M+H]^+$.

Compound (**187**) in its IR spectrum exhibited characteristic peaks at 3196 cm^{-1} for NH stretching and 1719 cm^{-1} for C=O stretching. In the PMR spectrum of compound (**187**), a broad singlet was observed at δ 9.15 (bs, NH_k) due to proton attached to amide nitrogen. Its aromatic protons gave signals as doublets at δ 7.54-7.52 (d, $2H_{i,\ j}$, J = 7.6 Hz) and 7.46-7.44 (d, $2H_{g,\ h}$, J = 8.0 Hz). Other aromatic protons offered multiplets at δ 7.38-7.30 (m, $6H_{a,\ b,\ c,\ d,\ e,\ f}$) and 7.28-7.21 (m, $4H_{r,\ s,\ t,\ u}$). Among aliphatic protons, benzylic protons appeared as a singlet at δ 3.41 (s, $2H_q$) while piperidine protons afforded signals at δ 2.98 (bs, $1H_l$), 2.91 (bs, $2H_{1o,\ 1p}$) and 2.04-1.92 (m, $6H_{m,\ n,\ 1o,\ 1p}$). A singlet was observed at δ 2.29 (s, $3H_v$) for methyl protons. The Mass spectrum of compound (**187**) displayed the quasimolecular ion peak at 464.5 $[M+H]^+$.

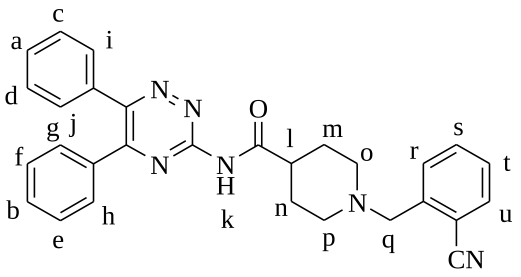


(**187**)

In the IR spectrum of compound (**188**), characteristic peaks were observed at 3215 cm-1 for NH stretching and 1729 cm-1 for C=O stretching. Its PMR spectrum showed a broad singlet at δ 8.78 (bs, NH_k) for amidic proton. Signals for aromatic protons appeared as multiplets at δ 7.68-7.64 (m, $3H_{i, j, u}$), 7.59-7.56 (m, $3H_{g, h, s}$) and 7.51-7.35 (m, $8H_{a, b, c, d, e, f, r, s}$). Among aliphatic protons, benzylic protons offered a singlet at δ 3.70 (s, $2H_q$) whereas protons of piperidine ring afforded broad singlets at δ 3.10 (bs, $1H_l$), 3.00 (bs, $1H_{1o}$), 2.97 (bs, $1H_{1p}$), 2.22 (bs, $2H_{1o, 1p}$) and 2.04 (bs, $4H_{m, n}$). The quasimolecular ion peak was observed at 518.5 $[M+H]^+$ in it mass spectrum.



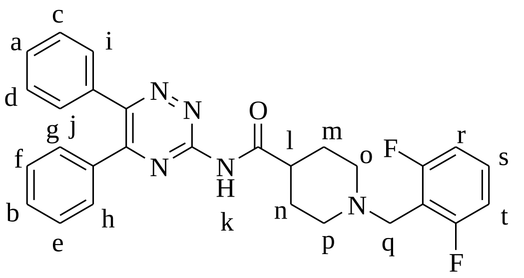
(188)



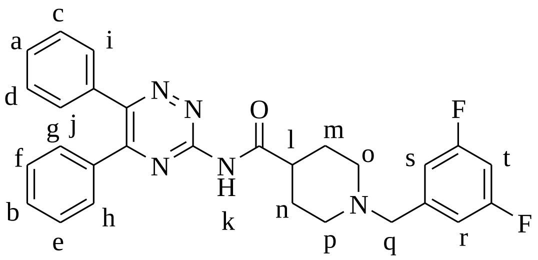
(189)

Compound (**189**) in its IR spectrum displayed characteristic peaks at 3197 cm^{-1} for NH stretching, 2225 cm^{-1} for CN stretching and 1718 cm^{-1} for C=O stretching. PMR spectrum of compound (**189**) offered a broad singlet at δ 9.32 (bs, NH_k) due to proton attached to amidic nitrogen. Aromatic protons offered signals as multiplets at δ 7.64-7.51 (m, $7H_{i, j, g, h, s, t, u}$), 7.45-7.38 (m, $4H_{c, d, e, f}$) and 7.36-7.32 (m, $3H_{a, b, r}$). Aliphatic protons were observed as a singlet at δ 3.66 (s, $2H_q$), as a broad singlet at δ 3.07 (bs, $1H_l$), and multiplets at 2.94-2.91 (m, $2H_{1o, 1p}$), 2.19-2.14 (m, $2H_{1o, 1p}$) and 2.02-1.92 (m, 4Hm, n).

IR spectrum of compound (**190**) showed characteristic peaks for NH stretching at 3213 cm^{-1} and C=O stretching at 1724 cm^{-1}. In the PMR spectrum of compound (**190**), a broad singlet was observed at δ 9.19 (bs, NH_k) due to amidic proton. Signals for aromatic protons appeared as a doublet at δ 7.61-7.59 (d, $2H_{i, j}$, J = 7.6 Hz) and as doublets of doublet at δ 7.54-7.51 (dd, $2H_{g, h}$, J = 1.6, 8.0 Hz). Four protons were observed as a multiplet at δ 7.47-7.37 (m, $4H_{c, d, e, f}$) while a triplet was obtained at δ 7.34-7.31 (t, $2H_{a, b}$, J = 7.6 Hz) for two aromatic protons. Other aromatic protons afforded multiplets at δ 7.27-7.22 (m, $1H_s$) and 6.94-6.87 (m, $2H_{r, t}$). Among aliphatic protons, a singlet was seen at δ 3.70 (s, 2H) for benzylic protons whereas signals were obtained at δ 3.04-2.90 (m, 3H), 2.19-2.14 (t, 2H, J = 11.4 Hz) and 2.03-1.90 (m, 4H) representing protons of piperidine ring.



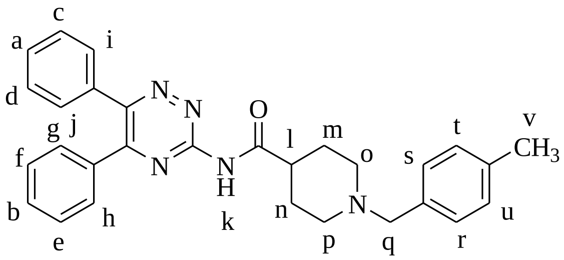
(190)



(191)

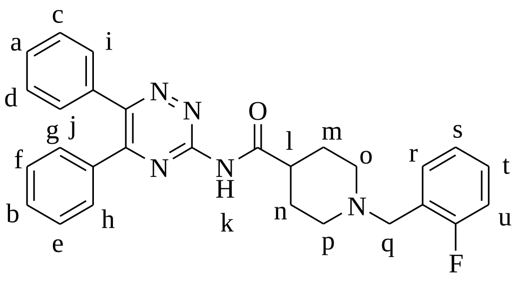
In its IR spectrum compound (**191**) displayed characteristic peaks for NH stretching at 3212 cm^{-1} and C=O stretching at 1724 cm^{-1}. PMR spectrum of compound (**191**) offered a broad singlet at δ 9.11 (bs, NH$_k$) indicating amidic proton. Aromatic protons provided signals as a doublet at δ 7.66-7.64 (d, 2H$_{i, j}$, J = 7.6 Hz) and a doublets of doublet at δ 7.58-7.56 (dd, 2H$_{g, h}$, J = 1.4, 8.2 Hz). Other aromatic protons were observed to show multiplets at δ 7.49-7.43 (m, 3H$_{c, d, e}$), 7.40-7.35 (m, 3H$_{a, b, f}$), 6.93-6.89 (m, 2H$_{r, s}$) and 6.75-6.70 (m, 1H$_t$). Two benzylic protons exhibited a singlet at δ 3.48 (s, 2H$_q$). Remaining aliphatic protons gave signals at δ 3.09 (bs, 1H$_l$), 2.97-2.93 (m, 2H$_{1o, 1p}$) and 2.05-1.95 (m, 6H$_{m, n, 1o, 1p}$).

