EXPERIMENTAL WORK
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Melting points reported are uncorrected. $^1$H NMR spectra were recorded on Brucker AC-300F, 300 MHz and Varian EM-360, 60 MHz NMR instrument using tetramethylsilane (TMS) as the internal standard (chemical shifts in $\delta$, ppm). IR spectra were recorded on Perkin-Elmer 882 spectrophotometer model. IR spectra were obtained with potassium bromide pellets ($\nu$ max in cm$^{-1}$). Ultraviolet spectra were recorded on Perkin-Elmer Lambda 15 spectrophotometer. The purity of the compounds were established by thin layer chromatography (TLC) and by elemental analysis (C, H, N). Elemental analyses were carried out on a Perkin-Elmer-2400. Mass spectra was recorded on a V6-11-250 J 70S. Anhydrous sodium sulfate was used as drying agent. Plates for TLC were prepared with silica gel G according to Stahl (E. Merck) using ethyl acetate. Iodine vapor was used to develop the plates. Silica gel (100-200 mesh) was used for column chromatography.

4-(2,3-EPOXYPROPOXY)-3-METHOXYBENZALDEHYDE (140)

4-Hydroxy-3-methoxybenzaldehyde (vanillin, 139) (5.0 g, 32.9 mmol) was refluxed in epichlorohydrin (50 ml) for 2 h, added anhydrous potassium carbonate (7.5 g) and refluxing was continued with stirring for 6 h. Completion of reaction was confirmed by TLC. The reaction mixture was filtered and the excess of epichlorohydrin removed under reduced pressure to obtain a solid residue, which was loaded onto a column of silica gel and eluted with chloroform. The solid obtained was crystallized from methanol to afford 140 (5.0 g, 73.1%), mp. 102-105°C.
IR (KBr): 2945, 2850, 1695, 1680, 1595, 1290, 1135 and 1020 cm\(^{-1}\).

\(^1\)H NMR (CDCl\(_3\)): \(\delta\) 2.78 (q, 1H, -CH\(_2\) of oxirane), 2.93 (t, 1H, -CH\(_2\) of oxirane), 3.43 (m, 1H, -CH of oxirane), 3.93 (s, 3H, -OCH\(_3\)), 4.08 (dd, 1H, -OCH\(_2\)-), 4.38 (dd, 1H, -OCH\(_2\)-), 7.02 (d, 1H, Ar), 7.43 (t, 2H, Ar) and 9.84 ppm (s, 1H, -CHO).

MS: m/z: 208 [M\(^+\)].

Calcd for C\(_{11}\)H\(_{12}\)O\(_4\): C, 63.46; H, 5.81. Found: C, 63.50; H, 5.81.

1-(ISOPROPYLAMINO)-3-(4-ISOPROPYLIMINOMETHYL-2-METHOXYPHENOX Y)PROPAN-2-OL (141)

4-(2,3-Epoxypropoxy)-3-methoxybenzaldehyde (140) (1.0 g, 4.8 mmol), isopropylamine (30 ml) and methanol (50 ml) were refluxed for 6 h. Completion of reaction was confirmed by TLC. Excess of isopropylamine was removed under reduced pressure to afford an oily residue 141 (1.4 g, 94.5%), which could not be crystallized and was used as such for further reaction.

Anal.:

\(^1\)H NMR (CDCl\(_3\)): \(\delta\) 1.08 (d, 6H, -NHCH(CH\(_3\))\(_2\)), 1.25 (d, 6H, -CH=NC(H\(_3\))\(_2\)), 2.37 (b, 1H, -OH, exchanged in D\(_2\)O ), 2.81 (m, 3H, -CH\(_2\)NHCH\(_3\)<), 3.47 (s, 1H, -NH-, exchanged in D\(_2\)O ), 3.53 (m, 1H, ArCH=NC\(_3\)<), 3.92 (s, 3H, -OCH\(_3\)), 4.04 (m, 3H, -OCH\(_2\)CH(OH)<), 6.90 (d, \(J=8.2\), 1H, Ar), 7.12 (dd, 1H, \(J=8.2\) Hz, \(J=1.8\) Hz, Ar), 7.41 (d, 1H, \(J=1.6\) Hz, Ar) and 8.20 ppm (s, 1H, ArCH=N-).

1-(ISOPROPYLAMINO)-3-(4-ISOPROPYLAMINOMETHYL-2-METHOXYPHENOX Y)PROPAN-2-OL (142)

1-(Isopropylamino)-3-(4-isopropylaminomethyl-2-methoxyphenoxy)propan-2-ol (141) (2.0 g, 6.5 mmol) in methanol (50 ml) was cooled to 5°C and reduced with 128
sodium borohydride (2.0 g, 52.8 mmol) over a period of 2 h, while stirring the contents magnetically. Completion of reaction was confirmed by TLC. Methanol was removed under reduced pressure and the residue dissolved in water, extracted with chloroform and the combined chloroform extract was washed with water. Dried and distilled the chloroform extract to give an oily residue 142 (1.5 g, 74.5%), which was used as such for the oxalate preparation.

Anal.:  
\[^1^H\] NMR (CDCl\(_3\)): \( \delta \) 1.08 (q, 12H, 2 \( \times \) -CH(CH\(_3\))\(_2\)), 2.69 (m, 1H, -CH(OH)CH\(_2\)-), 2.82 (m, 3H, -CH(OH)CH\(_3\)NHCH\(_2\) & ArCH\(_2\)NHCH\(_2\)), 3.68 (s, 2H, ArCH\(_2\)-), 3.80 (s, 3H, -OCH\(_3\)), 3.91 (m, 2H, -OCH\(_2\)-), 4.08 (bm, 1H, -CH(OH)-) and 6.79 ppm (m, 3H, Ar).

MS: \( m/z \) 310 [M\(^+\)].

1-(ISOPROPYLAMINO)-3-(4-ISOPROPYLAMINOMETHYL-2-METHOXYPHENOXY)PROPAN-2-OL (142) OXALATE [DPJ-634]

Oxalic acid (1.2 g, 9.5 mmol) was added to a solution of 142 (1.0 g, 2.5 mmol) in methanol (50 ml) and refluxed for 0.5 h. The reaction mixture was concentrated and left overnight to afford oxalate of 142 (1.0 g, 77.5%), mp. 244-246°C.

Anal.:  
IR (KBr): 3060, 2980, 2900, 1600, 1520, 1300, 1285, 1145 and 1020 cm\(^{-1}\).

\[^1^H\] NMR (D\(_2\)O): \( \delta \) 1.27 (q, 12H, 2 \( \times \) -CH(CH\(_3\))\(_2\)), 3.20 (m, 2H, -CH(OH)CH\(_2\)-), 3.39 (m, 2H, 2 \( \times \) -CH(CH\(_3\))\(_2\)), 3.81 (s, 3H, -OCH\(_3\)), 4.09 (m, 4H, -OCH\(_2\)- & ArCH\(_2\)-), 4.25 (m, 1H, -CH(OH)-) and 7.01 ppm (d, 3H, Ar).

Calcd for C\(_{19}\)H\(_{32}\)N\(_2\)O\(_7\): C, 56.99; H, 8.05; N, 6.99. Found: C, 56.69; H, 8.31; N, 6.88.
4-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)-3-METHOXYBENZALDEHYDE (143)

1-(Isopropylamino)-3-(4-isopropyliminomethyl-2-methoxyphenoxy)propan-2-ol (141) (2.0 g, 6.5 mmol) in 5% acetic acid (100 ml) was refluxed for 3 h, cooled, neutralized with sodium carbonate and extracted with chloroform. The chloroform extract was washed with water, dried and distilled to obtain an oily residue 143 (1.0 g, 57.7%).

*Anal.*

$^1$H NMR (CDCl$_3$): $\delta$ 1.09 (d, 6H, -CH(C$_3$H$_2$)), 2.83 (m, 3H, -CH$_2$NHCH(CH$_3$)$_2$), 3.30 (s, 2H, -OH & -NH-, exchanged in D$_2$O ), 3.89 (s, 3H, -OCH$_3$), 4.07 (m, 2H, -OCH$_2$-), 4.15 (m, 1H, -CH(OH)-), 6.98 (d, 1H, Ar), 7.39 (m, 2H, Ar) and 9.83 ppm (s, 1H, -CHO).

MS: m/z: 268 [MH$^+$].

4-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)-3-METHOXYBENZALDEHYDE (143) OXALATE [DPJ-898]

Oxalic acid (0.75 g, 5.9 mmol) was added to a solution of 143 (1.0 g, 2.8 mmol) in methanol (30 ml) and refluxed for 0.5 h. The solvent was removed under reduced pressure and the residue was crystallized from methanol-acetone mixture to afford oxalate of 143 (0.7 g, 52.4%), mp. 142-145°C.

*Anal.*

IR (KBr): 3290, 3260, 3235, 1665, 1590, 1460, 1400, 1275 and 1135 cm$^{-1}$.

$^1$H NMR (D$_2$O): $\delta$ 1.20 (d, 6H, -CH(CH$_3$)$_3$), 3.14 (m, 2H, -CH$_2$NH-), 3.34 (m, 1H, -CH(CH$_3$)$_2$), 3.70 (s, 3H, -OCH$_3$), 4.02 (m, 2H, -OCH$_2$-), 4.19 (m, 1H, -CH(OH)-),

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6.90 (d, J = 8.3, 1H, Ar_m to methoxy), 7.19 (d, J = 1.1, 1H, Ar_o to methoxy), 7.36 (dd, J = 8.1, J = 1.0, 1H, Ar_p to methoxy) and 9.49 ppm (s, 1H, -CHO).

Calcd for C_{16}H_{23}NO_8: C, 53.77; H, 6.49; N, 3.92. Found: C, 54.06; H, 6.29; N, 4.01.

1-(4-tert-BUTYLIMINOMETHYL-2-METHOXYPHENOXY)-3-(ISOPROPYLAMINO)PROPAN-2-OL (144)

4-(2-Hydroxy-3-isopropylaminopropoxy)-3-methoxybenzaldehyde (143) (3.0 g, 11.2 mmol), excess of tert-butylamine (20 ml) and methanol (50 ml) were refluxed for 6 h. Excess of tert-butylamine removed under reduced pressure to afford an oily residue 144 (3.5 g, 96.7%), which could not be crystallized and was used as such for further reaction.

Anal.: 

\[ ^1H \text{NMR (60 MHz) (CDCl}_3): \delta 1.0 (d, 6H, -CH(CH}_3)_2), 1.20 (s, 9H, -C(CH}_3)_3), 2.70 (m, 3H, -CH}_2NHCH<), 3.4 (s, 2H, \text{-OH & -NH-}, \text{exchanged in D}_2O ), 3.9 (s, 3H, -OCH}_3), 4.0 (s, 3H, -OCH}_2CH<), 6.8-7.5 (m, 3H, Ar) and 8.2 ppm (s, 1H, ArCH=N-). \]

1-(4-tert-BUTYLIMINOMETHYL-2-METHOXYPHENOXY)-3-(ISOPROPYLAMINO)PROPAN-2-OL (145)

1-(4-tert-Butyliminomethyl-2-methoxyphenoxy)-3-(isopropylamino)propan-2-ol (144) (2.0 g, 6.2 mmol) in methanol (50 ml) was cooled to 5°C and reduced with sodium borohydride (3.0 g, 79.3 mmol) over a period of 2 h, while stirring the contents magnetically. Completion of reaction was confirmed by TLC. Methanol was removed under reduced pressure, the residue dissolved in water and extracted with chloroform. The chloroform extract was washed with water, dried and distilled to give an oily residue 145 (1.5 g, 74.5%), which could not be crystallized.
Anal.

$^1$H NMR (CDCl$_3$): δ 1.07 (d, 6H, -CH(CH$_3$)$_2$), 1.19 (s, 9H, -C(CH$_3$)$_3$), 2.65-2.83 (m, 6H, -CH$_2$NHCH$<$, -OH & -NH$-$, three protons exchanged in D$_2$O ), 3.62 (s, 2H, ArCH$_2$), 3.81 (s, 3H, -OCH$_3$), 3.90 (m, 2H, -OCH$_2$), 4.05 (m, 1H, -CH(OH)-) and 6.70-6.84 ppm (m, 3H, Ar).

MS: m/z: 324 [M$^+$].

1-(4-tert-BUTYLAMINOMETHYL-2-METHOXYPHENOXY)-3-(ISOPROPYLAMINO)PROPAN-2-OL (145) OXALATE [DPJ-906]

Oxalic acid (0.5 g, 3.9 mmol) was added to a solution of 145 (0.75 g, 1.5 mmol) in methanol (50 ml) and refluxed for 0.5 h. The solvent was removed under reduced pressure and the residue was crystallized from methanol-acetone mixture to afford oxalate of 145 (0.78 g, 81.4%), mp. 258-260°C.

Anal.
IR (KBr): 3400, 3355, 2975, 2755, 2670, 2400, 1590, 1580, 1520, 1300, 1265, 1140 and 1015 cm$^{-1}$.

$^1$H NMR (D$_2$O): δ 1.22 (d, 6H, -CH(CH$_3$)$_2$), 1.31 (s, 9H, -C(CH$_3$)$_3$), 3.16 (m, 2H, -CH(OH)CH$_2$), 3.37 (m, 1H, -CH(CH$_3$)$_2$), 3.76 (s, 3H, -OCH$_3$), 4.04 (m, 4H, -OCH$_2$ & ArCH$_2$), 4.21 (m, 1H, -CH(OH)-), 6.93 (s, 2H, Ar) and 6.99 ppm (s, 1H, Ar).

Calcd for C$_{20}$H$_{34}$N$_2$O$_7$: C, 57.95; H, 7.97; N, 7.00.

4-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)-3-METHOXYBENZALDEHYDE OXIME (146)

To 4-(2-hydroxy-3-isopropylaminoproxy)-3-methoxybenzaldehyde (143) (0.5 g, 1.9 mmol) in refluxing aldehyde free alcohol (50 ml) was added a solution of
sodium acetate trihydrate (1.5 g, 11.0 mmol) in water (1 ml) and hydroxylamine hydrochloride (1.5 g, 21.6 mmol) in water (1 ml). Refluxing was continued for 6 h, and the completion of reaction was confirmed by TLC. The solvent was removed under reduced pressure to give a residue, which was dissolved in water, basified with ammonia solution and extracted with chloroform. The extract was washed with water, dried and distilled to give an oily residue 146 (0.2 g, 37.9%), which could not be crystallized and was used for preparation of oxalate.

*Anal.*:

$^1$H NMR (CDCl$_3$): $\delta$ 1.13 (d, 6H, -CH(CH$_3$)$_2$), 2.85 (m, 3H, -CH$_2$NH-), 3.78 (s, 3H, -OCH$_3$), 4.05 (m, 2H, -OCH$_2$), 4.23 (m, 1H, -CH(OH)-), 4.7-6.5 (b, 2H, ArCH=NOH & -OH, exchanged in D$_2$O), 6.81 (d, $J = 8.5$, 1H, Ar$_m$ to methoxy), 6.89 (dd, $J = 8.3$ Hz, $J = 1.6$ Hz, Ar$_p$ to methoxy), 7.13 (d, 1H, $J = 1.7$ Hz, Ar$_o$ to methoxy) and 8.00 ppm (s, 1H, ArCH=NOH).

MS: m/z: 282 [M$^+$].

**4-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)-3-METHOXYBENZALDEHYDE OXIME (146) OXALATE [DPJ-904]**

Oxalic acid (0.5 g, 3.9 mmol) was added to a solution of 146 (1.0 g, 3.5 mmol) in methanol (50 ml) and refluxed for 15 min. The solvent was removed under reduced pressure and the residue was crystallized from methanol-acetone mixture to afford oxalate of 146 (0.65 g, 49.3%), mp. 165-168°C.

*Anal.:

IR (KBr): 3515, 3460, 3410, 3375, 3290, 3150, 2920, 2340, 1620, 1595, 1510, 1310 and 1265 cm$^{-1}$. 

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\(^1\)H NMR (D$_2$O): \( \delta \) 1.21 (d, 6H, -CH(CH$_3$)$_2$), 3.15 (m, 2H, -CH$_2$NH-), 3.35 (m, 1H, -CH(CH$_3$)$_2$), 3.73 (s, 3H, -OCH$_3$), 4.01 (m, 2H, -OCH$_2$-), 4.19 (m, 1H, -CH(OH)-), 6.86 (d, 1H, \( J = 8.5 \) Hz, Ar$_m$ to methoxy), 7.00 (d, 1H, \( J = 8.3 \) Hz, Ar$_p$ to methoxy), 7.12 (s, 1H, Ar$_o$ to methoxy) and 7.98 ppm (s, 1H, ArCH=NOH).

Calcd for C$_{16}$H$_{24}$N$_2$O$_8$: C, 51.61; H, 6.50; N, 7.52. Found: C, 51.84; H, 6.74; N, 7.65.