Compound (**192**) in its IR spectrum displayed characteristic peaks for NH stretching at 3210 cm^{-1} and C=O stretching at 1724 cm^{-1}. In its PMR spectrum, a broad singlet appeared at δ 8.92 (bs, 1H) which represented proton attached to amide nitrogen. Aromatic protons were observed as multiplets at δ 7.66-7.63 (m, 2H$_{i, j}$), 7.58-7.55 (m, 2H$_{g, h}$) and 7.48-7.35 (m, 6H$_{a,b, c, d, e, f}$). Four aromatic protons offered doublets at δ 7.26-7.24 (d, 2H$_{r, s}$, J = 7.8 Hz) and 7.18-7.16 (d, 2H$_{t, u}$, J = 7.8 Hz) which coupled with each other. A singlet was seen at δ 3.50 (s, 2H$_q$) representing two benzylic protons whereas piperidine protons afforded signals at δ 3.02-2.98 (m, 3H$_{l, 1o, 1p}$) and 2.05-1.97 (m, 6H$_{m, n, 1o, 1p}$). Three aliphatic protons of methyl group offered a singlet at δ 2.38 (s 3H$_v$). Its mass spectrum showed quasimolecular ion peak at 464.5 [M+H]$^+$.

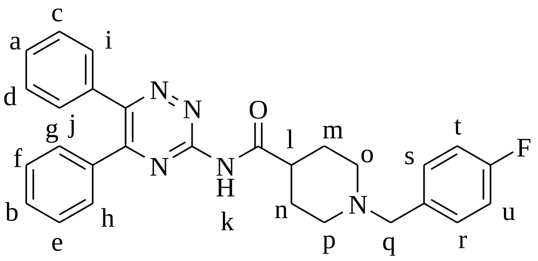


(192)

IR spectrum of compound (**193**) exhibited characteristic peaks for NH stretching at 3200 cm^{-1} and C=O stretching at 1720 cm^{-1}. Its PMR spectrum gave a signal at δ 9.51 (bs, NH$_k$) for an amidic proton. Signals for aromatic protons appeared as doublets at δ 7.63-7.61 (d, 2H$_{i, j}$, J = 8.0 Hz) and 7.53-7.52 (d, 2H$_{g, h}$, J = 8.4 Hz) while other aromatic protons were observed as multiplets at δ 7.42-7.30 (m, 7H$_{a, b, c, d, e, f, r}$), 7.25-7.20 (m, 1H$_s$), 7.12-7.08 (m, 1H$_t$) and 7.04-6.99 (m, 1H$_u$). Among aliphatic protons, benzylic protons gave a singlet peak at δ 3.53 (s, 2H$_q$) whereas protons of piperidine ring were observed as multiplets at δ 3.04-3.00 (m, 1H$_l$), 2.97-2.93 (m, 2H$_{1o, 1p}$) and 2.01-1.90 (m, 6H$_{m, n, 1o, 1p}$).



(193)



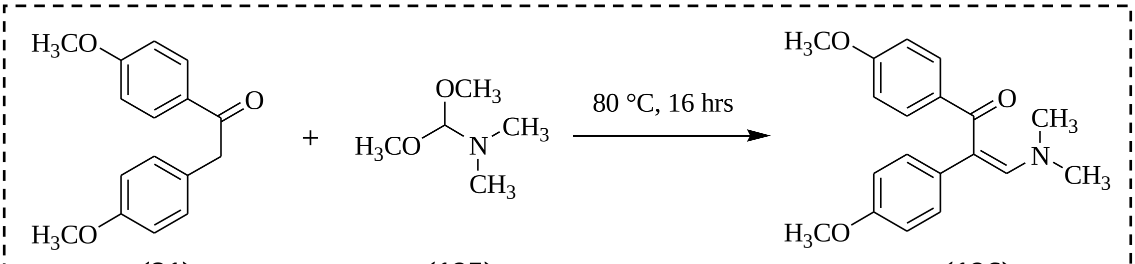
(194)

In the IR spectrum of compound (**194**), characteristic peaks were observed at 3205 cm^{-1} for NH stretching and 1721 cm-1 for C=O stretching. PMR spectrum of **194** displayed a broad singlet at δ 8.87 (bs, 1H) due to proton attached to amide nitrogen. Two doublets for four aromatic protons were observed at δ 7.60-7.58 (d, 2H$_{i, j}$, J = 8.4 Hz) and 7.52-7.50 (d, 2H$_{g, h}$, J = 8.0 Hz). Other aromatic protons offered signals as multiplets at δ 7.45-7.27 (m, 8H$_{a, b, c, d, e, f, r, s}$) and 7.02-6.97 (m, 2H$_{t, u}$). A singlet was observed at δ 3.46 (s, 2H$_q$) due to two benzylic protons whereas piperidine protons afforded multiplets at δ 2.99-2.91 (m, 3H$_{l, 1o, 1p}$) and 2.05-1.95 (m, 6H$_{m, n, 1o, 1p}$).

4.1.2 Synthesis of vicinal diaryl-substituted pyrimidines (202-215)

4.1.2.1 Synthesis of 3-(dimethylamino)-1,2-bis(4-methoxyphenyl)prop-2-en-1-one (196)

1,2-Bis(4-methoxyphenyl)ethanone (**81**) was reacted with neat *N,N*-dimethyl formamide dimethylacetal (DMF.DMA, **195**) at 80 ºC for 16 hrs as shown in **scheme-11** to obtain 3-(dimethylamino)-1,2-bis(4-methoxyphenyl)prop-2-en-1-one (**196**). IR spectrum of compound (**196**) showed characteristic peaks for the C=O stretching at 1653 cm^{-1} along with other peaks at 1246 and 1024 cm^{-1} for the C-O stretching.

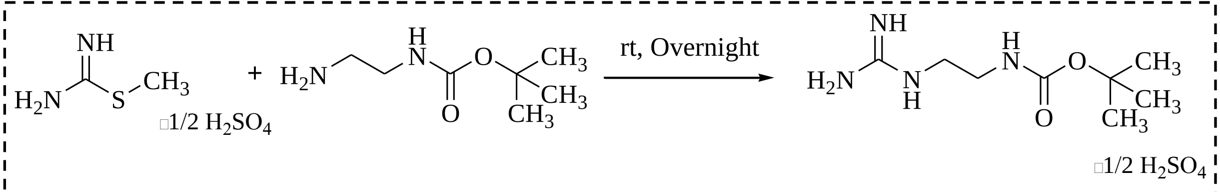


(81) (195) (196)

Scheme-11

4.1.2.2 Synthesis of *t*.butyl 2-guanidinoethylcarbamate (197)

As shown in **scheme-12**, *t*.butyl 2-guanidinylethylcarbamate (**197**) was prepared by treating with *S*-methylisothiourea hemisulphate (**O**) with *t*.butyl 2-aminoethylcarbamate (**P**) at room temperature. Compound (**197**) was used in the next step without any purification and analysis. Its mass spectrum confirmed its structure showing quasimolecular ion peak at 203.16 $[M+H]^+$.

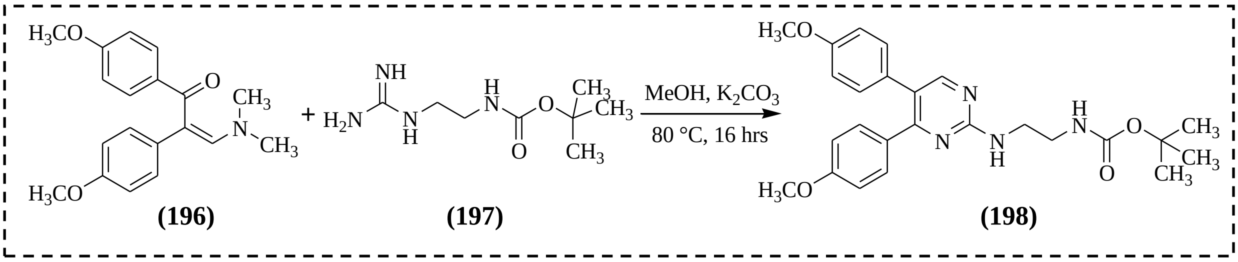


(O) (P) (197)

Scheme-12

4.1.2.3 Synthesis of *t*.butyl 2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-ylamino)ethyl carbamate (198)

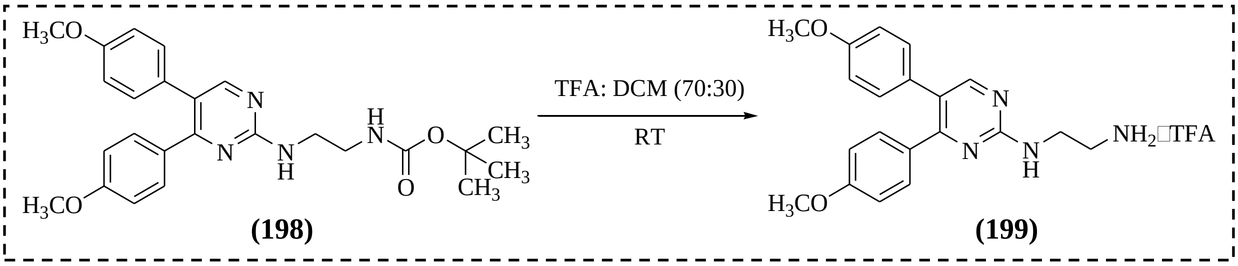
3-(Dimethylamino)-1,2-bis(4-methoxyphenyl)prop-2-en-1-one (**196**) was reacted with *t*.butyl 2-guanidinylethylcarbamate (**197**) as per **scheme-13** in presence of potassium carbonate and methanol at 80 ºC for 16 hrs to get *t*.butyl-2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-ylamino)ethyl carbamate (**198**). In the IR spectrum of compound (**198**), characteristic peaks were observed at 3358 and 3254 cm^{-1} for NH stretching while a peak appeared at 1698 cm^{-1} representing C=O stretching of carbamate group. Its mass spectrum displayed the quasimolecular ion peak at 451.2 $[M+H]^+$.



Scheme-13

4.1.2.4 Synthesis of *N*-(2-aminoethyl)-4,5-bis(4-methoxyphenyl)pyrimidin-2-amine (199)

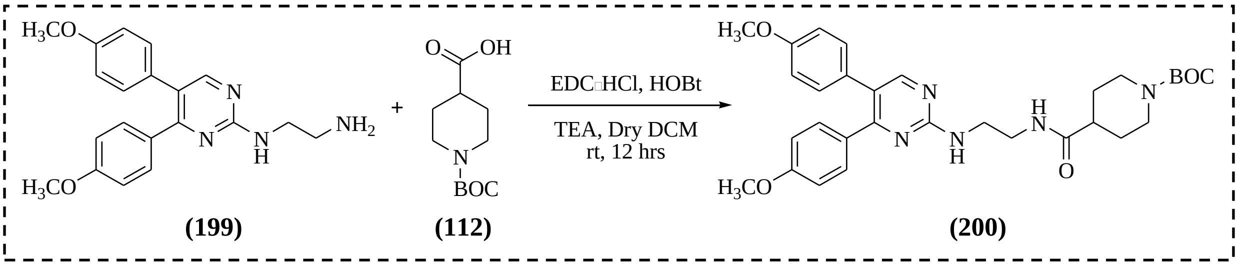
In the next step (**Scheme-14**), *t*.butyl 2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-yl amino)ethylcarbamate (**198**) was deprotected using trifluoroacetic acid and DCM to produce *N*-(2-aminoethyl)-4,5-bis(4-methoxyphenyl)pyrimidin-2-amine (**199**) which was used further without purification.



Scheme-14

4.1.2.5 Synthesis of *t*.butyl 4-(2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-ylamino)ethyl carbamoyl)piperidine-1-carboxylate (200)

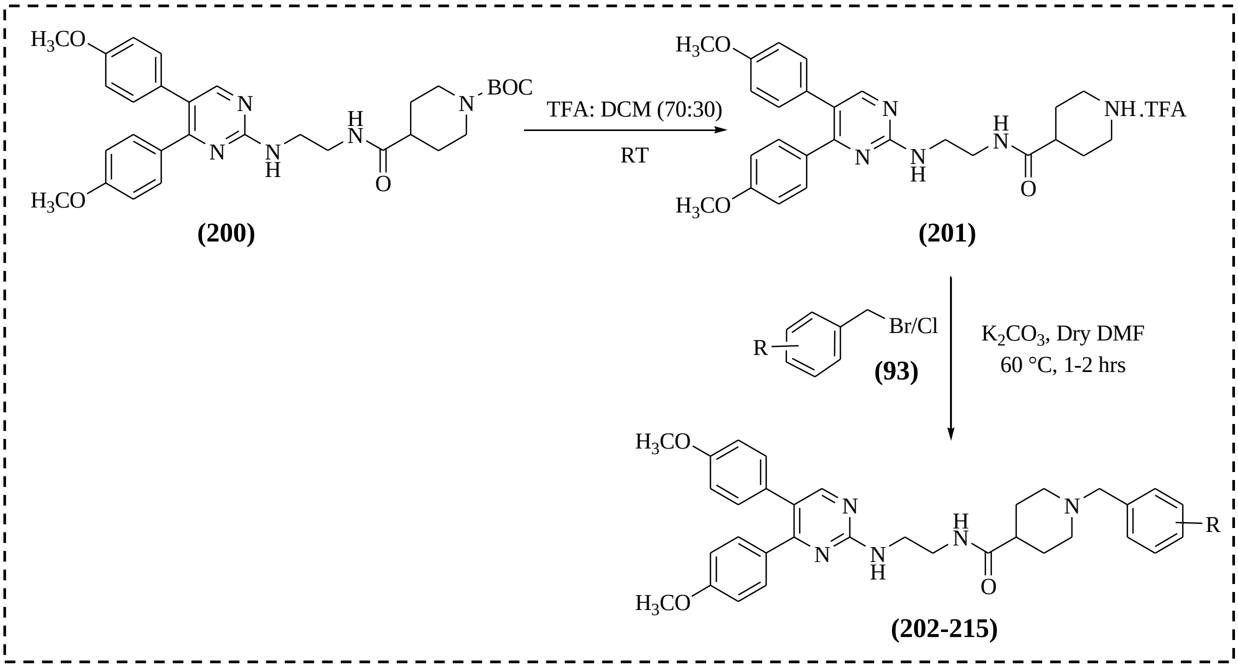
Acid-amine coupling reaction was carried out to synthesize *t*.butyl 4-(2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-ylamino)ethylcarbamoyl)piperidine-1-carboxylate (**200**) as shown in **scheme-15** wherein *N*-(2-aminoethyl)-4,5-bis(4-methoxyphenyl)pyrimidin-2-amine (**200**) was treated with 1-(*t*.butoxycarbonyl)piperidine-4-carboxylic acid (**112**) in presence of EDC.HCl and hydroxybenzotriazole under basic conditions. IR spectrum of compound (**200**) exhibited characteristic peaks at 3252 cm^{-1} for NH stretching, 1687 cm^{-1} for C=O stretching of carbamate and 1652 cm^{-1} for C=O stretching of amide. Its mass spectrum displayed $[M+2H]^+$ peak at 563.31.