4-[4-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)-3-METHOXY PHENYL]BUT-3-EN-2-ONE (147)

4-(2-Hydroxy-3-isopropylaminopropoxy)-3-methoxybenzaldehyde (143) (0.5 g, 1.9 mmol), potassium hydroxide (1.0 g, 17.8 mmol) and methanol (50 ml) were refluxed and then added acetone (5 ml). Refluxing was continued for 6 h, a yellowish-red color was produced. The solvents were removed under reduced pressure, added water (100 ml) and extracted with chloroform. The extract was washed with water, dried and distilled to give an oily residue. The residue was loaded onto a column of neutral alumina and eluted with pure chloroform, then with chloroform-methanol (99.5:0.5) and then with chloroform-methanol (99:1) mixture. After removal of solvents, the residue was crystallized from dry ether to afford 147 (0.14 g, 24.4%), mp. 104-107°C.

Anal.: [IR (KBr): 3415, 3380, 2920, 1660, 1600 1515, 1315, 1255, 1145 and 1035 cm$^{-1}$.  
\(^1\)H NMR (CDCl$_3$): \( \delta \) 1.08 (d, 6H, -CH(CH$_3$)$_2$), 2.37 (s, 3H, -COCH$_3$), 2.80 (m, 3H, -CH$_2$NHCH(-)), 2.9-3.2 (b, 2H, -OH & -NH-), 3.87 (s, 3H, -OCH$_3$), 4.03 (m, 2H, -OCH$_2$(-)), 4.11 (m, 1H, -CH(OH)-), 6.59 (d, 1H, \( J = 16.2 \) Hz, ArCH=CH(-)), 6.88 (d, 1H, Ar), 7.06 (m, 2H, Ar) and 7.44 ppm (d, 1H, \( J = 16.2 \) Hz, ArCH=CH-).

MS: m/z: 307 [M$^+$]

Calcd for C$_{17}$H$_{25}$N$_2$O$_4$: C, 66.42; H, 8.20; N, 4.56. Found: C, 66.45; H, 7.96; N, 4.78. 134
4-[(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)-3-METHOXYPHENYL]BUT-3-EN-2-ONE (147) OXALATE [DPJ-913]

To a solution of 147 (0.75 g, 2.4 mmol) in refluxing methanol (50 ml) was added oxalic acid (0.5 g, 3.9 mmol) and refluxing was continued for 10 min. The solvent was removed under reduced pressure and the residue crystallized from acetone to afford the oxalate of 147 (0.63 g, 65%), mp. 130-133°C.

Anal.:
IR (KBr): 3415, 3320, 2920, 1670, 1640, 1600, 1140 and 1035 cm⁻¹.
¹H NMR (D₂O): δ 1.21 (d, 6H, -CH(CH₃)₂), 2.25 (s, 3H, -COCH₃), 3.15 (m, 2H, -CH₂N<), 3.35 (m, 1H, -C(CH₃)₂), 3.76 (s, 3H, -OC₃H₃), 4.03 (m, 2H, -OCH₂-), 4.19 (m, 1H, -CH(OH)-), 6.54 (d, 1H, J = 16.2 Hz, ArCH=CH-), 6.90 (d, 1H, Ar), 7.14 (m, 2H, Ar) and 7.50 ppm (d, 1H, J = 16.2 Hz, ArCH=CH-).
Calcd for C₁₉H₂₇NO₄: C, 57.42; H, 6.85; N, 3.52. Found: C, 57.34; H, 6.70; N, 3.85.

1-[(tert-BUTYLAMINO)-3-(4-tert-BUTYLIMINOMETHYL-2-METHOXYPHENOXO)PROPAN-2-OL (148)

4-(2,3-Epoxypropoxy)-3-methoxybenzaldehyde (140) (2.0 g, 9.6 mmol), tert-butylamine (20 ml) and methanol (50 ml) were refluxed for 4 h. Completion of reaction was confirmed by TLC. Excess of tert-butylamine and methanol were removed under reduced pressure to afford an oily residue 148 (3.0 g, 92.8%), which could not be crystallized and was used as such for further reaction.

Anal.:
¹H NMR (60 MHz) (CDCl₃): δ 1.2 (s, 9H, -C(CH₃)₃), 1.3 (s, 9H, ArCH=NC(CH₃)₃), 2.8 (b, 2H, -CH₂NH-), 3.9 (s, 3H, -OC₃H₃), 4.1 (b, 5H, -OCH₂CH(OH)CH₂NH-, two protons exchanged in D₂O), 6.8-7.5 (m, 3H, Ar) and 8.2 ppm (s, 1H, ArCH=N-).
1-(tert-BUTYLAMINO)-3-(4-tert-BUTYLMETHINOMETHYL-2-METHOXYPHENOXY)PROPAN-2-OL (149)

1-(tert-Butylamino)-3-(4-tert-butyliminomethyl-2-methoxyphenoxy)propan-2-ol (148) (1.0 g, 3.0 mmol) in methanol (50 ml) was cooled to 5°C and reduced with sodium borohydride (1.0 g, 26.4 mmol) over a period of 2 h, while stirring the contents magnetically. Completion of reaction was confirmed by TLC. Methanol was removed under reduced pressure and the residue dissolved in water, extracted with chloroform. The chloroform extract was washed with water, dried and distilled to give an oily residue 149 (0.7 g, 69.6%), which could not be crystallized.

Anal.: 

$^1$H NMR (CDCl$_3$): $\delta$ 1.10 (s, 9H, -C(CH$_3$)$_3$), 1.18 (s, 9H, ArCH$_2$NHC(CH$_3$)$_3$), 2.72 (m, 2H, -CH(OH)CH$_2$), 3.64 (s, 2H, ArCH$_2$), 3.82 (s, 3H, -OCH$_3$), 3.91 (m, 2H, -OCH$_2$), 4.01 (bm, 1H, -OH), and 6.80 ppm (m, 3H, Ar)

MS: m/z: 339 [MH$^+$].

1-(tert-BUTYLAMINO)-3-(4-tert-BUTYLMETHINOMETHYL-2-METHOXYPHENOXY)PROPAN-2-OL (149) OXALATE [DPJ-633]

To a solution of 149 (0.3 g, 0.9 mmol) in refluxing methanol (50 ml) was added oxalic acid (0.3 g, 2.4 mmol) and refluxed for 0.5 h. The solvent was removed under reduced pressure and the residue was crystallized from methanol-acetone mixture to afford oxalate of 149 (0.3 g, 79%), mp 258-260°C.

Anal.: 

IR (KBr): 3340, 3300, 2980, 2810, 1600, 1515, 1310 and 1270 cm$^{-1}$. 

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$^1$H NMR (D$_2$O): $\delta$ 1.27 (s, 9H, -C(CH$_3$)$_3$), 1.31 (s, 9H, ArCH$_2$NHC(CH$_3$)$_3$), 3.09 (dd, 1H, -CH(OH)C$_2$-), 3.22 (dd, 1H, -CH(OH)C$_2$-), 3.76 (s, 3H, -OCH$_3$), 4.03 (m, 4H, -OCH$_2$- & ArC$_2$H$_2$), 4.17 (m, 1H, -CHOH-) 6.93 (s, 2H, Ar) and 6.99 ppm (s, 1H, Ar).

Calcd for C$_{21}$H$_{36}$N$_2$O$_7$: C, 58.86; H, 8.47; N, 6.54. Found: C, 58.68; H, 8.68; N, 6.65.

4-(3-tert-BUTYLAMINO-2-HYDROXYPROPOXY)-3-METHOXYBENZALDEHYDE (150)

1-(tert-Butylamino)-3-(4-tert-butylinomethyl-2-methoxyphenoxy)propan-2-ol (148) (1.0 g, 3.0 mmol) in 5% acetic acid (50 ml) was refluxed for 3 h, cooled, neutralized with sodium carbonate and extracted with chloroform. The chloroform extract was washed with water, dried and distilled to obtain an oily residue 150 (0.5 g, 59.8%).

Anal.:

$^1$H NMR (CDCl$_3$): $\delta$ 1.15 (s, 9H, -C(CH$_3$)$_3$), 2.77 (m, 1H, -CH$_2$NH-), 2.92 (m, 1H, -CH$_2$NH-), 3.91 (s, 3H, -OCH$_3$), 4.12 (t, 3H, -OCH$_2$CH(OH)-) 6.99 (d, 1H, Ar), 7.42 (m, 2H, Ar) and 9.84 ppm (s, 1H, -CHO).

MS: m/z: 282 [MH$^+$].

4-(3-tert-BUTYLAMINO-2-HYDROXYPROPOXY)-3-METHOXYBENZALDEHYDE (150) OXALATE [DPJ-811]

To a solution of 150 (2.0 g, 7.1 mmol) in refluxing methanol (50 ml) was added oxalic acid (1.5 g, 11.9 mmol) and refluxing was continued for 0.5 h. The reaction mixture was concentrated and left over night for crystallization to afford oxalate of 150 (1.0 g, 37.9%), mp. 196-199°C.

Anal.:

IR (KBr): 3290, 2975, 2915, 2830, 1685, 1580, 1500, 1285, 1250 and 1130 cm$^{-1}$. 

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1H NMR (D2O): δ 1.32 (s, 9H, -C(CH3)3), 3.16 (dd, 1H, -CH2NH-), 3.28 (dd, 1H, -CH2NH-), 3.63 (s, 3H, -OCH3), 4.16 (m, 2H, -OCH2-), 4.26 (m, 1H, -CH(OH)-), 7.06 (d, 1H, J = 8.4 Hz, Ar), 7.39 (d, 1H, J = 1.4 Hz, Ar), 7.51 (dd, 1H, J = 8.4 Hz, J = 1.7 Hz, Ar) and 9.64 ppm (s, 1H, -CHO).

Calcd for C17H25N08: C, 54.98; H, 6.79; N, 3.77. Found: C, 55.26; H, 6.99; N, 3.91.

1-(tert-BUTYLAMINO)-3-(4-ISOPROPYLIMINOMETHYL-2-METHOXYPHENOXY)PROPAN-2-OL (151)

4-(3-tert-Butylamino-2-hydroxypropoxy)-3-methoxybenzaldehyde (150) (2.0 g, 7.1 mmol) and isopropylamine (10 ml) in methanol (100 ml) were refluxed for 4 h. Excess of isopropylamine and methanol were removed under reduced pressure to afford an oily residue 151 (2.1 g, 91.6%), which could not be crystallized and was used as such for further reaction.

Anal.: 
1H NMR (60 MHz) (CDCl3): δ 1.1 (s, 9H, -C(CH3)3), 1.25 (d, 6H, -CH(CH3)2), 2.6 (b, 2H, -CH2NH-), 3.5 (s, 3H, -CH(CH3)2, -OH & -NH-, two protons exchanged in D2O), 3.8 (s, 3H, -OCH3), 4.1 (bs, 3H, -OCH2CH(OH)-), 6.8-7.5 (m, 3H, Ar) and 8.2 ppm (s, 1H, ArCH=N-)

1-(tert-BUTYLAMINO)-3-(4-ISOPROPYLAMINOMETHYL-2-METHOXYPHENOXY)PROPAN-2-OL (152)

1-(tert-Butylamino)-3-(4-isopropylaminomethyl-2-methoxyphenoxy)propan-2-ol (151) (1.0 g, 3.1 mmol) in methanol (50 ml) was cooled to 5°C and reduced with sodium borohydride (1.0 g, 26.4 mmol) over a period of 2 h while stirring the contents magnetically. Completion of reaction was confirmed by TLC. Methanol was removed under reduced pressure and the residue dissolved in water, extracted with chloroform.
The chloroform extract was washed with water, dried and distilled to give an oily residue 152 (0.7 g, 69.6%), which could not be crystallized.

\textit{Anal.}:

$^1$H NMR (CDCl$_3$): $\delta$ 1.10 (d, 15H, -CH(CH$_3$)$_2$ & -C(CH$_3$)$_3$), 2.71 (m, 1H, -CH(OH)CH$_2$-), 2.85 (m, 2H, -CH(OH)CH$_2$- & -CH(CH$_3$)$_2$), 3.72 (s, 2H, ArCH$_2$-), 3.86 (s, 3H, -OCH$_3$), 4.00 (t, 3H, -OCH$_2$CH(OH)-) and 6.84 ppm (m, 3H, Ar).

MS: m/z: 324 [M$^+$.]

1-(\textit{tert}-BUTYLAMINO)-3-(4-ISOPROPYLAMINOMETHYL-2-METHOXYPHENOXY)PROPAN-2-OL (152) OXALATE [DPJ-830]

Oxalic acid (1.0 g, 7.9 mmol) was added to a solution of 152 (1.0 g, 3.1 mmol) in methanol (50 ml) and refluxed for 0.5 h. The solvent was removed under reduced pressure and the residue was crystallized from methanol-acetone mixture to afford oxalate of 152 (1.02 g, 65.3%), mp. 158-161°C.

\textit{Anal.}:

IR (KBr): 3505, 3350, 2980, 2785, 1720, 1700, 1630, 1610, 1270 and 1230 cm$^{-1}$.

$^1$H NMR (D$_2$O): $\delta$ 1.33 (d, 6H, -CH(CH$_3$)$_2$), 1.36 (s, 9H, -C(CH$_3$)$_3$), 3.19 (dd, 1H, -CH(OH)CH$_2$-), 3.31 (dd, 1H, -CH(OH)CH$_2$-), 3.43 (m, 1H, -CH(CH$_3$)$_2$), 3.85 (s, 3H, -OCH$_3$), 4.13 (m, 4H, -OCH$_2$- & ArCH$_2$-), 4.28 (m, 1H, -CH(OH)-), 7.03 (s, 2H, Ar) and 7.10 ppm (s, 1H, Ar).

Calcd for C$_{22}$H$_{36}$N$_2$O$_{11}$: C, 52.38; H, 7.19; N, 5.55. Found. C, 52.56, H, 7.30, N, 5.45.

4-(\textit{tert}-BUTYLAMINO-2-HYDROXYPROPOXY)-3-METHOXYBENZALDEHYDE OXIME (153)

To 4-(\textit{tert}-butylamino-2-hydroxypropoxy)-3-methoxybenzaldehyde (150) (0.5 g, 1.8 mmol) in refluxing aldehyde free alcohol (50 ml) was added a solution of
sodium acetate trihydrate (1.5 g, 11.0 mmol) in water (1 ml) and hydroxylamine hydrochloride (1.5 g, 21.6 mmol) in water (1 ml). Refluxing was continued for 6 h and completion of reaction was confirmed by TLC. The solvent was removed under reduced pressure to give a residue, which was dissolved in water, basified with ammonia solution and extracted with chloroform. The extract was washed with water, dried and distilled to give an oily residue 153 (0.3 g, 57%), which could not be crystallized and used for preparation of oxalate.

**Anal.:**

$^1$H NMR (CDCl$_3$): δ 1.16 (s, 9H, -C(CH$_3$)$_3$), 2.77 (m, 1H, -CH$_2$NH-), 2.87 (m, 1H, -CH$_2$NH-), 3.78 (s, 3H, -OCH$_3$), 4.07 (d, 2H, -OCH$_2$-), 4.21 (m, 1H, -CH(OH)-), 4.90-5.60 (b, 3H, ArCH=NOH, -OH & -NH-, exchanged in D$_2$O ), 6.81 (d, 1H, $J = 8.2$ Hz, Ar$_m$ to methoxy), 6.89 (dd, 1H, $J = 8.2$ Hz, $J = 1.6$ Hz, Ar$_p$ to methoxy), 7.12 (d, 1H, $J = 1.5$ Hz, Ar$_o$ to methoxy) and 8.00 ppm (s, 1H, ArCH=NOH).

MS: m/z: 296 [M$^-$].

**4-(3-tert-BUTYLAMINO-2-HYDROXYPROPOXY)-3-METHOXYBENZALDEHYDE OXIME (153) OXALATE [DPJ-834]**

To a solution of 153 (0.5 g, 1.7 mmol) in refluxing methanol (50 ml) was added oxalic acid (0.3 g, 2.4 mmol) and refluxing was continued for 10 min The solvent was removed under reduced pressure and the residue was crystallized from dry acetone to afford oxalate of 153 (0.5 g, 76.7%), mp. 216-218°C.

**Anal.:**

IR (KBr): 3150, 3130, 3015, 2980, 2855, 2825, 2680, 2475, 1595, 1515, 1295, 1260, 1130 and 960 cm$^{-1}$.
$^1$H NMR (D$_2$O): $\delta$ 1.23 (s, 9H, -C(CH$_3$)$_3$), 3.04 (m, 1H, -CH$_2$NH-), 3.17 (m, 1H, -CH$_2$NH-), 3.68 (s, 3H, -OCH$_3$), 3.96 (m, 2H, -OCH$_2$-), 4.14 (m, 1H, -CH(OH)-) 6.81 (d, 1H, $J = 8.3$ Hz, Ar$_m$ to methoxy), 6.93 (dd, 1H, $J = 8.4$ Hz, $J = 1.7$ Hz, Ar$_p$ to methoxy); 7.04 (d, 1H, $J = 1.9$ Hz, Ar$_r$ to methoxy) and 7.91 ppm (s, 1H, ArCH=NOH).

Calcd for C$_{17}$H$_{26}$N$_2$O$_8$: C, 52.84; H, 6.78; N, 7.25. Found: C, 53.04; H, 7.04; N, 7.50.

4-[2-HYDROXY-3-(4-METHYLPIPERAZIN-1-YL)PROPOXY]-3-METHOXYBENZALDEHYDE (154)

4-(2,3-Epoxypropoxy)-3-methoxybenzaldehyde (140) (1.0 g, 4.8 mmol) and N-methylpiperazine (0.6 g, 5.9 mmol) in methanol (50 ml) were refluxed for 4 h. Completion of reaction was monitored by TLC. Methanol was removed under reduced pressure to give an oily residue, which was chromatographed over silica gel (35 g) using chloroform as eluent. The oily residue 154 (0.7 g, 47.3%) obtained was not crystallizable.

Anal.: $^1$H NMR (CDCl$_3$): $\delta$ 2.30 (s, 3H, >NCH$_3$), 2.61 (m, 10H, -CH$_2$N(CH$_2$CH$_2$)$_2$N-), 3.92 (s, 3H, -OCH$_3$), 4.10 (m, 2H, -OCH$_2$-), 4.18 (m, 1H, -CH(OH)-), 7.02 (d, 1H, Ar), 7.43 (m, 2H, Ar) and 9.85 ppm (s, 1H, -CHO).

MS: m/z: 308 [M$^+$]

4-[2-HYDROXY-3-(4-METHYLPIPERAZIN-1-YL)PROPOXY]-3-METHOXYBENZALDEHYDE (154) OXALATE [DPJ-832]

Oxalic acid (1.2 g, 9.5 mmol) was added to a solution of 154 (1.0 g, 3.2 mmol) in refluxing methanol (50 ml) and continued refluxing for 0.5 h, left overnight for crystallization and filtered to give oxalate of 154 (1.0 g, 63.1%), mp. 203-206°C.
**Anal.:**

IR (KBr): 3420, 3010; 2655, 2535, 1720, 1700, 1630, 1590, 1275, 1135 and 710 cm⁻¹.

¹H NMR (D₂O): δ 2.98 (s, 3H, >NCH₃), 3.49 (t, 2H, -CH₂N<), 3.67 (b, 8H, -N(CH₂CH₃)₂N-), 3.87 (s, 3H, -OCH₃), 4.17 (m, 2H, -OCH₂-), 4.50 (m, 1H, -CH(OH)-), 7.09 (d, 1H, J = 8.3 Hz, Ar), 7.44 (d, 1H, J = 1.6 Hz, Ar), 7.54 (dd, 1H, J = 8.3 Hz, J = 1.6 Hz, Ar) and 9.68 ppm (s, 1H, ArCHO).

Calcd for C₃₀H₃₈N₂O₁₂: C, 49.18; H, 5.78; N, 5.73. Found: C, 48.97, H, 5.50; N, 5.79.

1-(4-Isopropyliminomethyl-2-methoxyphenoxy)-3-(4-methylpiperazin-1-yl)propan-2-ol (155)

4-[2-Hydroxy-3-(4-methylpiperazin-1-yl)propoxy]-3-methoxybenzaldehyde (154) (1.0 g, 3.2 mmol) and isopropylamine (20 ml) in methanol (100 ml) were refluxed for 4 h. Excess of isopropylamine and methanol were removed under reduced pressure to afford an oily residue 155 (1.0 g, 88.2%), which could not be crystallized and was used as such for further reaction.

**Anal.:**

¹H NMR (60 MHz) (CDCl₃): δ 1.2 (d, 6H, -CH(CH₃)₂), 2.2 (s, 3H, >NCH₃), 2.4 (bs, 8H, -N(CH₂CH₃)₂N-), 3.3 (m, 3H, -CH₂N< & -CH(CH₃)₂), 3.9 (s, 3H, -OCH₃), 4.1 (s, 3H, -OCH₂CH(OH)-), 6.8-7.5 (m, 3H, Ar) and 8.3 ppm (s, 1H, ArCHO=N−).

1-(4-Isopropylaminomethyl-2-methoxyphenoxy)-3-(4-methylpiperazin-1-yl)propan-2-ol (156)

1-(4-Isopropylaminomethyl-2-methoxyphenoxy)-3-(4-methylpiperazin-1-yl)propan-2-ol (155) (1.0 g, 2.9 mmol) in methanol (75 ml) was cooled to 5°C and reduced with sodium borohydride (1.0 g, 26.4 mmol) over a period of 2 h, while
stirring the contents magnetically. Completion of reaction was confirmed by TLC. Methanol was removed under reduced pressure and the residue dissolved in water, extracted with chloroform. The chloroform extract was washed with water, dried and distilled to give an oily residue \(156\) (0.6 g, 59.7%), which could not be crystallized.

**Anal.:**

\(^1\)H NMR (CDCl\(_3\)): \(\delta\) 1.10 (d, 6H, \(-\text{CH(CH}_3\text{)}_2\)), 2.29 (s, 3H, \(>\text{NCH}_3\)), 2.57 (m, 10H, \(-\text{CH}_2\text{N(\text{CH}_3\text{CH}_2\text{)})}_2\text{N-}\)), 2.86 (m, 1H, \(-\text{CH(\text{CH}_3\text{)})}_2\)), 3.72 (s, 2H, \(\text{ArCH}_2\)), 3.86 (s, 3H, \(-\text{OCH}_3\)), 3.99 (m, 2H, \(-\text{OCH}_2\)), 4.12 (m, 1H, \(-\text{CH(OH)}\)) and 6.84 ppm (m, 3H, Ar).

MS: m/z: 351 [M⁺].

**1-(4-ISOPROPYLAMINOMETHYL-2-METHOXYPHENOXY)-3-(4-METHYLPIPERAZIN-1-YL)PROPAN-2-OL (156) OXALATE [DPJ-859]**

To a solution of \(156\) (1.5 g, 4.3 mmol) in refluxing methanol (100 ml) was added oxalic acid (2.2 g, 17.4 mmol) and refluxing was continued for 10 min. The reaction mixture was concentrated and left overnight to afford oxalate of \(156\) (2.18 g, 82.2%), mp 192-195°C.

**Anal.:**

IR (KBr): 3400, 2940, 2610, 1725, 1640, 1600, 1405 and 1215 cm\(^{-1}\).

\(^1\)H NMR (D\(_2\)O): \(\delta\) 1.24 (d, 6H, \(-\text{CH(\text{CH}_3\text{)})}_2\)), 2.94 (s, 3H, \(>\text{NCH}_3\)), 3.33 (m, 1H, \(-\text{CH(\text{CH}_3\text{)})}_2\)), 3.44 (d, 2H, \(-\text{CH}_2\text{N}<\)), 3.63 (b, 8H, \(-\text{N(\text{CH}_3\text{CH}_2\text{)})}_2\text{N-}\)), 3.77 (s, 3H, \(-\text{OCH}_3\)), 4.01 (m, 4H, \(-\text{OCH}_2\text{& ArCH}_2\)), 4.56 (m, 1H, \(-\text{CH(OH)}\)) and 6.93 ppm (d, 3H, Ar).

Calcd for C\(_{25}\)H\(_{39}\)N\(_3\)O\(_7\): C, 48.31; H, 6.32; N, 6.76. Found: C, 48.61; H, 5.38; N, 6.69.
1-(4-tert-BUTYLIMINOMETHYL-2-METHOXYPHENOXY)-3-(4-METHYLPIPERAZIN-1-YL)PROPAN-2-OL (157)

4-[2-Hydroxy-3-(4-methylpiperazin-1-yl)propoxy]-3-methoxybenzaldehyde (154) (1.0 g, 3.2 mmol) and tert-butylamine (20 ml) in methanol (100 ml) were refluxed for 4 h. The solvent was removed under reduced pressure to give an oily residue 157 (1.1 g, 93.3%), which could not be crystallized and was used as such for further reaction.

Anal.:

\[ \text{H NMR (CDCl}_3\text{): } \delta \text{ 1.3 (s, 9H, } -\text{C(C}_3\text{H}_3)\text{), 3.3 (s, 3H, } >\text{NCH}_3\text{), 3.4 (bs, 10H, } -\text{CH}_2\text{N(CH}_2\text{CH}_2\text{N})\text{, 3.5 (s, 1H, } >\text{OH, D}_2\text{O exchanged), 3.9 (s, 3H, } -\text{OCH}_3\text{), 4.1 (bs, 3H, } -\text{OCH}_2\text{CH}_2\text{)} \text{ ppm (m, 3H, Ar) and 8.3 ppm (s, 1H, ArC} = \text{N).} \]

MS: \text{m/z: 365 [M+]}. 

1-(4-tert-BUTYLIMINOMETHYL-2-METHOXYPHENOXY)-3-(4-METHYLPIPERAZIN-1-YL)PROPAN-2-OL (158)

1-(4-tert-Butyliminomethyl-2-methoxyphenoxy)-3-(4-methylpiperazin-1-yl)propan-2-ol (157) (1.0 g, 2.8 mmol) in methanol (75 ml) was cooled to 5°C and reduced with sodium borohydride (1.0 g, 26.4 mmol) over a period of 2 h, while stirring the contents magnetically. Completion of reaction was confirmed by TLC. Methanol was removed under reduced pressure and the residue dissolved in water, extracted with chloroform. The chloroform extract was washed with water, dried and distilled to give an oily residue 158 (0.7 g, 69.6%), which could not be crystallized.

Anal.:

\[ \text{H NMR (CDCl}_3\text{): } \delta \text{ 1.18 (s, 9H, } -\text{C(C}_3\text{H}_3)\text{), 2.29 (s, 3H, } >\text{NCH}_3\text{), 2.57 (m, 10H, } -\text{CH}_2\text{N(CH}_2\text{CH}_2\text{N})\text{, 3.66 (s, 2H, ArCH}_2\text{), 3.86 (s, 3H, } -\text{OCH}_3\text{), 3.99 (d, 2H, } -\text{OCH}_2\text{), 4.11 (m, 1H, } -\text{CH(OH)}\text{) and 6.87 ppm (m, 3H, Ar).} \]

MS: \text{m/z: 365 [M+]}.
To a solution of 158 (0.5 g, 1.4 mmol) in refluxing methanol (75 ml) was added oxalic acid (0.8 g, 6.4 mmol) and refluxing was continued for 0.5 h. The reaction mixture was concentrated and left overnight to afford oxalate of 158 (0.81 g, 93.2%), mp. 179-182°C.

Anal.:  
IR (KBr): 3410, 2940, 2570, 1725, 1605, 1405 and 1170 cm⁻¹.  
¹H NMR (D₂O): δ 1.36 (s, 9H, -C(CH₃)₃), 2.95 (s, 3H, >NC₃), 3.45 (d, 2H, =C=N<), 3.64 (b, 8H, -N(C₂H₅)₂N-), 3.80 (s, 3H, -OC₃), 4.06 (s, 4H, -OCH₂-), 4.57 (m, 1H, =CH₂OH), and 6.96 ppm (d, 3H, Ar).  
Calcd for C₂₆H₄₅N₃O₁₅: C, 49.13; H, 6.50; N, 6.61. Found: C, 48.89; H, 6.27; N, 6.60.

To 4-[2-hydroxy-3-(4-methylpiperezin-1-yl)propoxy]-3-methoxybenzaldehyde (154) (1.0 g, 3.2 mmol) in refluxing aldehyde free alcohol (25 ml) was added a solution of sodium acetate trihydrate (0.5 g, 3.7 mmol) in water (1 ml) and hydroxylamine hydrochloride (0.5 g, 7.2 mmol) in water (1 ml). Refluxing was continued for 6 h and completion of reaction was confirmed by TLC. The solvent was removed under reduced pressure to give a residue, which was dissolved in water, basified with ammonia solution and extracted with chloroform. Chloroform extract was washed with water, dried and distilled to give an oily residue 159 (0.6 g, 62.9%), which could not be crystallized and was used for preparation of oxalate.
Anal.:  
$^{1}$H NMR (CDCl$_3$): δ 2.34 (s, 3H, >NCH$_3$), 2.63 (m, 8H, -N(CH$_2$CH$_2$)$_2$N-), 2.77 (b, 2H, -CH$_2$N<), 3.79 (s, 3H, -OCH$_3$), 4.04 (m, 2H, -OCH$_2$-), 4.20 (m, 1H, -CH(OH)-), 6.2-7.5 (b, 2H, ArCH=NOH & -OH, exchanged in D$_2$O ), 6.87 (d, 1H, $J=8.2$ Hz, Ar$_m$ to methoxy), 6.98 (dd, 1H, $J=8.4$ Hz, $J=1.6$ Hz, Ar$_p$ to methoxy), 7.19 (d, 1H, $J=1.4$ Hz, Ar$_o$ to methoxy) and 8.03 ppm (s, 1H, ArCH=NOH).  
MS: m/z: 323 [M$^+$].  

4-[2-HYDROXY-3-(4-METHYLPIPERAZIN-1-YL)PROPoxy]-3-METHOXYBENZALDEHYDE OXIME (159) OXALATE [DPJ-933]  

Oxalic acid (1.0 g, 7.9 mmol) was added to a solution of 159 (1.0 g, 3.1 mmol) in refluxing methanol (50 ml) and refluxing was continued for 10 min. Collected the precipitate formed and crystallized from methanol to afford oxalate of 159 (1.1 g, 70.7%), mp. 198-200°C.  
Anal.:  
IR (KBr): 3420, 3400, 3345, 2970, 2930, 1630, 1585, 1510, 1450, 1270 and 1215 cm$^{-1}$.  
$^{1}$H NMR (D$_2$O): δ 3.00 (s, 3H, >NCH$_3$), 3.45 (t, 2H, -CH$_2$N<), 3.66 (b, 8H, -N(CH$_2$CH$_2$)$_2$N-), 3.87 (s, 3H, -OCH$_3$), 4.13 (m, 2H, -OCH$_2$-), 4.49 (m, 1H, -CH(OH)-), 7.02 (d, 1H, $J=8.3$ Hz, Ar$_m$ to methoxy), 7.15 (dd, 1H, $J=8.3$ Hz, $J=1.7$ Hz, Ar$_p$ to methoxy), 7.30 (d, 1H, $J=1.5$ Hz, Ar$_o$ to methoxy) and 8.14 ppm (s, 1H, ArCH=NOH).  
Calcd for C$_{20}$H$_{29}$N$_3$O$_2$: C, 47.71; H, 5.81; N, 8.35. Found: C, 47.48; H, 5.55; N, 8.14.
2,3-EPOXYPROPOXY-1-(2-ISOPROPYL-5-METHYL)BENZENE (161)

2-Isopropyl-5-methylphenol (thymol, 160) (5.0 g, 33.3 mmol), epichlorohydrin (50 ml) and potassium carbonate (5.0 g) were refluxed for 12 h while stirring. TLC confirmed completion of reaction. Filtered the residue and distilled off the excess epichlorohydrin under reduced pressure to give an oily residue, which was chromatographed over silica gel (100-200 mesh), using chloroform as the eluent to give an oily residue 161 (4.0 g, 58.3%).

Anal.:

$^1$H NMR (CDCl₃): δ 1.20 (d, 6H, -CH(C₃H₇)₂), 2.30 (s, 3H, -C(CH₃)₃), 2.75 (dd, 1H, -C₄H₂ of oxirane), 2.87 (t, 1H, -CH₂ of oxirane), 3.31 (m, 2H, -CH of oxirane & -CH(CH₃)₃), 3.95 (dd, 1H, -OCH₂-), 4.20 (dd, 1H, -OCH₂-), 6.64 (s, 1H, Ar), 6.75 (d, 1H, J = 7.7 Hz, Ar) and 7.09 ppm (d, 1H, J = 7.7 Hz, Ar).

M/S: m/z: 206 [M⁺]

1-(ISOPROPYLAMINO)-3-(2-ISOPROPYL-5-METHYLPHENOXY)PROPAN-2-OL (162)

2,3-Epoxypropoxy-1-(2-isopropyl-5-methyl)benzene (161) (2.0 g, 9.7 mmol) and isopropylamine (10 ml), were refluxed for 12 h. Completion of reaction was confirmed by TLC. Removed excess of isopropylamine under reduced pressure to give an only residue 162 (2.5 g, 97.2%).