Scheme-15

4.1.2.6 Synthesis of *N*-(2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-ylamino)ethyl)-1-substituted benzyl-4-carboxamide (202-215)

In the final step as per **scheme-16**, deprotection of *t*.butyl-4-(2-(4,5-bis(4-methoxy phenyl)pyrimidin-2-amino)ethylcarbamoyl)piperidine-1-carboxylate (**200**) in presence of trifluoroacetic acid (TFA) and DCM afforded *N*-(2-(4,5-bis(4-methoxyphenyl)pyrimidin-2-yl amino)ethyl)piperidine-4-carboxamide (**201**) which was further used without purification. Compound (**201**) in its IR spectrum showed characteristic peaks for NH stretching at 3372 cm^{-1} and C=O stretching at 1683 cm^{-1}. In its mass spectrum [M+2] ion peak was observed at 463.09.

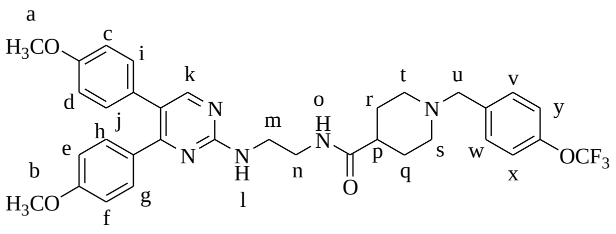


Scheme-16

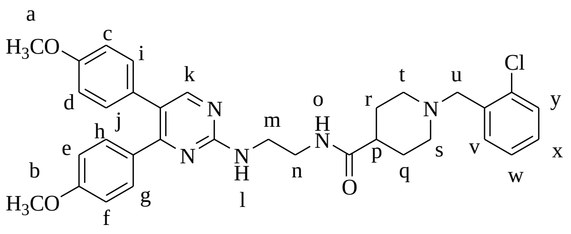
Deprotected compound (**201**) was then reacted with substituted benzyl bromides (**93**) in presence of potassium carbonate and dry DMF to yield the targeted compounds, *N*-(2-(4,5-

bis(4-methoxyphenyl)pyrimidin-2-ylamino)ethyl)-1-substituted benzyl-4-carboxamides (**202-215**).

IR spectrum of compound (**202**) showed the characteristic peaks for NH stretching at 3262 cm^{-1} and C=O stretching at 1640 cm^{-1}. Its PMR spectrum gave signals for aromatic protons at δ 8.22 (s, $1H_k$) as a singlet and 7.38-7.34 (m, $4H_{i, j, v, w}$) as a multiplet. A doublet was observed at δ 7.14-7.12 (d, $2H_{x, y}$, J = 8.0 Hz) comprising of two aromatic protons while a multiplet at δ 7.05-7.02 (m, $3H_{g, h, o}$) represented three protons. Signals for other aromatic protons appeared at δ 6.84-6.82 (d, $2H_{e, f}$, J = 8.8 Hz) and 6.76-6.74 (d, $2H_{c, d}$, J = 8.8 Hz). Proton attached to *sec.* amine demonstrated a triplet at δ 5.61-5.58 (t, NH_l) whereas six protons of two methoxyl groups offered two individual singlets at δ 3.81 (s, $3H_a$) and 3.78 (s, $3H_b$). Two protons of ethylene linker were observed as a multiplet at δ 3.70-3.66 (m, $2H_m$) while signals for the other two protons of ethylene linker and two benzylic protons merged together to give a multiplet at δ 3.51-3.47 (m, $4H_{n, u}$). Other aliphatic protons afforded a broad singlet at δ 2.82 (bs, $2H_{1s, 1t}$) and a multiplet at δ 1.85-1.66 (m, $7H_{p, q, r, 1s, 1t}$). Compound (**202**) in its mass spectrum showed the quasimolecular ion peak at 637.14 $[M+2H]^+$.



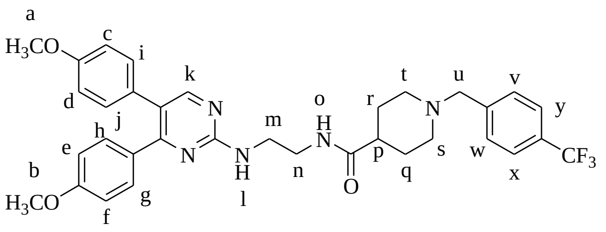
(202)



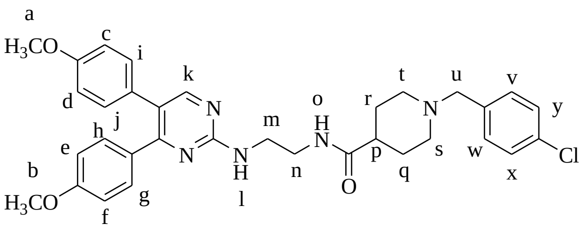
(203)

Compound (**203**) in its IR spectrum offered characteristic peaks at 3274 cm^{-1} for NH stretching and 1647 cm^{-1} for C=O stretching. PMR spectrum of compound (**203**) displayed a singlet at δ 8.23 (s, $1H_k$) for an aromatic proton and a broad singlet δ 7.57 (bs, NH_o) for proton attached to amide nitrogen. Two separate multiplets appeared at δ 7.38-7.31 (m, $4H_{i, j, w, y}$) and 7.23-7.17 (m, $2H_{v, x}$) for six aromatic protons. A doublet was obtained at δ 7.05-7.03 (d, $2H_{g, h}$, J = 8.8 Hz) for two protons which coupled with protons at δ 6.84-6.82 (d, $2H_{e, f}$, J = 8.8 Hz). Other aromatic protons afforded a doublet at δ 6.77-6.75 (d, $2H_{c, d}$, J = 8.4 Hz). Signal for a *sec.*amine proton appeared as a triplet at δ 5.63-5.60 (t, NH_l). Six aliphatic protons of two methoxyl groups gave two singlet peaks at δ 3.81 (s, $3H_a$) and 3.78 (s, $3H_b$). A multiplet was seen at δ 3.70-3.64 (m, $4H_{m, u}$) representing two protons of ethylene linker and two protons of benzylic protons. Other aliphatic protons afforded signals at δ 3.51-3.47 (m, $2H_n$), 2.90 (bs, $2H_{1s, 1t}$) and 1.86-1.70 (bs, $7H_{p, q, r, 1s, 1t}$).

In the IR spectrum of compound (**204**), characteristic peaks were observed for NH stretching at 3250 cm^{-1} and C=O stretching at 1649 cm^{-1}. Its PMR spectrum exhibited signals for aromatic protons at δ 8.24 (s, 1H$_{k}$) and 7.57-7.55 (m, 4H$_{v, w, x, y}$). Aromatic protons at δ 7.38-7.36 (d, 2H$_{i, j}$, J = 8.8 Hz) exhibited *ortho* coupling with protons observed at δ 6.76-6.74 (d, 2H$_{c, d}$, J = 8.8 Hz). Similarly, an *ortho* coupling was observed between aromatic protons showing doublets at δ 7.04-7.02 (d, 2H$_{g, h}$, J = 8.4 Hz) and 6.84-6.82 (d, 2H$_{e, f}$, J = 8.4 Hz). A broad singlet appeared at δ 5.63 (bs, NH$_{l}$) for proton of *sec.*amine. Among aliphatic protons, protons of methoxyl groups displayed singlets at δ 3.81 (s, 3H$_{a}$) and 3.78 (s, 3H$_{b}$). Signals for protons of three methylene groups were observed as multiplets at δ 3.70-3.63 (m, 4H$_{m, u}$) and 3.51-3.47 (m, 2H$_{n}$). Protons of piperidine ring afforded a broad singlet at δ 2.87 (bs, 2H$_{1s, 1t}$) and a multiplet at δ 1.95-1.84 (m, 7H$_{p, q, r, 1s, 1t}$). The mass spectrum of compound (**204**) showed quasimolecular ion peak at 621.20 [M+2H]$^{+}$.