Anal.:

$^1$H NMR (CDCl₃): δ 1.09 (d, 6H, -NHCH(CH₃)₂), 1.20 (d, 6H, ArCH(CH₃)₂), 2.30 (s, 3H, ArCH₃), 2.71-3.02 (m, 5H, -CH(OH)CH₂NHCH₃, two protons exchanged in D₂O), 3.27 (m, 1H, ArCH(CH₃)₂), 3.92 (m, 1H, -OCH₂-), 4.00 (m, 1H, -OCH₂-), 4.08
(bm, 1H, -CH(OH)-), 6.67 (s, 1H, Ar), 6.75 (d, 1H, J = 7.7 Hz, Ar) and 7.09 ppm (d, 1H, J = 7.7 Hz, Ar).

M/S: m/z: 265 [M⁺].

1-(ISOPROPYLAMINO)-3-(2-ISOPROPYL-5-METHYLPHENOXY)PROPAN-2-OL (162) OXALATE [DPJ-576]

To a solution of 162 (2.0 g, 7.5 mmol) dissolved in acetone (50 ml), added a hot solution of oxalic acid (1.25 g, 9.9 mmol) in acetone (10 ml) and refluxed for 0.5 h. The reaction mixture was concentrated and left for crystallization to afford oxalate of 162 (1.72 g, 64.3%), mp. 143-146°C.

Anal.: IR (KBr): 3396, 3246, 3100, 2963, 1725, 1643, 1102, 811, 743 and 498 cm⁻¹.

¹H NMR (CDCl₃): δ 1.17 (d, 6H, -NHCH(CH₃)₂), 1.39 (d, 6H, ArCH(CH₃)₂), 2.28 (s, 3H, -OH3), 3.21 (m, 2H, 2 × -CH(CH₃)₂), 3.39 (m, 1H, -CH₂NH-), 3.51 (m, 1H, -CH₂NH-), 3.90 (m, 1H, -OCH₂-), 4.03 (m, 1H, -OCH₂-), 6.58 (s, 1H, Ar), 6.75 (d, 1H, J = 7.7 Hz, Ar) and 7.08 ppm (d, 1H, J = 7.7 Hz, Ar).

Calcd for C₂₉H₅₀NO₆: C, 60.82; H, 8.22; N, 3.94. Found: C, 60.29; H, 8.36; N, 4.06.

1-(tert-BUTYLAMINO)-3-(2-ISOPROPYL-5-METHYLPHENOXY)PROPAN-2-OL (163)

2,3-Epoxypropoxy-1-(2-isopropyl-5-methyl)benzene (161) (2.0 g, 9.7 mmol) and tert-butylamine (10 ml), were refluxed for 12 h. Completion of reaction was confirmed by TLC. Removed excess of tert-butylamine under reduced pressure to give an oily residue 163 (2.5 g, 92.3%).
Anal.

$^1$H NMR (CDCl$_3$): $\delta$ 1.13 (s, 9H, -C(CH$_3$)$_3$), 1.20 (d, 6H, ArCH(CH$_3$)$_2$), 2.31 (s, 3H, ArCH$_3$), 2.71-2.92 (m, 4H, -CH(OH)CH$_2$NH$^-$), two protons exchanged in D$_2$O), 3.26 (m, 1H, -CH(0H)C=O), 3.97 (m, 3H, -OCH$_2$CH(OH)$^-$), 6.68 (s, 1H, Ar), 6.75 (d, 1H, $J$ = 7.7 Hz, Ar) and 7.09 ppm (d, 1H, $J$ = 7.7 Hz, Ar).

M/S: m/z: 279 [M$^+$].

1-(tert-BUTYLAMINO)-3-(2-ISOPROPYL-5-METHYLPHENOXY)PROPAN-2-OL (163) OXALATE [DPJ-577]

The compound 163 (1.5 g, 5.4 mmol) was dissolved in acetone (50 ml) by warming, added a hot solution of oxalic acid (1.0 g, 7.9 mmol) in acetone (10 ml) and refluxed the mixture for 0.5 h. Removed excess of solvent under reduced pressure and the oily residue given washing with dry ether. Crystallized the residue from acetone to afford oxalate of 163 (0.9 g, 46%), mp. 193-196°C.

Anal.: IR (KBr): 3289, 3077, 2981, 2873, 1907, 1712, 1625, 1202, 1119, 845 and 726 cm$^{-1}$.

$^1$H NMR (CDCl$_3$): $\delta$ 1.19 (d, 6H, ArCH(CH$_3$)$_2$), 1.40, (s, 9H, -C(CH$_3$)$_3$), 2.31 (s, 3H, ArCH$_3$), 3.01 (t, 1H, -C=NH), 3.24 (m, 2H, -CH$_2$NHCH$_2$), 3.91 (m, 1H, -OCH$_2$), 4.10 (m, 1H, -OCH$_2$), 4.41 (m, 1H, -CH(OH)$^-$), 6.66 (s, 1H, Ar), 6.75 (d, 1H, $J$ = 7.7 Hz, Ar) and 7.07 ppm (d, 1H, $J$ = 7.7 Hz, Ar).

Calcd for C$_{19}$H$_{26}$N$_2$O$_6$: C, 61.76; H, 8.46; N, 3.79. Found: C, 61.95; H, 8.60; N, 3.89.

1-(2-ISOPROPYL-5-METHYLPHENOXY)-3-(4-METHYLPIPERAZIN-1-YL)PROPAN-2-OL (164)

2,3-Epoxypropoxy-1-(2-isopropyl-5-methyl)benzene (161) (1.0 g, 4.9 mmol) was refluxed in methanol (50 ml), added N-methylpiperazine (0.5 g, 5.6 mmol) and
continued refluxing for 6 h. Completion of reaction was confirmed by TLC. Excess solvent was removed under reduced pressure to give an oily residue 164 (0.75 g, 50.5%).

Anal.:  
$^1$H NMR (CDCl$_3$): $\delta$ 1.20 (d, 6H, ArCH(CH$_3$)$_2$), 2.30 (s, 3H, -CH$_3$), 2.31 (s, 3H, -CH$_3$), 2.60 (bm, 10H, -CH$_2$N(CH$_2$CH$_2$)$_2$N-), 3.27 (m, 1H, -CH(CH$_3$)$_2$), 3.98 (m, 2H, -OCH$_2$-), 4.11 (m, 1H, -CH(OH)-), 6.67 (s, 1H, Ar), 6.75 (d, 1H, $J=7.8$ Hz, Ar), 7.09 (d, 1H, $J=7.8$ Hz, Ar).

M/S: m/z: 306 [M$^+$].

1-(2-ISOPROPYL-5-METHYLPHENOXY)-3-(4-METHYLPIPERAZIN-1-YL)PROPAN-2-OL (164) OXALATE [DPJ-912]

To a solution of 164 (0.5 g, 1.6 mmol) in refluxing methanol (50 ml) added oxalic acid (0.5 g, 4.0 mmol) and continued refluxing for 0.5 h. Filtered off the precipitate to give oxalate of 164 (0.34 g, 42.8%), mp. 216-219°C.

Anal.:  
IR (KBr): 3330, 2935, 2440, 1725, 1615, 1640, 1410, 1195, 1180, 1110, 1060 and 710 cm$^{-1}$.

$^1$H NMR (D$_2$O): $\delta$ 1.01 (d, 6H, ArCH(CH$_3$)$_2$), 2.15 (s, 3H, ArCH$_3$), 2.88 (s, 3H, -NCH$_3$), 3.12 (m, 1H, -CH(CH$_3$)$_2$), 3.34 (d, 2H, -CH$_2$N-), 3.55 (b, 8H, -N(CH$_2$CH$_2$)$_2$N-), 3.89 (dd, 1H, -OCH$_2$-), 3.97 (dd, 1H, -OCH$_2$-), 4.37 (m, 1H, -CH(OH)-), 6.72 (s, 1H, Ar), 6.76 (d, 1H, $J=7.7$ Hz, Ar) and 7.10 ppm (d, 1H, $J=7.7$ Hz).

Calcd for C$_{22}$H$_{34}$N$_2$O$_5$: C, 54.31; H, 7.04; N, 5.75. Found: C, 54.83; H, 7.43; N, 5.67.
**N-(4-HYDROXYPHENYL)-3,4-DIMETHOXYBENZAMIDE (165)**

4-Aminophenol (1.0 g, 9.2 mmol) was refluxed in tetrahydrofuran (50 ml) and added 3,4-dimethoxybenzoyl chloride (0.8 g, 4.0 mmol) dissolved in tetrahydrofuran (10 ml) and continued refluxing for 1 h. Completion of reaction was confirmed by TLC. Removal of tetrahydrofuran under reduced pressure gave a sticky black mass, which was crystallized from methanol to afford 165 (0.9 g, 35.9%), mp. 224-227°C.

**Anal.:**

IR (KBr): 3540, 3500, 3320, 2930, 1640, 1510, 1265, 1225, 1020 and 820 cm⁻¹.

¹H NMR (CDCl₃-DMSO-d₆): δ 3.93 (s, 6H, 2 x -OCH₃), 6.82 (q, 2H, Ar), 6.91 (d, 1H, J = 8.63 Hz, Ar), 7.52 (m, 4H, Ar) and 9.12 ppm (s, 1H, -N=CO-, exchanged in D₂O).


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**N-(2,3-EPOXYPROPLOXYPHENYL)-3,4-DIMETHOXYBENZAMIDE (166)**

N-(4-Hydroxyphenyl)-3,4-dimethoxybenzamide (165) (2.0 g, 7.3 mmol) was refluxed in epichlorohydrin (50 ml) for 2 h, added anhydrous potassium carbonate (5.0 g) and refluxing was continued for 6 h with stirring. TLC confirmed completion of reaction. The reaction mixture was filtered and the excess of epichlorohydrin removed under reduced pressure to obtain a solid residue, which was refluxed with acetone and then with methanol to remove impurities to afford 166 (1.7 g, 70.5%), mp 188-191°C. The product 166 was used for further reaction without crystallization.

**Anal.:**

IR (KBrl): 3300, 1635, 1505, 1260, 1230, 1155, 1030 and 810 cm⁻¹.

¹H NMR (CDCl₃-DMSO-d₆): δ 2.77(m, 1H, -CH₂ of oxirane), 2.92 (m, 1H, -CH₂ of oxirane), 3.36 (m, 1H, -CH of oxirane), 3.90 (m, 1H, -OCH₂), 3.94 (s, 3H, -OCH₃), 3.95 (s,
3H, -OCH$_3$), 4.29 (dd, 1H, -OCH$_2$-), 6.92 (m, 3H, Ar), 7.61 (m, 4H, Ar) and 9.53 ppm (s, 1H, -N/HCO-).

Calcd for C$_{19}$H$_{19}$N$_2$O$_5$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.40; H, 5.68; N, 4.60.

N-[4-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)PHENYL]-3,4-DIMETHOXYBENZAMIDE (167)

N-(2,3-Epoxypropoxyphenyl)-3,4-dimethoxybenzamide (166) (0.5 g, 1.5 mmol) was refluxed in methanol (50 ml), added isopropylamine (15 ml) and refluxing was continued for 2.5 h. Excess of reagent was removed under reduced pressure to give a solid residue. The solid residue was crystallized from acetone to afford 167 (0.36 g, 61.1%), mp. 135-138°C.

Anal.: IR (KBr): 3300, 2920, 1640, 1510, 1265, 1240, 1025 and 815 cm$^{-1}$.

$^1$H NMR (CDCl$_3$-DMSO-d$_6$): $\delta$ 1.08 (d, 6H, -CH(CH$_3$)$_2$), 2.69 (m, 1H, -CH$_2$NH-), 2.87 (m, 2H, -CH$_2$NH- & -CH(CH$_3$)$_2$), 3.96 (m, 8H, 2 x -OCH$_3$ & -OCH$_2$-), 4.03 (m, 1H, -CH(OH)-), 6.91 (m, 3H, Ar), 7.61 (m, 4H, Ar) and 9.52 ppm (s, 1H, -N/HCO-, exchanged in D$_2$O).

Calcd for C$_{21}$H$_{28}$N$_2$O$_5$: C, 64.93; H, 7.27; N, 7.21. Found: C, 64.86; H, 7.22; N, 7.18.

N-[4-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)PHENYL]-3,4-DIMETHOXYBENZAMIDE (167) OXALATE [DPJ-888]

To a solution of 167 (1.25 g, 3.2 mmol) in refluxing methanol (50 ml) added oxalic acid (0.5 g, 3.9 mmol) and the refluxing continued for 0.5 h. The solvent was removed under reduced pressure and the residue crystallized from methanol-acetone mixture to afford oxalate of 167 (0.88 g, 57.2%), mp. 198-201°C.
**Anal.:**

IR (KBr): 3410, 3340, 2990, 1650, 1600, 1540, 1510, 1265 and 1220 cm\(^{-1}\).

\(^1\)H NMR (D\(_2\)O): 5 1.24 (d, 6H, \(-\mathrm{CH}(CH_3)_2\)), 3.12 (m, 2H, \(-\mathrm{CH}_2\mathrm{NH}\)), 3.38 (m, 1H, \(-\mathrm{CH}(CH_3)_2\)), 3.67 (s, 3H, \(-\mathrm{OCH}_3\)), 3.69 (s, 3H, \(-\mathrm{OCH}_3\)), 3.88 (m, 2H, \(-\mathrm{OCH}_2\)), 4.16 (m, 1H, \(-\mathrm{CH}(\mathrm{OH})\)), 6.78 (d, 3H, Ar) and 7.17 ppm (m, 4H, Ar).

Calcd for C\(_{23}\)H\(_{30}\)N\(_2\)O\(_9\): C, 57.73; H, 6.32; N, 5.85. Found: C, 57.61; H, 6.33; N, 5.91.

**N-[4-(3-\textit{tert}-\text{butylamino}-2-\text{hydroxypropoxy})phenyl]-3,4-dimethoxybenzamide (168)**

N-(2,3-Epoxypropoxyphenyl)-3,4-dimethoxybenzamide (166) (1.5 g, 4.6 mmol) was refluxed in methanol (100 ml), added tert-butylamine (25 ml) and refluxing was continued for 3 h. Completion of reaction was confirmed by TLC. The solvent was removed under reduced pressure and the solid residue was crystallized from acetone to afford 168 (1.26 g, 68.7%), mp. 105-108°C.

**Anal.:**

IR (KBr): 3310, 2960, 2925, 1665, 1505, 1260, 1235, 1210 and 1025 cm\(^{-1}\).

\(^1\)H NMR (CDCl\(_3\)-DMSO-\(d_6\)): 5 1.14 (s, 9H, \(-\mathrm{C}(\mathrm{CH}_3)_3\)), 2.69 (m, 1H, \(-\mathrm{CH}_2\mathrm{NH}\)), 2.82 (m, 1H, \(-\mathrm{CH}_2\mathrm{NH}\)), 3.96 (m, 9H, 2 x \(-\mathrm{OCH}_3\) & \(-\mathrm{OCH}_2\mathrm{CH}(\mathrm{OH})\)), 6.92 (m, 3H, Ar), 7.62 (m, 4H, Ar) and 9.64 ppm (s, 1H, \(-\mathrm{NHCO}\), exchanged in D\(_2\)O).

Calcd for C\(_{22}\)H\(_{30}\)N\(_2\)O\(_5\): C, 65.65; H, 7.51; N, 6.96. Found: C, 65.16; H, 7.65; N, 6.98.

**N-[4-(3-\textit{tert}-\text{butylamino}-2-\text{hydroxypropoxy})phenyl]-3,4-dimethoxybenzamide (168) Oxalate [DPJ-890]**

To a solution of 168 (1.25 g, 3.1 mmol) in refluxing methanol (50 ml), added oxalic acid (0.4 g, 3.2 mmol) and refluxing was continued for 0.5 h. The solvent was
removed under reduced pressure and the residue was crystallized from methanol-acetone mixture to afford oxalate of 168 (0.6 g, 39.2%), mp. 195-198°C.

**Anal.:**
IR (KBr): 3410, 3345, 3000, 1735, 1660, 1605, 1510, 1265 and 1225 cm⁻¹.
¹H NMR (D₂O): δ 1.27 (s, 9H, -C(CH₃)₃), 3.12 (m, 2H, -CH₂NH-), 3.65 (s, 3H, -OCH₃), 3.67 (s, 3H, -OCH₃), 3.85 (m, 2H, -OCH₂-), 4.11 (m, 1H, -CH(OH)-), 6.76 (d, 3H, Ar) and 7.11 ppm (m, 4H, Ar).
Calcd for C₂₄H₃₂N₂O₉: C, 58.53; H, 6.55; N, 5.69. Found: C, 58.67; H, 6.57; N, 5.75.

**N-{4-[2-HYDROXY-3-(4-METHYLPIPERAZIN-1-YL)PROPOXY]PHENYL}-3,4-DIMETHOXYBENZAMIDE (169)**

A mixture of N-(2,3-epoxypropoxyphenyl)-3,4-dimethoxybenzamide (166) (1.5 g, 4.6 mmol) and N-methylpiperazine (1 ml, 9.0 mmol) in methanol (75 ml) was refluxed for 4 h. Completion of reaction was confirmed by TLC. The solvent was removed under reduced pressure and the solid residue was crystallized from ethyl acetate to afford 169 (1.23 g, 62.6%), mp. 140-143°C.

**Anal.:**
IR (KBr): 3460, 3285, 2935, 2795, 1640, 1510, 1270, 1235, 1140, 1020 and 815 cm⁻¹.
¹H NMR (CDCl₃): δ 2.30 (s, 3H, >NC(CH₃)₃), 2.40-2.72 (bm, 10H, -CH₂(CH₂CH₂)₂N-), 3.94 (s, 6H, 2 x -OCH₃), 3.98 (d, 2H, -OCH₂-), 4.10 (m, 1H, -CH(OH)-), 6.91 (m, 3H, Ar), 7.38 (dd, 1H, Ar), 7.51 (m, 3H, Ar) and 7.78 ppm (s, 1H, -NHCO-, exchanged in D₂O).
Calcd for C₂₃H₂₁N₃O₅: C, 64.32; H, 7.27; N, 9.78. Found: C, 64.75; H, 7.32; N, 10.18.
N-(4-[2-HYDROXY-3-(4-METHYLPIPERAZIN-1-YL)PROPOXY]PHENYL)-3,4-DIMETHOXYBENZAMIDE (169) OXALATE [DPJ-893]

Oxalic acid (0.7 g, 5.5 mmol) was added to a solution of 169 (1.0 g, 2.3 mmol) in refluxing methanol (50 ml) and refluxing was continued for 15 min. Filtered the precipitates and crystallized from methanol to afford oxalate of 169 (0.65 g, 45.8%), mp. 209-212°C.

Anal.:

IR (KBr): 3470, 3435, 3380, 2930, 2330, 1720, 1640, 1505, 1410, 1265, 1230, 1080 and 1020 cm\(^{-1}\).

\(^1\)H NMR (D\(_2\)O): \(\delta\) 2.90 (s, 3H, >NC(/3), 3.37-3.58 (bm, 10H, -Ctf2N(C/H2)2N-), 3.74 (s, 6H, 2x -OC(/3), 3.95 (m, 2H, -OC\(H_2\)-), 4.35 (m, 1H, -C(/H(OH)-)), 6.88 (dd, 3H, Ar), 7.23 (d, 3H, Ar) and 7.33 ppm (d, 1H, Ar).

Caled for C\(_{27}\)H\(_{35}\)N\(_3\)O\(_3\): C, 53.20; H, 5.79; N, 6.89. Found: C, 53.18; H, 5.72; N, 6.80.

N-(4-HYDROXYPHENYL)-3,4,5-TRIMETHOXYBENZAMIDE (170)

4-Aminophenol (5.0 g, 45.8 mmol) was refluxed in tetrahydrofuran (100 ml) and then added 3,4,5-trimethoxybenzoyl chloride (4.0 g, 17.3 mmol) dissolved in tetrahydrofuran (10 ml) in small portions and refluxing was continued for 7 h. Completion of reaction was confirmed by TLC. Removal of tetrahydrofuran under reduce pressure gave a solid residue, which was crystallized from methanol to afford 170 (2.5 g, 18%), mp. 225-228°C.

Anal.:

IR (KBr) 3335, 1655, 1585, 1545, 1505, 1460, 1340, 1245, 1210 and 1020 cm\(^{-1}\).
$^1$H NMR (CDCl$_3$-DMSO-$d_6$): $\delta$ 3.89 (s, 3H, -OCH$_3$), 3.93 (s, 6H, 2 x -OCH$_3$), 6.84 (d, 2H, $J = 8.8$ Hz, Ar), 7.21 (s, 2H, Ar), 7.49 (d, 2H, $J = 8.7$ Hz, Ar), 8.57 (s, 1H, -N=CO-, exchanged in D$_2$O) and 8.92 ppm (s, 1H, -OH, exchanged in D$_2$O).

Calcd for C$_{16}$H$_{17}$NO$_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.53; H, 5.42; N, 4.75.

**N-(2,3-EPOXYPROPOXYPHENYL)-3,4,5-TRIMETHOXYBENZAMIDE (171)**

$N$-(4-Hydroxyphenyl)-3,4,5-trimethoxybenzamide (170) (5.0 g, 16.5 mmol) was refluxed in epichlorohydrin (60 ml) for 2 h, added anhydrous potassium carbonate (6.0 g) and refluxing was continued for 7 h. Completion of reaction was determined by TLC. The reaction mixture was filtered and excess of epichlorohydrin removed under reduced pressure to obtain a solid residue, which was crystallized from acetone to afford 171 (3.0 g, 50.6%), mp. 140-143°C.

Anal.: 
IR (KBr): 3300, 2830, 1640, 1580, 1520, 1500, 1420, 1340, 1230 and 1120 cm$^{-1}$.

$^1$H NMR (CDCl$_3$): $\delta$ 2.78 (q, 1H, -CH$_2$ of oxirane), 2.93 (t, 1H, -CH$_2$ of oxirane), 3.73 (m, 1H, -CH of oxirane), 3.95 (m, 10H, -OCH$_2$- & 3 x -OCH$_3$), 4.25 (dd, 1H, -OCH$_2$-), 6.94 (d, 2H, $J = 8.9$ Hz, Ar), 7.08 (s, 2H, Ar), 7.54 (d, 2H, $J = 8.8$ Hz, Ar) and 7.74 ppm (s, 1H, -NHCO-).

Calcd for C$_{19}$H$_{21}$NO$_6$: C, 63.50; H, 5.89; N, 3.90. Found: C, 63.67, H, 5.83; N, 4.32.

**N-[4-(2-HYDROXY-3-ISOPROPYLAMINO)PROPOXYPHENYL]-3,4,5-TRIMETHOXYBENZAMIDE (172)**

$N$-(2,3-Epoxypropoxyphenyl)-3,4,5-trimethoxybenzamide (171) (2.50 g, 7.0 mmol) was refluxed in methanol (50 ml), added isopropylamine (5 ml) and refluxing was continued for 2 h. Completion of reaction was determined by TLC. The solvent
was removed under reduced pressure and the residue was crystallized from ether-acetone mixture to afford 172 (2.5 g, 85.9%), mp. 125-128°C.

**Anal.:**
IR (KBr): 3280, 2920, 1640, 1585, 1515, 1455, 1405, 1335, 1235, 1125 and 810 cm⁻¹.

¹H NMR (CDCl₃): δ 1.10 (d, 6H, -CH(CH₃)₂), 2.72-2.89 (m, 3H, -C(CH₂NHC(CH₃)₂)-), 3.91 (s, 3H, -OCH₃), 3.94 (s, 6H, 2 x -OCH₃), 4.01 (m, 3H, -OCH₂CH(OH)-), 6.94 (d, 2H, J = 8.9 Hz, Ar), 7.07 (s, 2H, Ar), 7.52 ppm (s, 1H, -NCO-).

Calcd for C₂₂H₃₀N₂O₆: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.43; H, 7.22; N, 6.39.

**N-[4-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)PHENYL]-3,4,5-TRIMETHOXYBENZAMIDE (172) OXALATE [DPJ-782]**

To a refluxing solution of 172 (1.5 g, 3.6 mmol) in methanol (50 ml), added oxalic acid (0.5 g, 3.9 mmol) and refluxing was continued for 0.5 h. The solvent was removed under reduced pressure and the residue crystallized from acetone to afford oxalate of 172 (1.5 g, 82.3%), mp. 228-231°C.

**Anal.:**
IR (KBr): 3320, 1640, 1620, 1580, 1510, 1230 and 1125 cm⁻¹.

¹H NMR (D₂O): δ 1.22 (d, 6H, -CH(CH₃)₂), 3.11 (m, 2H, -CH₂NH-), 3.36 (s, 1H, -CH(CH₃)₂), 3.64 (s, 3H, -OCH₃), 3.70 (s, 6H, 2 x -OCH₃), 3.87 (b, 2H, -OCH₂-), 4.13 (b, 1H, -CH(OH)-), 6.77 (d, 2H, J = 7.7 Hz, Ar), 6.89 ppm (s, 2H, Ar) and 7.19 ppm (d, 2H, J = 7.7 Hz, Ar).

Calcd for C₂₄H₃₂N₂O₁₀: C, 56.69; H, 6.34; N, 5.51. Found: C, 56.77; H, 6.39; N, 5.60.
N-[4-(3-tert-BUTYLAMINO-2-HYDROXYPROPOXY)PHENYL]-3,4,5-TRIMETHOXYBENZAMIDE (173)

N-(2,3-Epoxypropoxyphenyl)-3,4,5-trimethoxybenzamide (171) (3.0 g, 8.4 mmol) was refluxed in (50 ml), added tert-butylamine (5 ml) and refluxing was continued for 4 h. Completion of reaction was confirmed by TLC. The solvent was removed under reduced pressure to give an oily residue 173 (3.5 g, 96.9%).

Anal.:

$^1$H NMR (CDCl$_3$): $\delta$ 1.13 (s, 9H, -C(CH$_3$)$_3$), 2.50 (b, 2H, -NH- & -OH, exchanged in D$_2$O), 2.69 (q, 1H, -CH$_2$NH-), 2.85 (t, 1H, -CH$_2$NH-), 3.86 (s, 6H, 2 $\times$ -OCH$_3$), 3.88 (s, 3H, -OCH$_3$), 3.96 (m, 3H, -OCH$_2$CH-), 6.87 (d, 2H, $J = 8.9$ Hz, Ar), 7.07 (s, 2H, Ar), 7.51 (d, 2H, $J = 8.9$ Hz, Ar) and 8.13 ppm (s, 1H, -NHCO-, exchanged in D$_2$O).

N-[4-(3-tert-BUTYLAMINO-2-HYDROXYPROPOXY)PHENYL]-3,4,5-TRIMETHOXYBENZAMIDE (173) OXALATE [DPJ-784]

Oxalic acid (0.75 g, 6.0 mmol) was added to a solution of 173 (1.5 g, 3.5 mmol) in refluxing methanol (50 ml) and continued refluxing for 0.5 h. Concentrated the reaction mixture and left overnight for crystallization to afford oxalate of 173 (1.1 g, 57.7%), mp. 231-232°C.

Anal.:

IR (KBr): 3380, 3160, 2980, 2780, 1660, 1620, 1590, 1510, 1235 and 1125 cm$^{-1}$.

$^1$H NMR (CDCl$_3$-DMSO-d$_6$): $\delta$ 1.35 (s, 9H, -C(CH$_3$)$_3$), 2.95 (t, 1H, -CH$_2$NH-), 3.14 (d, 1H, -CH$_2$NH-), 3.60-4.15 (bm, 13H, -OCH$_2$CH(OH)CH$_2$NH- & 3 $\times$ -OCH$_3$), 4.34 (bs, 1H, -CH(OH)-), 6.88 (d, 2H, $J = 8.8$ Hz, Ar), 7.31 (s, 2H, Ar), 7.64 (d, 2H, $J = 8.7$ Hz, Ar) and 9.94 ppm (s, 1H, -NHCO-).

Calcd for C$_{25}$H$_{34}$N$_2$O$_6$: C, 57.46; H, 6.56; N, 5.36. Found: C, 57.32; H, 6.55; N, 5.44
N-{4-[2-HYDROXY-3-(4-METHYLPIPERAZIN-1-YL)PROPOXY]PHENYL}-3,4,5-TRIMETHOXYBENZAMIDE (174)

N-(2,3-Epoxypropoxyphenyl)-3,4,5-trimethoxybenzamide (171) (1.5 g, 4.2 mmol) and N-methylpiperazine (1.0 ml, 9.0 mmol) were refluxed in methanol (75 ml) for 8 h. Completion of reaction was confirmed by TLC. The solvent was removed under reduced pressure and the oily residue was dissolved in dry acetone, any insoluble portion was filtered out. The acetone portion was evaporated to give an oily residue of 174 (1.5 g, 78.2%).

Anal.

$^1$H NMR (CDCl$_3$): $\delta$ 2.30 (s, 3H, $>\text{NCH}_3$), 2.60 (bm, 10H, $-\text{CH}_2\text{N(CH}_2\text{CH}_2\text{)}_2\text{N-}$), 3.88 (s, 9H, 3 $\times$ -OCH$_3$), 3.97 (t, 2H, -OCH$_2$-), 4.08 (m, 1H, -CH(OH)-), 6.90 (d, 2H, $J = 9.0$ Hz, Ar), 7.06 (s, 2H, Ar), 7.52 (d, 2H, $J = 8.9$ Hz, Ar) and 7.95 ppm (s, 1H, -NHCO-, exchanged in D$_2$O).

N-{4-[2-HYDROXY-3-(4-METHYLPIPERAZIN-1-YL)PROPOXY]PHENYL}-3,4,5-TRIMETHOXYBENZAMIDE (174) OXALATE [DPJ-786]

To a solution of 174 (1.0 g, 2.2 mmol) in refluxing methanol (50 ml), added oxalic acid (0.8 g, 6.3 mmol) and refluxing was continued for 0.5 h. Concentrated and left for crystallization to afford oxalate of 174 (0.43 g, 31.1%), mp. 202-205°C.

Anal.

IR (KBr): 3470, 3425, 3380, 2930, 2525, 1630, 1590, 1225 and 1120 cm$^{-1}$.

$^1$H NMR (D$_2$O): $\delta$ 2.89 (s, 3H, $>\text{NCH}_3$), 3.33 (m, 2H, $-\text{CH}_2\text{N}<$), 3.50-3.70 (bd, 17H, $-\text{N(CH}_2\text{CH}_2\text{)}_2\text{N-} \& 3 \times$ -OCH$_3$), 3.81 (b, 2H, -OCH$_2$-), 4.31 (b, 1H, -CH(OH)-), 6.69 (d, 2H, $J = 7.5$ Hz, Ar), 6.80 (s, 2H, Ar) and 7.14 ppm (d, 2H, $J = 7.2$ Hz, Ar).

Calcd for C$_{28}$H$_{37}$N$_3$O$_{14}$: C, 52.58; H, 5.83; N, 6.57. Found: C, 52.34; H, 5.89; N, 6.47.
**N-(5-HYDROXYNAPHTHALEN-1-YL)ACETAMIDE (175)**

To a suspension of 5-amino-1-naphthol (3.0 g, 18.8 mmol) in water (30 ml) was added acetic anhydride (6 ml), the reaction mixture was manually stirred and warmed on a water bath (60°C) for 5 min to get a clear solution. The reaction mixture was allowed to stand overnight and filtered to afford 175 (3.0 g, 79.1%), mp. 155-158°C. The product was used for next step without crystallization.

**Anal.:**

IR (KBr): 3280, 1620, 1580, 1535, 1410, 1370, 1270 and 770 cm⁻¹.

¹H NMR (CDCl₃-DMSO-d₆): δ 2.28 (s, 3H, -NHCOC₂H₅), 6.91 (d, 1H, Ar), 7.30 (t, 1H, Ar), 7.42 (m, 2H, Ar), 7.76 (d, 1H, Ar), 8.12 (d, 1H, Ar) and 8.83 ppm (s, 1H, -N7/CO-, exchanged in D₂O).

Calcd for C₁₂H₁₁NO₂: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.77; H, 5.22; N, 6.51.

**N-[5-(2,3-EPOXYPROPOXY)NAPHTHALEN-1-YL]ACETAMIDE (176)**

N-(5-Hydroxynaphthalen-1-yl)acetamide (175) (3.0 g, 14.9 mmol) was refluxed in epichlorohydrin (75 ml) for 0.5 h, added anhydrous potassium carbonate (5.0 g) and refluxing was continued for 5 h. Completion of reaction was confirmed by TLC. The reaction mixture was filtered and excess of epichlorohydrin removed under reduced pressure to obtain a solid residue, which was crystallized from acetone to obtain 176 (1.0 g, 26.1%), mp. 150-153°C.

**Anal.:**

IR (KBr): 3240, 3040, 1650, 1540, 1405, 1270, 1240, 1040 and 770 cm⁻¹.

¹H NMR (CDCl₃-DMSO-d₆): δ 2.27 (s, 3H, -NHCOC₂H₅), 2.86 (q, 1H, -CH₂ of oxirane), 2.96 (t, 1H, -CH₂ of oxirane), 3.50 (m, 1H, -CH of oxirane), 4.09 (dd, 1H, -OCH₂), 160
4.47 (dd, 1H, -OCH₂-), 6.86 (d, 1H, Ar), 7.42 (m, 2H, Ar), 7.64 (d, 1H, Ar), 7.74 (d, 1H, Ar), 8.14 (d, 1H, Ar) and 9.46 ppm (s, 1H, -N/CO-).

Calcd for C₁₅H₁₄N₂O₅: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.62; H, 5.61; N, 5.52.