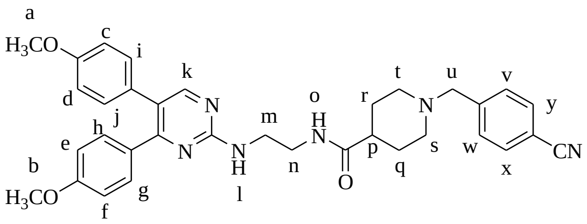
(204)



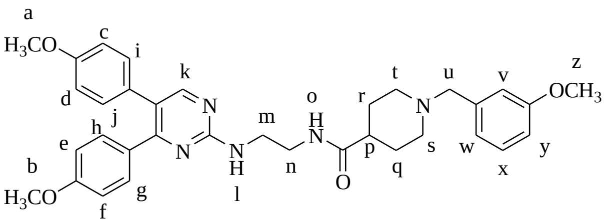
(205)

IR spectrum of compound (**205**) showed characteristic peaks at 3255 cm^{-1} for NH stretching and 1639 cm^{-1} for C=O stretching. In its PMR spectrum, a singlet for one aromatic proton was obtained at δ 8.25 (s, 1H$_{k}$). A doublet was observed at δ 7.40-7.38 (d, 2H$_{i, j}$, J = 8.6 Hz) coupled with protons showing doublets at δ 6.78-6.76 (d, 2H$_{c, d}$, J = 8.6 Hz). A signal for an amidic proton merged with that of aromatic protons appeared as a multiplet at δ 7.28-7.19 (m, 5H$_{o, v, w, x, y}$). Other aromatic protons appearing at δ 7.07-7.05 (d, 2H$_{g, h}$) and 6.87-6.85 (d, 2H$_{e, f}$) coupled with each other with a coupling constant of 8.8 Hz. Proton of *sec.*amine gave a triplet at δ 5.63-5.60 (t, NH$_{l}$). Two individual singlets were obtained at δ 3.84 (s, 3H$_{a}$) and 3.80 (s, 3H$_{b}$). Four aliphatic protons of ethylene linker afforded multiplets at δ 3.70-3.67 (m, 2H$_{m}$) and 3.52-3.48 (m, 2H$_{n}$). A singlet was observed at δ 3.36 (s, 2H$_{u}$) for two benzylic protons while protons of piperidine ring offered signals as a multiplet at δ 2.97-2.73 (m, 2H$_{1s, 1t}$) and broad singlets at δ 1.85 (bs, 3H$_{p, 1s, 1t}$) and 1.59 (bs, 4H$_{q, r}$).The mass spectrum of compound (**205**) displayed the quasimolecular ion peak at 587.00 [M+2H]$^{+}$.

In the IR spectrum of compound (**206**), characteristic peaks were seen at 3385 cm-1 for NH stretching, 2227 cm^{-1} for CN stretching and 1643 cm^{-1} for C=O stretching. PMR spectrum of compound (**206**) offered a singlet for one aromatic proton at δ 8.25 (s, $1H_k$). Signals for other aromatic protons appeared as a doublet at δ 7.57-7.55 (d, $2H_{x, y}$, J = 7.6 Hz) and a multiplet at δ 7.40-7.36 (m, $4H_{i, j, v, w}$). Two aromatic protons at δ 7.05-7.03 (d, $2H_{g, h}$, J = 8.2 Hz) coupled with protons observed at δ 6.85-6.83 (d, $2H_{e, f}$, J = 8.2 Hz). An amidic proton was seen at δ 7.00 (bs, $1NH_o$) whereas a proton attached to *sec.*amine gave a broad singlet at δ 5.58 (bs, $1NH_l$). Other aromatic protons showed a doublet at δ 6.77-6.75 (d, $2H_{c, d}$, J = 8.8 Hz). Two singlets at δ 3.82 (s, $3H_a$) and 3.78 (s, $3H_b$) were obtained for six protons of two methoxyl groups. Protons of ethylene linker were observed as two multiplets at δ 3.70-3.66 (m, $2H_m$) and 3.51-3.47 (m, $2H_n$). Two benzylic protons afforded a singlet at δ 3.44 (s, $2H_u$) whereas piperidine protons offered two broad singlets at δ 2.72-2.69 (bs, $2H_{1s, 1t}$) and 1.79 (bs, $7H_{p, q, r, 1s, 1t}$).



(206)

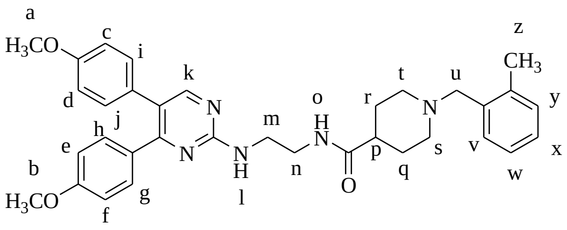


(207)

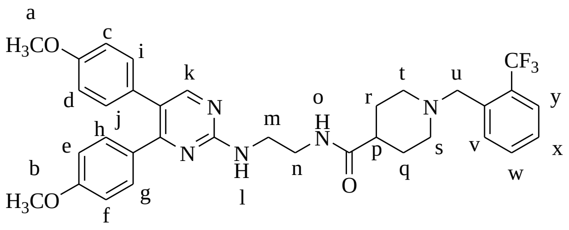
Compound (**207**) in its IR spectrum displayed characteristic peaks for NH stretching at 3294 cm^{-1} and C=O stretching at 1648 cm^{-1}. The ^1H-NMR spectrum of compound (**207**) demonstrated peaks for aromatic protons at δ 8.22 (s, $1H_k$), 7.38-7.36 (d, $2H_{i, j}$, J = 8.8 Hz), and 7.22-7.18 (t, $1H_x$, J = 7.8 Hz), 7.04-7.02 (d, $2H_{g, h}$, J = 8.8 Hz). An amidic proton gave a broad singlet at δ 6.92 (bs, NH_o) while remaining aromatic protons afforded a multiplet at δ 6.85-6.74 (m, $7H_{c, d, e, f, v, w, y}$). A triplet was observed at δ 5.67-5.64 (t, NH_l) for proton attached to *sec.*amine. Among aliphatic protons, signals appeared at δ 3.81 (s, $3H_a$) and 3.78 (s, $6H_b$) representing nine protons of three methoxyl groups. Two protons of ethylene linker offered a multiplet at δ 3.70-3.65 (m, $2H_m$, J = 5.8 Hz) while a multiplet was observed at δ 3.53-3.47 (m, $4H_{n, u}$) representing two protons of ethylene linker and two benzylic protons. Other aliphatic protons afforded signals at δ 2.89-2.86 (m, $2H_{1s, 1t}$) and1.68 (bs, $7H_{p, q, r, 1s, 1t}$). Its mass spectrum showed quasimolecular ion peak at 583.04 $[M+2H]^+$.

IR spectrum of compound (**208**) showed characteristic peaks for NH stretching at 3379 cm^{-1} and for C=O stretching at 1641 cm^{-1}. Its PMR spectrum gave a singlet at δ 8.23 (s, 1H) for one aromatic proton. Among aromatic protons, two protons at δ 7.38-7.36 (d, $2H_{i, j}$, J

= 8.8 Hz) showed *ortho* coupling with other two protons observed at δ 6.76-6.74 (d, 2H$_{c,\,d}$, *J* = 8.8 Hz). A multiplet was seen at δ 7.20-7.08 (m, 4H) for four aromatic protons. Four aromatic protons appeared at δ 7.05-7.03 (d, 2H$_{g,\,h}$, *J* = 8.8 Hz) and 6.85-6.83 (d, 2H$_{e,\,f}$, *J* = 8.8 Hz) showing an *ortho* coupling with a coupling constant of 8.8 Hz. Proton attached to amidic nitrogen offered a broad singlet at δ 6.90 (bs, 1NH$_{o}$) while a *sec.*amine proton gave a triplet at δ 5.54-5.51 (t, 1NH$_{l}$). Methoxyl protons afforded two individual singlets at δ 3.82 (s, 3H$_{a}$) and 3.78 (s, 3H$_{b}$). Four protons of ethylene linker showed multiplets at δ 3.70-3.65 (m, 2H$_{m}$) and 3.51-3.47 (m, 2H$_{n}$). A singlet was observed at δ 3.55 (s, 2H$_{u}$) for benzylic protons and at δ 2.30 (s, 3H$_{z}$) for methyl protons. Signals for piperidine protons were seen at δ 2.75-2.73 (bs, 2H$_{1s,\,1t}$) as broad singlet and 1.57 (m, 7H$_{p,\,q,\,r,\,1s,\,1t}$) as multiplet. The mass spectrum of compound (**208**) showed quasimolecular ion peak at 566.98 $[M+2H]^+$.