**N-[5-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)NAPHTHALEN-1-YL]ACETAMIDE (177)**

_**N-[5-(2,3-Epoxypropoxy)naphthalen-1-yl]acetamide (176)**_ (1.0 g, 3.9 mmol) was refluxed in methanol (50 ml), added isopropylamine (10 ml) and refluxing was continued for 3 h. Completion of reaction was confirmed by TLC. The excess reagent was removed under reduced pressure. The solid residue was crystallized from acetone to afford 177 (0.8 g, 65.1%), mp. 155-158°C.

**Anal.**:

IR (KBr): 3415, 3270, 2925, 1655, 1545, 1415, 1270, 1040 and 770 cm⁻¹.

¹H NMR (CDCl₃-DMSO-d₆): δ 1.10 (d, 6H, -CH(CH₃)₂), 2.28 (s, 3H, -NHOCH₃), 2.83 (m, 2H, -CH₂NHCH₃), 2.98 (t, 1H, -CH₂NH-), 4.16 (m, 3H, -OCH₂CH₂-), 6.86 (d, 1H, Ar), 7.42 (m, 2H, Ar), 7.61 (d, 1H, Ar), 7.76 (d, 1H, Ar), 8.16 (d, 1H, Ar) and 9.33 ppm (s, 1H, -N/CO-, exchanged in D₂O).

Calcd for C₁₈H₂₄N₂O₅: C, 68.33; H, 7.65; N, 8.85. Found: C, 68.58; H, 7.40; N, 8.58

**N-[5-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)NAPHTHALEN-1-YL]ACETAMIDE (177) OXALATE [DPJ-953]**

To a solution of 177 (0.8 g, 2.5 mmol) in refluxing methanol (50 ml), added oxalic acid (0.4 g, 3.2 mmol) and refluxing was continued for 0.5 h. The solvent was removed under reduced pressure and the residue crystallized from methanol-acetone mixture to afford oxalate of 177 (0.73 g, 70.6%), mp. 177-180°C.
IR (KBr): 3395, 3245, 3040, 2980, 2930, 2855, 2780, 1655, 1535, 1405, 1260, 1230, 1085, 1030, 770 and 710 cm⁻¹.

¹H NMR (D₂O): δ 1.29 (d, 6H, -CH(CH₃)₂), 2.23 (s, 3H, -NHCOC₃), 3.28 (m, 2H, -CH₂NH-), 4.20 (m, 4H, -OCH₂-), 4.38 (m, 1H, -CH(OH)-), 6.95 (t, 1H, Ar), 7.47 (m, 4H, Ar) and 8.19 ppm (d, 1H, Ar).

Calcd for C₂₀H₂₆N₂O₇: C, 59.10; H, 6.45; N, 6.89. Found: C, 59.22; H, 6.43; N, 6.93.

N-[5-(3-tert-BUtylamino-2-Hydroxypropoxy)Naphthalen-1-yl]Acetamide (178)

N-[5-(2,3-Epoxypropoxy)naphthalen-1-yl]acetamide (176) (0.94 g, 3.6 mmol) was refluxed in methanol (50 ml), added tert-butylamine (15 ml) and refluxing was continued for 2 h. Completion of reaction was confirmed by TLC. The excess reagent was removed under reduced pressure and the solid residue was crystallized from acetone to afford 178 (0.93 g, 77.1%), mp. 82-85°C.

¹H NMR (CDCl₃-DMSO-d₆): δ 1.14 (s, 9H, -C(CH₃)₃), 2.26 (s, 3H, -NHCOC₃), 2.79 (dd, 1H, -CH₂NH-), 2.94 (dd, 1H, -CH₂NH-), 4.14 (m, 3H, -OCH₂CH₃), 6.83 (d, 1H, Ar), 7.38 (m, 2H, Ar), 7.54 (d, 1H, Ar), 7.77 (d, 1H, Ar), 8.11 (d, 1H, Ar) and 8.33 ppm (s, 1H, -N=CO-, exchanged in D₂O).

Calcd for C₁₉H₂₆N₂O₃: C, 69.06; H, 7.93; N, 8.48. Found: C, 68.98; H, 8.02; N, 8.36.
**N-[5-(3-tert-BUTYLAMINO-2-HYDROXYPROPOXY)NAPHTHALEN-1-YL]ACETAMIDE (178) OXALATE [DPJ-955]**

Added oxalic acid (0.4 g, 3.2 mmol) to a solution of 178 (0.92 g, 2.8 mmol) in refluxing methanol (50 ml) and refluxing was continued for 0.5 h. The solvent was removed under reduced pressure and the residue crystallized from methanol-acetone mixture to afford oxalate of 178 (0.91 g, 77.3%), mp. 202-205°C.

**Anal.:**

IR (KBr): 3350, 3300, 3270, 3070, 3030, 2980, 2920, 2850, 1650, 1510, 1405, 1295, 1260, 1230 and 730 cm⁻¹.

¹H NMR (D₂O): δ 1.37 (s, 9H, -C(CH₃)₃), 2.27 (s, 3H, -NHCOC₂H₅), 3.29 (m, 2H, -CH₂NH-), 4.24 (m, 2H, -OCH₂-), 4.39 (m, 1H, -CH(OH)-), 6.99 (t, 1H, Ar), 7.50 (m, 4H, Ar) and 8.22 ppm (d, 1H, Ar).

Calcd for C₂₁H₂₅N₂O₇: C, 59.99; H, 6.71; N, 6.66. Found: C, 60.03; H, 6.80; N, 6.69.

**N-(5-HYDROXYNAPHTHALEN-1-YL)-3,4-DIMETHOXYBENZAMIDE (179)**

5-Amino-1-naphthol (1.0 g, 6.3 mmol) was refluxed in tetrahydrofuran (50 ml), and added 3,4-dimethoxybenzoyl chloride (1.0 g, 5.0 mmol) dissolved in tetrahydrofuran (10 ml) and continued refluxing for 1 h. Completion of reaction was confirmed by TLC. Removal of tetrahydrofuran under reduced pressure gave a solid residue, which was crystallized from methanol to yield 179 (1.0 g, 49.2%), mp. 242-244°C.

IR (KBr): 3515, 3255, 1635, 1580, 1495, 1350, 1260, 1210, 1125, 1015 and 770 cm⁻¹.

¹H NMR (CDCl₃-DMSO-d₆): δ 3.94 (s, 6H, 2 x -OCH₃), 6.91 (d, 1H, Ar), 6.98 (d, 1H, Ar), 7.29 (t, 1H, Ar), 7.45 (q, 2H, Ar), 7.71 (m, 3H, Ar), 8.17 (d, 1H, Ar) and 9.78 ppm (s, 1H, -N/HCO-, exchanged in D₂O).

Calcd for C₁₉H₁₇N₂O₆: C, 70.58; H, 5.30; N, 4.33. Found: C, 70.59; H, 5.56; N, 4.66.
N-[5-(2,3-epoxypropoxy)naphthalen-1-yl]-3,4-dimethoxybenzamide (180)

N-(5-Hydroxynaphthalen-1-yl)-3,4-dimethoxybenzamide (179) (1.0 g, 3.1 mmol) was refluxed in epichlorohydrin (50 ml) for 2 h, added anhydrous potassium carbonate (2.0 g), continued refluxing for 4 h. Completion of reaction was confirmed by TLC. The reaction mixture was filtered while hot to remove solid materials. The excess of epichlorohydrin was removed under vacuum to give a solid residue, which was crystallized from methanol to afford 180 (0.75 g, 63.9%), mp. 167-170°C.

Anal.: IR (KBr): 3225, 2995, 2915, 1625, 1500, 1395, 1260, 1025 and 765 cm⁻¹.

¹H NMR (CDCl₃-DMSO-d₆): δ 2.87 (q, 1H, -CH₂ of oxirane), 2.98 (q, 1H, -CH₂ of oxirane), 3.51 (m, 1H, -CH₂ of oxirane), 3.96 (s, 6H, 2 × -OCH₃), 4.12 (dd, 1H, -OCH₂-), 4.47 (dd, 1H, -OCH₂-), 6.86 (d, 1H, Ar), 6.97 (d, 1H, Ar), 7.40 (m, 1H, Ar), 7.51 (t, 1H, Ar), 7.61 (d, 1H, Ar), 7.73 (m, 3H, Ar), 8.23 (d, 1H, Ar) and 9.41 ppm (s, 1H, -N=CO-).

Calcd for C₂₂H₂₁NO₅: C, 69.64; H, 5.58; N, 3.69. Found: C, 69.75; H, 5.49; N, 3.77.

N-[5-(2-hydroxy-3-isopropylaminoproxy)naphthalen-1-yl]-3,4-dimethoxybenzamide (181)

N-[5-(2,3-epoxypropoxy)naphthalen-1-yl]-3,4-dimethoxybenzamide (180) (0.5 g, 1.3 mmol) was refluxed in methanol (50 ml), added isopropylamine (5 ml) and refluxing was continued for 2 h. Completion of reaction was confirmed by TLC. The excess reagent was removed under reduced pressure and the residue was crystallized from acetone-ether mixture to afford 181 (0.5 g, 86.5%), mp. 162-165°C.

Anal.: IR (KBr): 3310, 2965, 2900, 1650, 1585, 1490, 1260, 1225, 1155, 1020 and 770 cm⁻¹.
'H NMR (CDCl\textsubscript{3}-DMSO-\textit{d}_6): \delta 1.11 (d, 6H, -C(CH\textsubscript{3})\textsubscript{2}), 2.78-3.01 (brm, 3H, -CH\textsubscript{2}NHCH<), 3.95 (s, 6H, 2 \times -OCH\textsubscript{3}), 4.18 (m, 3H, -OCH\textsubscript{2}CH<), 6.88 (d, 1H, Ar), 6.98 (d, 1H, Ar), 7.39 (t, 1H, Ar), 7.48 (t, 1H, Ar), 7.69 (m, 4H, Ar), 8.24 (d, 1H, Ar) and 9.79 ppm (s, 1H, -N\textsubscript{\textit{\textit{\textbar}}}CO-, exchanged in D\textsubscript{2}O)

Calcd for C\textsubscript{25}H\textsubscript{30}N\textsubscript{2}O\textsubscript{5}: C, 68.47; H, 6.90; N, 6.39. Found: C, 68.32; H, 6.43; N, 6.83.

Y-[5-(2-HYDROXY-3-ISOPROPYLAMINOPROPOXY)NAPHTHALEN-1-YL]-3,4-DIMETHOXYPHENAZAMIDE (181) OXALATE [DPJ-983]

Oxalic acid (0.3 g, 2.4 mmol) was added to a solution of 181 (0.75 g, 1.7 mmol) in refluxing methanol (50 ml) and refluxing was continued for 10 min. Concentrated the reaction mixture and left for crystallization to afford oxalate of 181 (0.7 g, 77.4%), mp. 251-254°C.

Anal.:
IR (KBr): 3380, 3245, 2930, 2840, 2700, 1620, 1580, 1520, 1500, 1400, 1285, 1160, 1010 and 770 cm\textsuperscript{-1}.

'\textsuperscript{1}H NMR (CDCl\textsubscript{3}-CF\textsubscript{3}COOH): \delta 1.49 (d, 6H, -C(CH\textsubscript{3})\textsubscript{2}), 3.63 (bd, 2H, -CH\textsubscript{2}NH-), 3.86 (m, 1H, -CH(CH\textsubscript{3})\textsubscript{2}), 4.01 (s, 6H, 2 \times -OCH\textsubscript{3}), 4.35 (q, 2H, -OCH\textsubscript{2}-), 4.76 (bs, 1H, -CH(OH)-), 6.89 (d, 1H, Ar), 7.11 (d, 1H, Ar), 7.44 (m, 6H, Ar), 8.19 (d, 1H, Ar) and 8.72 ppm (s, 1H, -N\textsubscript{\textit{\textbar}}}CO-).

Calcd for C\textsubscript{27}H\textsubscript{32}N\textsubscript{2}O\textsubscript{9}: C, 61.36; H, 6.10; N, 5.30. Found: C, 61.84; H, 6.20; N, 5.41.

N-[5-(3-\textit{\textbar}\textit{\textbar}BUTYLAMINO-2-HYDROXYPROPOXY)NAPHTHALEN-1-YL]-3,4-DIMETHOXYPHENAZAMIDE (182)

N-[5-(3,3-Epoxypropoxy)naphthalen-1-y1)-3,4-dimethoxyphenazamide (180) (1.0 g, 2.6 mmol) was refluxed in methanol (50 ml), added tert-butylamine (10 ml) and refluxing was continued for 2 h. Completion of reaction was confirmed by TLC.
Removed the excess reagent under reduced pressure and the residue was crystallized from acetone-ether mixture to afford 182 (1.1 g, 90.6%), mp. 148-151°C.

**Anal.:**

IR (KBr): 3260, 2940, 1640, 1590, 1510, 1330, 1265, 1215, 1125, 1025 and 770 cm⁻¹.

¹H NMR (CDCl₃-DMSO-d₆): δ 1.15 (s, 9H, -C(CH₃)₃), 2.79 (q, 1H, -CH₂NH-), 2.95 (t, 1H, -CH₂NH-), 3.03 (b, 2H, -NH₂ & -OH, exchanged in D₂O), 3.94 (s, 6H, 2 x -OCH₃), 4.16 (m, 3H, -OCH₂CH₂-), 6.86 (d, 1H, Ar), 6.94 (d, 1H, Ar), 7.38 (t, 1H, Ar), 7.47 (t, 1H, Ar), 7.58 (d, 1H, Ar), 7.71 (m, 3H, Ar), 8.22 (d, 1H, Ar) and 9.59 ppm (s, 1H, -NHCO-, exchanged in D₂O).

Calcd for C₂₆H₃₂N₂O₅: C, 69.00; H, 7.13; N, 6.19. Found: C, 68.81; H, 6.98; N, 6.05.

**N-[5-(3-tert-BUTYLAMINO-2-HYDROXYPROPOXY)NAPHTHALEN-1-YL]-3,4-DIMETHOXYBENZAMIDE (182) OXALATE [DPJ-985]**

To a solution of 182 (0.75 g, 1.7 mmol) in refluxing methanol (50 ml), added oxalic acid (0.3 g, 2.4 mmol) and refluxing was continued for 10 min. Concentrated the reaction mixture and left for crystallization to afford oxalate of 182 (0.45 g, 50%), mp. 257-260°C.

**Anal.:**

IR (KBr): 3475, 3380, 3230, 2960, 2800, 1615, 1585, 1540, 1500, 1400, 1260, 1220, 1020 and 760 cm⁻¹.

¹H NMR (CDCl₃-CF₃COOH): δ 1.52 (s, 9H, -C(CH₃)₃), 3.52 (bs, 2H, -CH₂NH-), 4.00 (s 3H, -OCH₃), 4.02 (s 3H, -OCH₃), 4.32 (bs, 2H, -OCH₂-), 4.72 (b, 1H, -CH(OH)-), 6.88 (d, 1H, Ar), 7.08 (d, 1H, Ar), 7.52 (d, 5H, Ar), 7.65 (s, 1H, Ar), 8.16 (d, 1H, Ar) and 8.58 ppm (s, 1H, -NHCO-).

Calcd for C₃₈H₄₂N₂O₇: C, 61.98; H, 6.32; N, 5.16. Found: C, 62.10; H, 6.48; N, 5.06.
METHYL 2-(4-ALLYL-2-METHOXYPHENOXY)ACETATE (186)

A mixture of 4-allyl-2-methoxyphenol (eugenol, 183) (2.0 g, 12.2 mmol) and anhydrous potassium carbonate (2.0 g) were refluxed in anhydrous ethyl methyl ketone (50 ml) while stirring magnetically for 2 h. Methyl chloroacetate (2 ml, 22.8 mmol), catalytic amounts of potassium iodide and triethylamine were added to the reaction mixture and continued refluxing for 10 h. The solid materials were filtered and the solvent was removed under reduced pressure. The viscous oily product obtained was column chromatographed over silica gel (100-200 mesh) using chloroform as eluent to give 186 (2.0 g, 69.5%)

Anal.:

$^1$H NMR (CDCl₃): δ 3.33 (d, 2H, -CH₂CH=CH₂) 3.78 (s, 3H, -COOC₂H₃), 3.85 (s, 3H, ArOCH₃), 4.66 (s, 2H, -OCH₂-), 5.07 (m, 2H, -CH₂CH=CH₂), 5.94 (m, 1H, -CH₂CH=CH₂) and 6.76 ppm (m, 3H, Ar)

2-(4-ALLYL-2-METHOXYPHENOXY)-N-(2-DIETHYLAMINOETHYL)-ACETAMIDE (187)

Methyl 2-(4-allyl-2-methoxyphenoxo)acetate (186) (2.0 g, 8.5 mmol) and 2-diethylaminoethylamine (2.0 ml, 14.2 mmol) were mixed together and heated at 80°C for 8 h. TLC determined the completion of reaction. The product obtained was left on sodium carbonate solution (10%) overnight, and then extracted with chloroform (3 x 30 ml). Combined the chloroform layers, washed with water and distilled to give an oily residue 187 (1.5 g, 55.3%), which could not be crystallized and was used as such for the preparation of oxalate.
'H NMR (CDCl₃): δ 0.98 (t, 6H, -N(CH₂CH₃)₂), 2.53 (m, 6H, -CH₂N(CH₂CH₃)₂), 3.37 (m, 4H, -CONH(CH₂)₂ & -CH₂CH=CH₂), 3.86 (s, 3H, ArOCH₃), 4.51 (s, 2H, -OCH₂-), 5.10 (m, 2H, -CH₂CH=CH₂), 5.93 (m, 1H, -CH₂CH=CH₂), 6.76 (m, 3H, Ar) and 7.42 ppm (b, 1H, -CONH-, exchanged in D₂O).