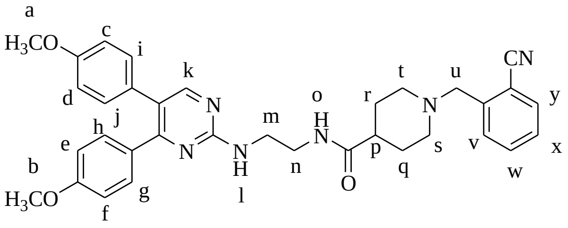
(208)



(209)

In its IR spectrum, compound (**209**) showed characteristic peaks at 3344 cm^{-1} for NH stretching and 1643 cm^{-1} for C=O stretching. PMR spectrum of compound (**209**) offered peaks for aromatic protons as a singlet at δ 8.24 (s, 1H$_{k}$), doublets at δ 7.76-7.74 (d, 1H$_{y}$, *J* = 7.6 Hz) and 7.59-7.57 (d, 1H$_{v}$, *J* = 7.7 Hz), and a triplet at δ 7.47-7.43 (t, 1H$_{x}$, *J* = 7.6 Hz). An *ortho* coupling was observed between four aromatic protons showing doublets at δ 7.39-7.37 (d, 2H$_{i,\,j}$, *J* = 9.2 Hz) and 6.77-6.75 (d, 2H$_{c,\,d}$, *J* = 9.2 Hz). A triplet appeared at δ 7.30-7.27 (t, 1H$_{w}$, *J* = 7.6 Hz) due to one aromatic proton while a doublet was obtained at δ 7.05-7.03 (d, 2H$_{g,\,h}$, *J* = 8.6 Hz) for two aromatic protons which coupled with other protons at δ 6.84-6.82 (d, 2H$_{e,\,f}$, *J* = 8.6 Hz). Two separate singlet peaks were observed at δ 3.81 (s, 3H$_{a}$) and 3.77 (s, 3H$_{b}$). Protons of ethylene linker appeared as multiplets at δ 3.69-3.66 (m, 2H$_{m}$) and 3.52-3.48 (m, 2H$_{n}$) while a singlet at δ 3.54 (s, 1H$_{u}$) represented two benzylic protons. Other aliphatic protons offered peaks at δ 2.74 (bs, 1H$_{1s}$), 2.71 (bs, 1H$_{1t}$) and 1.65-1.59 (m, 7H$_{p,\,q,\,r,\,1s,\,1t}$).

Compound (**210**) in its IR spectrum showed characteristic peaks at 3379 cm^{-1} for NH stretching, 2225 cm^{-1} for CN stretching and 1650 cm^{-1} for C=O stretching. Its PMR spectrum gave signals for aromatic protons at δ 8.24 (s, 1H$_{k}$), 7.61-7.59 (d, 1H$_{y}$, *J* = 8.4 Hz), 7.55-7.51 (m, $2H_{w, x}$) and 7.34-7.30 (m, $1H_{v}$). Four aromatic protons appearing at δ 7.39-7.37 (d, $2H_{i, j}$, J = 8.8 Hz) and 6.78-6.76 (d, $2H_{c, d}$, J = 8.8 Hz) coupled with each other with a coupling constant of 8.8 Hz whereas other aromatic protons were observed at δ 7.06-7.04 (d, $2H_{g, h}$, J = 8.6 Hz) and 6.85-6.83 (d, $2H_{e, f}$, J = 8.6 Hz) showing an *ortho* coupling with a coupling constant of 8.6 Hz. A *sec.*amine proton was obtained as a broad singlet at δ 5.53 (bs, $1NH_{l}$). Two singlets were seen at δ 3.82 (s, $3H_{a}$) and 3.80 (s, $3H_{b}$) representing six protons of methoxyl groups whereas protons of ethylene linker afforded multiplets at δ 3.69-3.66 (m, $2H_{m}$) and 3.51-3.47 (m, $2H_{n}$). Benzylic protons appeared at δ 3.60 (s, $2H_{u}$) while two broad singlets at δ 2.76-2.73 (bs, $2H_{1s, 1t}$) and 1.86-1.72 (bs, $7H_{p, q, r, 1s, 1t}$) represented protons of piperidine ring. Quasimolecular ion peak was obtained at 578.00 $[M+2H]^+$ in the mass spectrum of compound (**210**).



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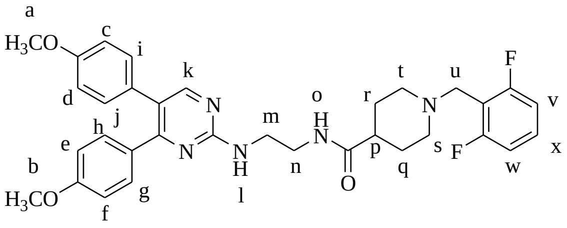
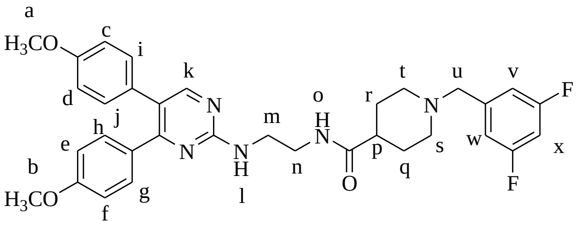


(211)

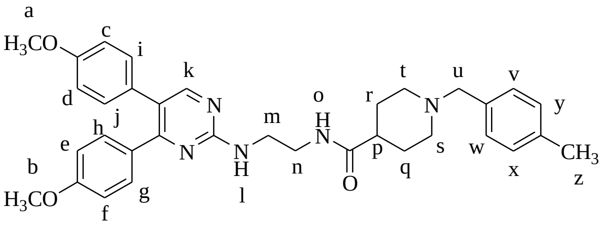
IR spectrum of compound (**211**) exhibited characteristic peaks for NH stretching at 3379 cm^{-1} and C=O stretching at 1640cm^{-1}. In the PMR spectrum, compound (**211**) displayed peaks for aromatic protons as a singlet at δ 8.22 (s, $1H_{k}$), as a doublet at δ 7.37-7.35 (d, $2H_{i, j}$, J = 8.8 Hz), as a multiplet at δ 7.28-7.20 (m, $1H_{x}$) and a doublet at δ 7.05-7.03 (d, $2H_{g, h}$, J = 8.8 Hz). An amidic proton was observed at δ 6.95 (bs, NH_{o}) whereas other aromatic protons offered signals at δ 6.90-6.82 (m, $4H_{e, f, v, w}$) and 6.76-6.74 (d, $2H_{c, d}$, J = 8.8 Hz). A triplet appeared at δ 5.58-5.54 (t, NH_{l}) for the proton of *sec.*amine. Aliphatic protons afforded singlets at δ 3.81 (s, $3H_{a}$) and 3.79 (s, $3H_{b}$) representing six protons of two methoxyl groups. Other aliphatic protons offered multiplets at δ 3.68-3.64 (m, $4H_{m, u}$) and 3.48-3.44 (m, $2H_{n}$). Protons of piperidine ring were obtained as broad singlets at δ 2.87 (bs, $1H_{1s}$), 2.84 (bs, $1H_{1t}$) and 1.74-1.63 (bs, $7H_{p, q, r, 1s, 1t}$). Its mass spectrum exhibited $[M+2H]^+$ peak at 589.30.