2-(4-ALLYL-2-METHOXYPHENOXY)-N-(2-DIETHYLAMINOETHYL)ACETAMIDE (187) OXALATE [DPJ-632]

Added oxalic acid (1.0 g, 7.9 mmol) to a solution of 187 (1.0 g, 3.1 mmol) in methanol (50 ml) and refluxed for 0.5 h. The solvent was removed under reduced pressure and the product obtained was crystallized from dry acetone to afford oxalate of 187 (1.0 g, 76.5%), mp 100-103°C.

Anal.: IR (KBr): 3511, 3412, 2652, 1679, 1516, 1226, 1143, 1033, 813 and 761 cm⁻¹.

3.67 (q, 2H, -CONHCH₂-), 3.81 (s, 3H, ArOCH₃), 4.45 (s, 2H, -OCH₂-), 5.05 (m, 2H, -CH₂CH=CH₂), 5.88 (m, 1H, -CH₂CH=CH₂), 6.65 (m, 2H, Ar), 6.75 (d, 1H, Ar) and 7.94 ppm (t, 1H, -CONH-, exchanged in D₂O).

Calcd for C₂₀H₃₀N₂O₇: C, 58.52; H, 7.37; N, 6.82. Found: C, 57.95; H, 7.25; N, 6.96.

METHYL 2-(2-ISOPROPYL-5-METHYLPHENOXY)ACETATE (188)

A mixture of 2-isopropyl-5-methylphenol (thymol, 160) (2.0 g, 13.3 mmol) and anhydrous potassium carbonate (2.0 g) in anhydrous ethyl methyl ketone (50 ml) were refluxed while stirring magnetically for 2 h. Methyl chloroacetate (4 ml, 45.6 mmol), catalytic amounts of potassium iodide and triethylamine were added to the reaction mixture and continued refluxing for 10 h. The solid material was removed by
filtering the reaction mixture. The solvent was removed under reduced pressure to give a viscous oily product, which was column chromatographed over silica gel (100-200 mesh) using chloroform as eluent to give 188 (2.0 g, 67.6%).

Anal.:  
$^1$H NMR (CDCl$_3$): $\delta$ 1.22 (d, 2H, -CH(CH$_3$)$_2$), 2.29 (s, 3H, ArCH$_3$), 3.37 (m, 1H, -CH(CH$_3$)$_2$), 3.77 (s, 3H, -OCH$_3$), 4.62 (s, 2H, -OCH$_2$), 6.52 (s, 1H, Ar), 6.77 (d, 1H, $J = 7.7$ Hz, Ar) and 7.12 ppm (d, 1H, $J = 7.8$ Hz, Ar).

$N$-(2-DIETHYLAMINOETHYL)-2-(2-ISOPROPYL-5-METHYLPHENOXY)-ACETAMIDE (189)  
Methyl 2-(2-isopropyl-5-methylphenoxy)acetate (188) (2.0 g, 9.0 mmol) and 2-diethylaminoethylamine (2.0 ml, 14.2 mmol) were mixed together and heated at 80°C for 8 h. The completion of reaction was confirmed by TLC. The product obtained was left on sodium carbonate solution (10%) overnight, and then extracted with chloroform (3 $\times$ 30 ml) The chloroform layers were combined, washed with water and distilled to give an oily residue 189 (0.7 g, 23.6%), which could not be crystallized and was used as such for the preparation of oxalate.

Anal.:  
$^1$H NMR (CDCl$_3$): $\delta$ 0.98 (t, 6H, -N(CH$_2$CH$_3$)$_2$), 1.23 (d, 6H, -CH(CH$_3$)$_2$), 2.31 (s, 3H, ArCH$_3$), 2.55 (m, 6H, -CH$_3$N(CH$_2$CH$_3$)$_2$), 3.39 (m, 3H, -CONHCH$_2$ & -CH(CH$_3$)$_2$), 4.49 (s, 2H, -OCH$_2$), 6.61 (s, 1H, Ar), 6.81 (d, 1H, $J = 7.6$ Hz, Ar), 7.13 (d, 1H, $J = 7.7$ Hz, Ar) and 7.36 ppm (b, 1H, -CONH-).
N-(2-DIETHYLAMINOETHYL)-2-(2-ISOPROPYL-5-METHYLPHENOXY)-ACETAMIDE (189) OXALATE [DPJ-629]

To a solution of 189 (1.0 g, 3.3 mmol) in methanol (50 ml) added oxalic acid (1.0 g, 7.9 mmol) and refluxed for 0.5 h. The solvent was removed under reduced pressure and the product obtained was crystallized from dry acetone to afford oxalate of 189 (0.7 g, 54.1%), mp 116-119°C.

Anal.: IR (KBr): 3405, 2962, 2483, 2366, 2309, 1653, 1406, 1113, 814 and 719 cm$^{-1}$.

$^1$H NMR (CDCl$_3$): $\delta$ 1.21 (d, 6H, -CH(CH$_3$)$_2$), 1.30 (t, 6H, -N(CH$_2$CH$_3$)$_2$), 2.20 (s, 3H, ArCH$_3$), 3.25 (m, 7H, -CH$_2$N(CH$_2$CH$_3$)$_2$ & -CH(CH$_3$)$_2$), 3.77 (q, 2H, -CONH$\cdot$CH$_2$-), 4.50 (s, 2H, -OCH$_2$), 6.58 (s, 1H, Ar), 6.81 (d, 1H, $J$ = 7.7 Hz, Ar), 7.12 (d, 1H, $J$ = 7.7 Hz, Ar) and 7.62 ppm (t, 1H, -CONH$\cdot$, exchanged in D$_2$O).

Calcd for C$_{20}$H$_{32}$N$_2$O$_6$: C, 60.59; H, 8.13; N, 7.07. Found: C, 60.22; H, 8.23; N, 7.20.

METHYL 2-(NAPHTHALENE-1-YLOXY)ACETATE (190)

A mixture of 1-naphthol (5.0 g, 34.7 mmol) and anhydrous potassium carbonate (5.0 g) were refluxed in anhydrous ethyl methyl ketone (100 ml) while stirring magnetically for 2 h. Methyl chloroacetate (4 ml, 45.6 mmol), catalytic amounts of potassium iodide and triethylamine were added to the reaction mixture and continued refluxing for 12 h. The solid materials were removed by filtration. The solvent was removed under reduced pressure to give a viscous oily product which was column chromatographed over silica gel (100-200 mesh) using chloroform as eluent to give 190 (6.0 g, 80%)
Anal.:

$^1$H NMR (CDCl$_3$): $\delta$ 3.82 (s, 3H, -COOCH$_3$), 4.82 (s, 2H, -OCH$_2$-), 6.70 (d, 1H, Ar), 7.34 (t, 1H, Ar), 7.49 (m, 3H, Ar), 7.80 (m, 1H, Ar) and 8.36 ppm (q, 1H, Ar).

METHYL 2-(NAPHTHALENE-2-YLOXY)ACETATE (191)

A mixture of 2-naphthol (5.0 g, 34.7 mmol) and anhydrous potassium carbonate (5.0 g) were refluxed in anhydrous ethyl methyl ketone (100 ml) while stirring magnetically for 2 h. Methyl chloroacetate (4 ml, 45.6 mmol), catalytic amounts of potassium iodide and triethylamine were added to the reaction mixture and continued refluxing for 12 h. The reaction mixture was filtered and the solvent was removed under reduced pressure. The residue crystallized from acetone to afford 191 (5.5 g, 73.3%), mp. 70-72°C.

Anal.:

IR (KBr): 3070, 2960, 1760, 1440, 1210, 1180, 1080, 850 and 755 cm$^{-1}$.

$^1$H NMR (CDCl$_3$): $\delta$ 3.83 (s, 3H, -COOCH$_3$), 4.76 (s, 2H, -OCH$_2$-), 7.07 (d, 1H, Ar), 7.24 (dd, 1H, Ar), 7.36 (m, 1H, Ar), 7.45 (m, 1H, Ar), 7.72 (d, 1H, Ar) and 7.77 ppm (d, 2H, Ar).

Calcd for C$_{13}$H$_{12}$O$_3$: C, 72.21; H, 5.59. Found: C, 72.05; H, 5.26.

METHYL 2-(5-ACETYLAMINONAPHTHALEN-1-YLOXY)ACETATE (192)

A mixture of N-(5-hydroxynaphthalen-1-yloxy)acetamide (175) (4.5 g, 22.4 mmol) and anhydrous potassium carbonate (10.0 g) were refluxed in anhydrous ethyl methyl ketone (100 ml) while stirring magnetically for 2 h. Methyl chloroacetate (5 ml, 57.0 mmol) was added to the reaction mixture and continued refluxing for 4 h. The reaction mixture was filtered and the solvent was removed under reduced
pressure. The residue obtained was crystallized from a mixture of ethyl methyl ketone and acetone to afford 192 (4.0 g, 65.5%), mp. 181-184°C.

*Anal.*:

IR (KBr): 3265, 1740, 1650, 1530, 1410, 1230, 1085 and 775 cm\(^{-1}\).

\(^1\)H NMR (CDCl\(_3\)-DMSO-\(d_6\)): \(\delta\) 2.26 (s, 3H, -NHCOC\(_3\)), 3.82 (s, 3H, -COOC\(_3\)), 4.83 (s, 2H, -OCH\(_2\)-), 6.73 (d, 1H, Ar), 7.36 (t, 1H, Ar), 7.45 (t, 1H, Ar), 7.63 (d, 1H, Ar), 7.76 (d, 1H, Ar), 8.19 (d, 1H, Ar) and 9.16 ppm (s, 1H, -N\(\text{HCO}\)-, exchanged in D\(_2\)O).


N-(2-DIETHYLAMINOETHYL)-2-(NAPHTHALENE-1-YLOXY)ACETAMIDE (193)

Methyl 2-(naphthalene-1-yloxy)acetate (190) (2.0 g, 9.3 mmol) and 2-diethylaminoethylamine (2.0 ml, 14.2 mmol) were mixed together and heated at 80°C for 10 h. The completion of reaction was confirmed by TLC. The product obtained was left on sodium carbonate solution (10%) overnight, and then extracted with chloroform (3 \(\times\) 30 ml). Combined the chloroform extracts, washed with water and distilled to give an oily residue 193 (1.5 g, 55.3%), which could not be crystallized and was used as such for the preparation of oxalate.

*Anal.:

\(^1\)H NMR (CDCl\(_3\)): \(\delta\) 0.95 (t, 6H, -N(CH\(_2\)CH\(_3\))\(_2\)), 2.51 (m, 6H, -CH\(_2\)N(CH\(_2\)CH\(_3\))\(_2\)), 3.40 (q, 2H, -CONHCH\(_2\)-), 4.63 (s, 2H, -OCH\(_2\)-), 6.73 (d, 1H, Ar), 7.31 (t, 1H, Ar), 7.47 (m, 3H, Ar), 7.61 (b, 1H, -CONH-), 7.78 (m, 1H, Ar) and 8.28 ppm (q, 1H, Ar).

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**N-(2-DIETHYLAMINOETHYL)-2-(NAPHTHALENE-1-YLOXY)ACETAMIDE (193) OXALATE [DPJ-574]**

To a solution of 193 (2.0 g, 6.7 mmol) in methanol (50 ml) added oxalic acid (1.0 g, 7.9 mmol) and refluxed for 0.5 h. The solvent was removed under reduced pressure and the product obtained was crystallized from dry acetone to afford oxalate of 193 (1.2 g, 45.2%), mp 93-96°C.

IR (KBr): 3443, 3055, 2985, 2650, 1674, 1399, 1106, 794 and 716 cm\(^{-1}\)

\(^1\)H NMR (CDCl\(_3\)): \(\delta\) 1.27 (t, 6H, -N(CH\(_2\)CH\(_3\))\(_2\)), 3.15 (q, 4H, -N(CH\(_2\)CH\(_3\))\(_2\)), 3.24 (t, 2H, -CH\(_2\)CH\(_2\)N<), 3.73 (d, 2H, -CONHC\(_2\)-), 4.70 (s, 2H, -OCH\(_2\)-), 6.79 (d, 1H, Ar), 7.35 (t, 1H, Ar), 7.50 (m, 3H, Ar), 7.80 (q, 1H, Ar), 8.40 (q, 1H, Ar) and 8.55 ppm (s, 1H, -CONH\(_2\)-, exchanged in D\(_2\)O).

Calcd for C\(_{20}\)H\(_{26}\)N\(_2\)O\(_6\): C, 61.53; H, 6.71; N, 7.17. Found: C, 61.23; H, 6.51; N, 7.47.

**N-(2-DIETHYLAMINOETHYL)-2-(NAPHTHALENE-2-YLOXY)ACETAMIDE (194)**

Methyl 2-(naphthalene-2-yloxy)acetate (191) (2.0 g, 9.3 mmol) and 2-diethylaminoethylamine (2.0 ml, 14.2 mmol) were mixed together and heated at 80°C for 8 h. The completion of reaction was confirmed by TLC. The product obtained was left on sodium carbonate solution (10%) overnight, and then extracted with chloroform (3 x 30 ml). The chloroform layers were combined, washed with water and distilled to give an oily residue 194 (0.9 g, 32.4%), which could not be crystallized and was used as such for the preparation of oxalate.

\(\text{Anal.:}\)

\(\text{\(^1\)H NMR (CDCl}_3\): \(\delta\) 0.95 (t, 6H, -N(CH}_2CH}_3)_2), 2.48 (q, 4H, -N(CH}_2CH}_3)_2), 2.55 (t, 2H, -NHCH}_2CH}_2N<), 3.38 (q, 2H, -CONHCH}_2), 4.61 (s, 2H, -OCH}_2), 7.16 (m, 2H, Ar), 7.36 (bm, 2H, Ar, -CONH<), 7.45 (m, 1H, Ar) and 7.74 ppm (m, 3H, Ar).
N-(2-DIETHYLAMINOETHYL)-2-(NAPHTHALENE-2-YLOXY)ACETAMIDE (194) OXALATE [DPJ-595]

Oxalic acid (1.0 g, 7.9 mmol) was added to a solution of 194 (2.0 g, 5.1 mmol) in methanol (50 ml) and refluxed for 0.5 h. The solvent was removed under reduced pressure and the product obtained was crystallized from dry acetone to afford oxalate of 194 (1.1 g, 42.3%), mp. 114-117°C.

Anal.: IR (KBr): 3303, 3057, 2975, 2649, 1669, 1395, 1219, 854 and 717 cm⁻¹.

¹H NMR (CDCl₃): δ 1.24 (t, 6H, -N(CH₂CH₃)₂), 3.17 (m, 6H, -CH₂N(CH₂CH₃)₂), 3.64 (d, 2H, -CONHC₂-), 4.63 (s, 2H, -OCH₂-), 7.20 (d, 1H, Ar), 7.27 (dd, 1H, Ar), 7.35 (t, 1H, Ar), 7.44 (t, 1H, Ar), 7.77 (t, 3H, Ar) and 8.64 ppm (s, 1H, -CONH₂-).


2-(5-ACETYLAMINONAPHTHALEN-1-YLOXY)-N-(2-DIETHYLAMINOETHYL)-ACETAMIDE (195)

Methyl 2-(5-acetylaminonaphthalen-1-yloxy)acetate (192) (1.0 g, 3.7 mmol) and 2-diethylaminoethylamine (1.0 ml, 7.1 mmol) were mixed together and heated at 100°C for 6 h. The completion of reaction was confirmed by TLC. Dissolved the solid residue in acetone, filtered of any insoluble material and crystallized from acetone-ether mixture to afford 195 (0.5 g, 38.2%), mp. 134-137°C.

Anal.: IR (KBr): 3280, 2970, 2930, 1655, 1505, 1410, 1265, 1055 and 780 cm⁻¹.