In the IR spectrum of compound (**212**) characteristic peaks were observed for NH stretching at 3470 cm^{-1} and C=O stretching at 1643 cm^{-1}. Compound (**212**) in its PMR spectrum provided signals for aromatic protons as a singlet at δ 8.23 (s, $1H_{k}$) and a doublet at δ 7.38-7.36 (d, $2H_{i, j}$, J = 9.0 Hz) which coupled with other protons observed at δ 6.77-6.75

(d, $2H_{c, d}$, J = 9.0 Hz). Other aromatic protons were observed at δ 7.04-7.02 (d, $2H_{g, h}$, J = 8.8 Hz), 6.86-6.81 (m, $5H_{e, f, o, v, w}$) and 6.70-6.65 (m, $1H_{x}$). A peak for proton of *sec.*amine appeared as a triplet at δ 5.59-5.56 (t, NH_{l}). Among aliphatic protons, six protons of methoxyl groups offered two singlets at δ 3.81 (s, $3H_{a}$) and 3.78 (s, $3H_{b}$) whereas protons of ethylene linker afforded two multiplet peaks at δ 3.70-3.66 (m, $2H_{m}$) and 3.51-3.47 (m, $2H_{n}$). A singlet was obtained at δ 3.42 (s, $2H_{u}$) due to benzylic protons while protons of piperidine ring offered three broad singlets at δ 2.77 (bs, $1H_{1s}$), 2.75 (bs, $1H_{1t}$) and 1.90-1.82 (bs, $7H_{p, q, r, 1s, 1t}$).



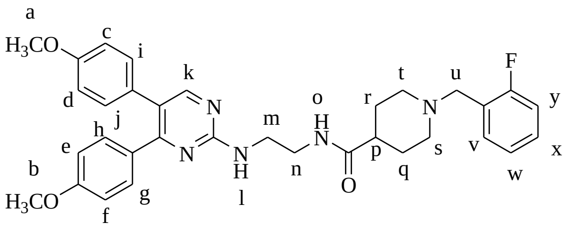
(212)



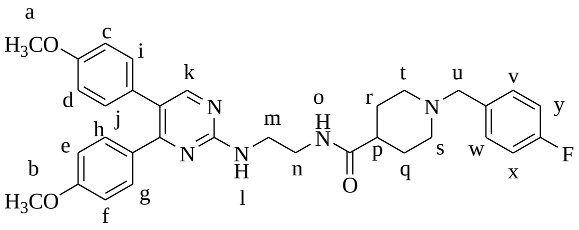
(213)

Compound (**213**) in its IR spectrum exhibited characteristic peaks at 3290 cm-1 for NH stretching and 1648 cm-1 for C=O stretching. PMR spectrum of compound (**213**) showed a singlet at δ 8.23 (s, $1H_{k}$) for one aromatic proton. Aromatic protons showing doublets at δ 7.39-7.37 (d, $2H_{i, j}$, J = 9.0 Hz) coupled with protons observed at δ 6.79-6.76 (d, $2H_{c, d}$, J = 9.0 Hz) whereas protons at δ 7.21-7.19 (d, $2H_{v, w}$, J = 7.8 Hz) showed ortho coupling with other protons at δ 7.14-7.12 (d, $2H_{x, y}$, J = 7.8 Hz). Another ortho coupling was observed between aromatic protons showing signals at δ 7.07-7.05 (d, $2H_{g, h}$, J = 8.8 Hz) and 6.87-6.84 (d, $2H_{e, f}$, J = 8.8 Hz). Two separate singlets appeared at δ 3.83 (s, $3H_{a}$) and 3.81 (s, $3H_{b}$) representing six protons of two methoxyl groups. Protons of ethylene linker afforded peaks as multiplets at δ 3.71-3.67 (m, $2H_{m}$) and 3.51-3.48 (m, $2H_{n}$) while benzylic protons offered a singlet peak at δ 3.55 (s, $2H_{u}$). Signals for other aliphatic protons were observed at δ 2.89 (bs, $2H_{1s, 1t}$), 2.34 (s, $3H_{z}$), 2.06 (s, $2H_{1s, 1t}$) and 1.69 (m, $5H_{p, q, r}$).

IR spectrum of compound (**214**) displayed characteristic peaks for NH stretching at 3379 cm-1 and C=O stretching at 1643 cm^{-1}. In its PMR spectrum, peaks for aromatic protons were observed at δ 8.23 (s, $1H_{k}$) as a singlet, 7.39-7.30 (m, $3H_{i, j, v}$) as a multiplet. Two multiplets were obtained at δ 7.25-7.18 (m, $1H_{x}$) and 7.08-6.96 (m, $5H_{g, h, o, w, y}$) for other aromatic protons while remaining aromatic protons offered two doublets at δ 6.85-6.83 (d, $2H_{e, f}$, J = 8.8 Hz) and 6.76-6.74 (d, $2H_{c, d}$, J = 8.8 Hz). Proton attached to *sec.*amine gave a triplet at δ 5.57-5.54 (t, NH_{l}). Signals for six aliphatic protons of methoxyl groups were observed at δ 3.81 (s, $3H_a$) and 3.78 (s, $3H_b$). Two multiplets appeared at δ 3.69-3.64 (m, $2H_m$) and 3.50-3.46 (m, $4H_{n,\ u}$) representing four protons of ethylene linker and two benzylic protons. Three broad singlets were seen at δ 2.79 (bs, $1H_{1s}$), 2.76 (bs, $1H_{1t}$) and 1.80-1.59 (bs, $7H_{p,\ q,\ r,\ 1s,\ 1t}$) comprising of nine protons of piperidine ring.



(214)



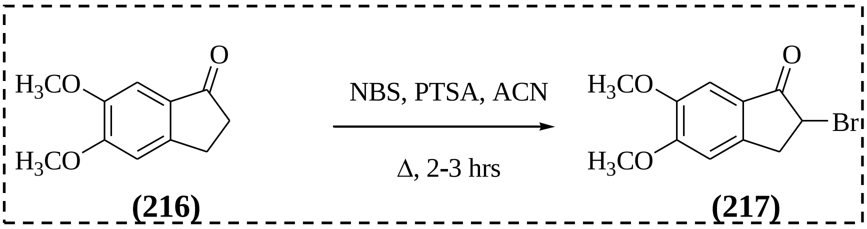
(215)

In the IR of compound (**215**) characteristic peaks were observed at 3278 cm^{-1} for NH stretching and 1646 cm^{-1} for C=O stretching. Its PMR spectrum offered signals for aromatic protons as a singlet at δ 8.22 (s, $1H_k$) and a doublet at δ 7.38-7.36 (d, $2H_{i,\ j}$, J = 9.0 Hz) which coupled with protons at δ 6.77-6.75 (d, $2H_{c,\ d}$, J = 9.0 Hz). A broad singlet was observed at δ 7.30 (bs, NH_o) due to an amidic proton. Other remaining aromatic protons afforded a multiplet at δ 7.05-6.96 (m, $6H_{g,h,\ v,\ w,\ x,\ y}$) and a doublet at δ 6.84-6.82 (d, $2H_{e,\ f}$, J = 8.8 Hz). Proton of *sec.*amine provided a signal at δ 5.56-5.53 (t, NH_l). Among aliphatic protons, signals appeared at δ 3.81 (s, $3H_a$) and 3.78 (s, $3H_b$) representing six protons of methoxyl groups. Signals at δ 3.70-3.66 (m, $2H_m$) and 3.51-3.47 (m, $4H_{n,\ u}$) demonstrated protons of ethylene linker and benzyl group. Broad singlet were obtained at δ 2.83 (bs, $2H_{1s,\ 1t}$) and 1.87-1.69 (bs, $7H_{p,\ q,\ r,\ 1s,\ 1t}$) due to nine protons of piperidine ring. The mass spectrum of **216** displayed $[M+2H]^+$ peak at 571.30.

4.1.3 Synthesis of vicinal diaryltriazine-donepezil hybrids

4.1.3.1 Synthesis of 2-bromo-5,6-dimethoxyindan-1-one (217)

5,6-Dimethoxyindanone (**216**) was refluxed with *N*-bromosuccinimide (NBS) in presence of *p*-toluenesulfonic acid (**Scheme-17**) to yield 2-bromo-5,6-dimethoxyindan-1-one (**217**).

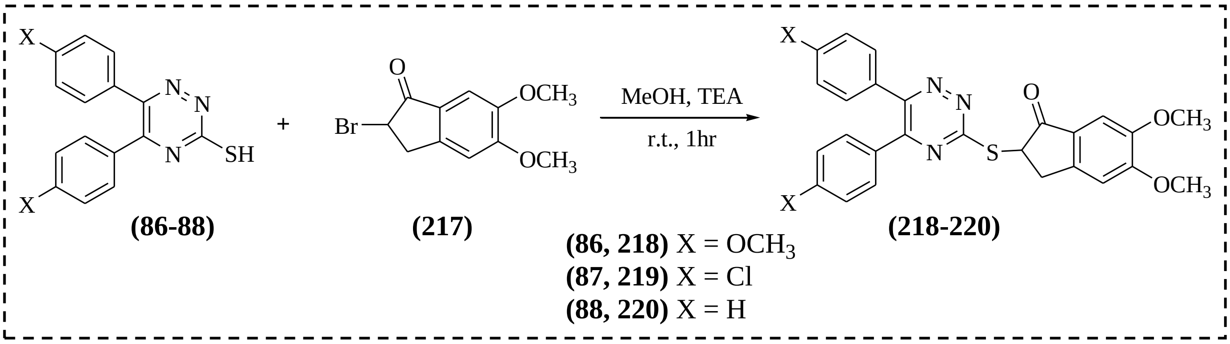


(216) (217)

Scheme-17

4.1.3.2 Synthesis of 2-(5,6-diaryl-1,2,4-triazin-3-ylthio)-5,6-dimethoxyindan-1-one (218-220)

As depicted in **scheme-18**, 5,6-diaryl-1,2,4-triazine-3-thiol (**86-88**) on nucleophilic substitution reaction with 2-bromo-5,6-dimethoxyindan-1-one (**217**) in presence of triethylamine afforded vicinal diaryltriazine-donepezil hybrids, 2-(5,6-diaryl-1,2,4-triazin-3-ylthio)-5,6-dimethoxyindan-1-ones (**218-220**).

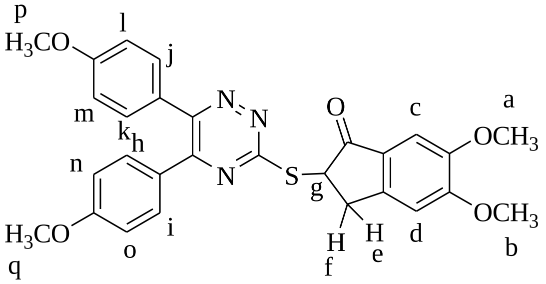


(86-88) **(217)** **(218-220)**

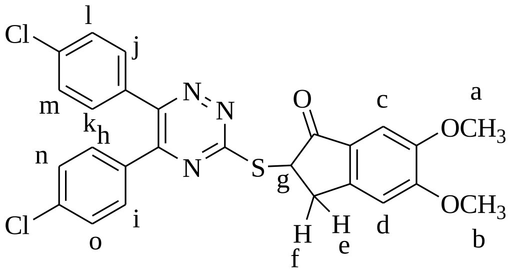
(86, 218) X = OCH_3
(87, 219) X = Cl
(88, 220) X = H

Scheme-18

Compound (**218**) in its IR spectrum showed characteristic peak for C=O stretching at 1704 cm^{-1}. In the PMR spectrum of compound (**218**), signals for aromatic protons were observed at δ 7.45-7.43 (d, $2H_{j,\ k}$, J = 8.8 Hz) which coupled with other protons at δ 6.65-6.63 (d, $2H_{l,\ m}$, J = 8.8 Hz). A singlet appeared in the spectrum at δ 7.25 (s $1H_c$) for one aromatic proton whereas the other aromatic protons offered signals at δ 7.20-7.18 (d, $2H_{h,\ i}$, J = 8.8 Hz) and 6.90-6.86 (m, $3H_{d,\ n,\ o}$). Among the aliphatic protons, proton next to carbonyl group afforded a doublets of doublet at δ 4.48-4.45 (dd, $1H_g$, J = 4.5, 7.8 Hz) while six protons of two methoxyl groups gave singlets at δ 4.00 (s, $3H_a$) and 3.95 (s, $3H_b$). Other aliphatic protons furnished a multiplet at δ 3.84-3.78 (m, $7H_{e,\ p,\ q}$) comprising seven protons while a single proton produced a peak at δ 3.42-3.37 (dd, $1H_f$, J = 4.5, 17.2 Hz) showing germinal and vicinal couplings.

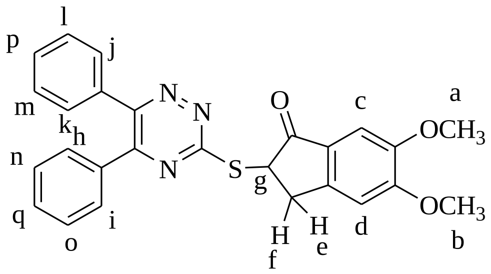


(218)



(219)

IR spectrum of compound (**219**) exhibited characteristic peak for carbonyl group at 1715 cm^{-1}. Its PMR spectrum provided signals for aromatic protons as doublets at δ 7.45-7.43 (d, 2H$_{j,\ k}$, J = 8.4 Hz) and 7.38-7.36 (d, 2H$_{h,\ i}$, J = 8.8 Hz). A singlet for one aromatic proton was observed at δ 7.26 (s 1H$_c$) while other aromatic protons afforded signals at δ 7.18-7.17 (d, 4H$_{l,\ m,\ n,\ o}$, J = 2.0 Hz) and 6.92 (s, 1H$_d$). The aliphatic proton adjacent to carbonyl group gave a doublet of doublet at δ 4.53-4.50 (dd, 1H$_g$, J = 4.7, 7.8 Hz). Two individual singlets were seen at δ 4.02 (s, 3H$_a$) and 3.95 (s, 3H$_b$) representing six protons of two methoxyl groups. Remaining two aliphatic protons offered two doublets of doublet at δ 3.86-3.80 (dd, 1H$_e$, J = 7.8, 17.0 Hz) and 3.42-3.37 (dd, 1H$_f$, J = 4.7, 17.0 Hz).



(220)

In the IR spectrum of compound (**220**) characteristic peak was observed at 1702 cm^{-1} for C=O stretching. PMR spectrum of compound (**220**) exhibited signals for aromatic protons at δ 7.48-7.45 (m, 2H$_{j,\ k}$), 7.42-7.31 (m, 4H$_{h,\ i,\ l,\ m}$) and 7.24 (s 1H$_c$). Other aromatic protons appeared as multiplet at δ 7.20-7.12 (m, 4H$_{n,\ o,\ p,\ q}$) and a singlet at δ 6.90 (s, 1H$_d$). Aliphatic proton at δ 4.49-4.46 (dd, 1H$_g$, J = 4.7, 7.8 Hz) showed vicinal coupling with two protons observed at δ 3.85-3.79 (dd, 1H$_e$, J = 7.8, 17.1 Hz) and 3.44-3.39 (dd, 1H$_f$, J = 4.7, 17.1 Hz). Other six aliphatic protons of methoxyl groups were observed at δ 4.00 (s, 3H$_a$) and 3.93 (s, 3H$_b$).

4.2 Biological Studies

All the aimed final compounds have been submitted for biological evaluation of their potential as Anti-Alzheimer's agents.