¹H NMR (CDCl₃): δ 0.98 (t, 6H, -N(CH₂CH₃)₂), 2.32 (s, 2H, -NCOCH₃). 2.57 (m, 6H, -CH₂N(CH₂CH₃)₂), 3.44 (q, 2H, -CONHCH₂-), 4.67 (s, 2H, -OCH₂-), 6.82
(d, 1H, Ar), 7.49 (m, 5H, Ar, -CONH-, one proton exchanged in D2O), 7.96 (d, 1H, Ar) and 8.19 ppm (d, 1H, Ar).

Calcd for C20H27N3O3: C, 67.20; H, 7.61; N, 11.76. Found: C, 67.37; H, 8.12; N, 11.66

2-(5-ACETYLMIDONAPHTHALEN-1-YL-OXY)-N-(2-DIETHYLAMINOETHYL)-ACETAMIDE (195) OXALATE [DPJ-973]

To a solution of 195 (0.5 g, 1.4 mmol) in methanol (50 ml), added oxalic acid (0.2 g, 1.6 mmol) and refluxed for 10 min. The solvent was removed under reduced pressure and the product obtained was crystallized from methanol-acetone mixture to afford oxalate of 195 (0.4 g, 63.9%), mp. 148-151°C.

Anal.: IR (KBr): 3380, 3285, 1660, 1525, 1405, 1365, 1225 and 790 cm⁻¹.

1H NMR (D2O): δ 1.18 (t, 6H, -N(CH2)3), 2.27 (s, 3H, -NHCOC3), 3.15 (q, 4H, -N(CH2CH3)2), 3.25 (t, 2H, -NHCH2CH2N<), 3.62 (t, 2H, -CONHC2), 4.77 (s, 2H, -OC2), 6.88 (d, 1H, Ar), 7.49 (m, 4H, Ar) and 8.26 ppm (d, 1H, Ar),


2-(4-ALLYL-2-METHOXYPHENOXY)-N-[2-(3,4-DIMETHOXYPHENYL)ETHYL]-ACETAMIDE (196) [DPJ-844]

Methyl 2-(4-allyl-2-methoxyphenoxy)acetate (186) (1.8 g, 7.6 mmol) and homoveratrylamine (2 ml, 11.9 mmol) were mixed thoroughly and left at room temperature for 24 h to give a solid product. The solid residue was given washings several times with hexane to remove unreacted homoveratrylamine. The solid residue was column chromatographed over silica gel (100-200 mesh) using chloroform as eluent. The product was then crystallized from acetone-ether mixture to give 196 (1.1 g, 37.5%), mp. 94-96°C.
A nal.:
IR (KBr): 3330, 2960, 2930, 1655, 1510, 1265, 1230, 1140, 1020 and 805 cm\(^{-1}\).

\(^1\)H NMR (CDCl\(_3\)): \(\delta\) 2.79 (t, 2H, -NH\(\text{CH}_2\)=CH\(\text{CH}_2\)), 3.84 (d, 2H, -CH\(\text{CH}_2\)=CH\(\text{CH}_2\)), 3.58 (q, 2H, -NHCH\(\text{CH}_2\)=CH\(\text{CH}_2\)), 3.77 (s, 3H, -OCH\(_3\)), 3.82 (s, 3H, -OCH\(_3\)), 3.85 (s, 3H, -OCH\(_3\)), 4.49 (s, 2H, -OCH\(_2\)=CH\(\text{CH}_2\)), 5.09 (m, 2H, -CH\(\text{CH}_2\)=CH\(\text{CH}_2\)), 5.95 (m, 1H, -CH\(\text{CH}_2\)=CH\(\text{CH}_2\)), 6.71 (m, 4H, Ar), 6.78 (dd, 2H, Ar) and 7.07 ppm (b, 1H, -CONH\(-\)).

Calcd for C\(_{22}\)H\(_{25}\)N\(_2\)O\(_5\): C, 68.55; H, 7.06; N, 3.64. Found: C, 68.46; H, 7.00; N, 3.88.

\(N\)-[2-(3,4-DIMETHOXYPHENYL)ETHYL]-2-(NAPHTHALENE-1-YLOXY)-ACETAMIDE (197) [DPJ-835]

Methyl 2-(naphthalene-1-yloxy)acetate (190) (1.0 g, 4.6 mmol) and homoveratrylamine (1 ml, 5.9 mmol) were mixed thoroughly and left at room temperature for 24 h. The oily residue was given washings several times with hexane till a solid residue was obtained to remove unreacted excess of homoveratrylamine. The solid residue was column chromatographed over silica gel (100-200 mesh) using chloroform as eluent. The product was then crystallized from methanol to afford 197 (0.5 g, 29.6%), mp. 106-109°C.

A nal.:
IR (KBr): 3300, 1660, 1550, 1510, 1260, 1230, 1020 and 765 cm\(^{-1}\).

\(^1\)H NMR (CDCl\(_3\)): \(\delta\) 2.79 (t, 2H, -NH\(\text{CH}_2\)=CH\(\text{CH}_2\)), 3.85 (q, 2H, -NHCH\(\text{CH}_2\)=CH\(\text{CH}_2\)), 3.80 (s, 3H, -OCH\(_3\)), 3.81 (s, 3H, -OCH\(_3\)), 4.66 (s, 2H, -OCH\(_2\)=CH\(\text{CH}_2\)), 6.67 (m, 5H, Ar, -CONH\(-\)), 7.35 (t, 1H, Ar), 7.49 (m, 3H, Ar), 7.82 (d, 1H, Ar) and 7.91 ppm (d, 1H, Ar).

Calcd for C\(_{22}\)H\(_{23}\)N\(_2\)O\(_4\): C, 72.31; H, 6.34; N, 3.84. Found: C, 72.17; H, 6.25; N, 3.63.
**N-[2-(3,4-DIMETHOXYPHENYL)ETHYL]-2-(NAPHTHALENE-2-YLOXY)-ACETAMIDE (198) [DPJ-843]**

Methyl 2-(naphthalene-2-yloxy)acetate (191) (1.0 g, 4.6 mmol) and homoveratrylamine (2 ml, 11.9 mmol) were mixed thoroughly and left at room temperature for 24 h. The oily residue was given washings several times with hexane till all of homoveratrylamine is removed. The solid residue was crystallized from methanol to give 198 (1.1 g, 62.1%), mp. 132-135°C.

**Anal.:**

IR (KBr): 3370, 2940, 1655, 1535, 1510, 1260, 1230, 1140 and 835 cm⁻¹

¹H NMR (CDCl₃): δ 2.79 (t, 2H, -NHCH₂C₆H₄-), 3.60 (q, 2H, -NHC₆H₄CH₂-), 3.81 (s, 3H, -OC₆H₃), 3.82 (s, 3H, -OC₆H₃), 4.59 (s, 2H, -OC₆H₂-), 6.67 (m, 4H, Ar), 7.08 (m, 2H, Ar), 7.37 (m, 1H, Ar), 7.47 (m, 1H, Ar) and 7.75 ppm (m, 3H, Ar).

Calcd for C₂₂H₂₃N₀₄: C, 72.31; H, 6.34; N, 3.84. Found: C, 72.81; H, 6.35; N, 4.09.

**METHYL 2-[4-(3,4,5-TRIMETHOXYBENZAMIDO)PHENOXY]ACETATE (199)**

A mixture of N-(4-hydroxyphenyl)-3,4,5-trimethoxybenzamide (170) (2.0 g, 6.6 mmol) and anhydrous potassium carbonate (4.0 g) were refluxed in anhydrous ethyl methyl ketone (100 ml) while stirring for 2 h. Methyl chloroacetate (2 ml, 22.8 mmol), catalytic amounts of potassium iodide and triethylamine were added to the reaction mixture and continued refluxing with stirring for 6 h. Completion of reaction was confirmed by TLC. The reaction mixture was filtered and the solvent was removed under reduced pressure to obtain a solid residue, which was crystallized from acetone-ether mixture to afford 199 (1.8 g, 72.7%), mp. 140-141°C.
**N-[2-(3,4-DIMETHOXYPHENYL)ETHYL]-2-[4-(3,4,5-TRIMETHOXYBENZAMIDO)PHENOXY]ACETAMIDE (200) [DPJ-848]**

Methyl 2-[4-(3,4,5-trimethoxybenzamido)phenoxy]acetate (199) (1.0 g, 2.7 mmol) and homoveratrylamine (1.5 ml, 8.9 mmol) were mixed thoroughly by warming on a water bath, and left at room temperature for 24 h. The solid material was given washings several times with hexane to remove excess of homoveratrylamine. The solid residue was crystallized from methanol to afford 200 (1.2 g, 85.9%), mp. 144-146°C.

**Anal.**

IR (KBr): 3440, 3280, 1645, 1560, 1500, 1230, 1120, 815 and 785 cm\(^{-1}\).

\( ^1\)H NMR (CDCl\(_3\)): \( \delta \) 2.78 (t, 2H, -NHCH\(_2\)CH\(_2\)-), 3.56 (q, 2H, -NHCH\(_2\)CH\(_2\)-), 3.82 (s, 3H, -OCH\(_3\)), 3.85 (s, 3H, -OCH\(_3\)), 3.90 (s, 9H, 3 x -OCH\(_3\)), 4.44 (s, 2H, -OCH\(_2\)-), 6.61 (t, 1H, -CONH-), 6.69 (m, 2H, Ar), 6.80 (m, 3H, Ar), 7.12 (s, 2H, Ar), 7.53 (dd, 2H, Ar) and 8.09 ppm (s, 1H, ArNHCO\(_-\), exchanged in D\(_2\)O)

Calcd for C\(_{28}\)H\(_{32}\)N\(_2\)O\(_8\): C, 64.11; H, 6.15; N, 5.34. Found: C, 63.89; H, 6.25; N, 5.22.
PHARMACOLOGICAL TESTING

β-ADRENOCEPTOR BINDING ASSAY

Chemicals

All the used solvents and drugs were for analysis. [3H]Dihydroalprenolol ([3H]DHA) having a specific activity of 99.9 Ci/Mol and radiochemical purity > 98.5%, was used as ligand.

β1-Adrenoceptor binding assay

Pellets containing β1 type adrenergic receptors were obtained from turkey erythrocyte membranes as described in the literature. [3H]dihydroalprenolol ([3H]DHA) (NEN), having a specific activity of 99.9 Ci/mmol and radiochemical purity > 98.5%, was used as ligand.

β1-adrenergic receptor binding assay was determined as follows: 300 μl of membrane (~1.2 mg/ml of protein, dilution 1:8 v/v) were incubated for 15 min at 37 °C with 100 μl of 4 nM [3H]DHA and 100 μl of various concentrations of the test compounds (dissolved in water or 5% DMSO and diluted with saline buffer) and 12 mM Tris-HCl, pH=7.5 (total vol. 1ml). The incubations were stopped adding 4 ml of cold buffer (12mM Tris-HCl) followed by rapid filtration through glass fiber filter disks (Whatman GF/B). The samples were subsequently washed 3 times with 4.5 ml of the same buffer and placed into scintillation vials. 10ml of Filter-Count (Packard) liquid scintillation cocktail was then added to each vial and
counting was carried out by scintillation spectrometer (Packard TRI-CARB® 2000CA).

Non-specific binding was defined as non-displaceable binding in the presence of 100 μl of 10 μM propranolol. Blank experiments were carried out to determine the effects of 5% DMSO on the binding: no effects were evidenced.

Competition experiments were analyzed by the "EasyFit" program (EasyFit 1.4, 1989-1991, Matteo Vaccari & Mario Negri Institute) to obtain the concentration of unlabelled drug that caused 50% inhibition of ligand binding (IC50), with six concentrations of displacers, each performed in triplicate. The IC50 values obtained were used to calculate apparent inhibition constants (Ki) by the method of Cheng and Prussoff, from the following equation: 

\[ \text{Ki} = \frac{\text{IC50}}{(1 + S/K_D)} \]

where S represents the concentration of the ligand used and K_D its receptor dissociation constant (K_D value, obtained by Scatchard analysis, for [3H]DHA is 3.6x10^{-9} M).

**β2-adrenoceptor binding assay**

Preparation of lung homogenate: male Sprague-Dawley rats were sacrificed by decapitation. The right lung was removed free of the major bronchi. Lungs were homogenized with Brinkman Polytron (setting 5 for 15 sec) in 50 volumes of buffer, 75 mM Tris-HCl (pH 7.65), 25 mM MgCl2 and then centrifuged at 30,000 x g for 10 min twice. The resulting pellets were resuspended in 100 volumes of buffer 75 mM Tris-HCl (pH 7.65), 25 mM MgCl2, then were
frozen at -80 °C before being assayed.\textsuperscript{384, 385} \([\text{^3}H]\)dihydroalprenolol was used as ligand.

300 \(\mu\)l of membrane of lung (~13.05 mg of fresh tissue, dilution 1:10) were incubated for 30 min at 37 °C with 100 \(\mu\)l of 6 nM \([\text{^3}H]\)DHA, 100 \(\mu\)l of ketanserine, \(10^{-7}\) M 5HT antagonist and 100 \(\mu\)l of various concentrations of the test compounds (dissolved in water or 5% DMSO and diluted with buffer) and 75 mM Tris-HCl (pH 7.65), 25 mM MgCl\(_2\) (total vol. 1 ml). The samples were subsequently washed with 4.5 ml of the same buffer and placed into scintillation vials. 10 ml of Filter-Count (Packard) liquid scintillation cocktail was then added to each vial and counting was carried out by scintillation spectrometer (Packard TRI-CARB\textsuperscript{®} 2000CA).

Non-specific binding was measured in the presence of 100 \(\mu\)l of 10 \(\mu\)M unlabelled ICI 118551, and specific binding as the difference between total and non-specific binding. Blank experiments were carried out to determine the effects of 5% DMSO on the binding: no effects were evidenced.

The concentration of the test compounds that inhibited \([\text{^3}H]\)DHA binding by 50% (IC\(_{50}\)) were determined as above reported.
β-ADRENOCEPTOR BLOCKING ACTIVITY

Materials and general techniques

Frogs of either sex of *Rana tigrina* species were obtained from Ganesh brothers, Mumbai, India. *Swiss albino* mice of either sex (20-30 g), female rats of *Wistar strain* (200-250 g) and New Zealand white rabbits of either sex (2-3.5 Kg) were purchased from National Toxicology Centre, Pune, India. All animals were housed in clean environment under 12 hr light and 12 hr dark cycle. The animals had free access to food pellets and water was made available ad libitum.

Isoprenaline, Adrenaline, Atenolol hydrochloride, Heparin and Urethane were diluted / dissolved to appropriate concentrations with physiological saline. Fresh drug solutions were prepared for each day's work.

Isolated frog heart preparation

Frog heart was isolated and mounted on a stand along with Syme’s cannula as per procedure described by Kulkarni. A constant flow rate of ringer solution was maintained. Apex of the ventricle was attached to starling’s heart lever writing and contractions were recorded on the smoked drum. Normal heart rate and contractile amplitude were recorded.

Adrenaline solution was administered into the ringer solution flowing through the Syme’s cannula and the changes in the heart rate and contractile amplitude were recorded. Appropriate contractions of the test compounds were made in ringer solution and the reservoir bottle containing ringer solution was replaced with test compound.
containing ringer solution. The test compound solution was perfused for 5 to 10 minutes after which various concentrations of adrenaline were administered and the responses were recorded.

**Mouse ECG experiments**

Mice of either sex weighing 25-35 g were anaesthetized with freshly prepared urethane (1.5 – 1.75 g/kg i.p.) and stainless steel needles of gauge 21×1/2 were inserted subcutaneously in the flexor aspect of limbs. The needles were clipped to SS2L electrodes of BIOPAC Student lab pro (Model MP 30, BIOPAC Systems, Inc., Santa Barba, CA, U.S.A).

The test compounds in the appropriate doses were administered intravenously through the tail vein. E.C.G. recordings (Lead I) were taken at 5 minutes, 15 minutes, 30 minutes, 45 minutes, one hour and then hourly response till the action of the drug ends. At the end of the experiment the needles were unclipped and detached from the limbs of the animals and the animals were observed intermittently till full recovery.

**Isolated rat uterus preparation**

Isolated rat uterus preparation was carried as described by Levy and Tozzi\(^\text{387}\). Spontaneous motility of the unprimed rat uterus was recorded by means of force transducer of Student’s Physiograph (Bio-Devices, Ambala, India). The drugs were injected into the isolated organ bath (INCO, Ambala, India) and the effects on the contraction of the uterus were recorded.
LOCAL ANAESTHETIC ACTIVITY

Materials and general techniques

Male guinea pigs of Dunkin-Hartley strain (300-400 g) and New Zealand white rabbits of either sex (2-3.5 Kg) were obtained from National Toxicology Centre, Pune (India). Sprague-Dawley rats of either sex (150-200 g) were obtained from Hindustan Antibiotics Ltd., Pune (India). All animals were housed in clean environment under 12 hr light and 12 hr dark cycle. The animals had free access to food pellets and water was made available ad libitum.

Procaine (procaine hydrochloride) was used after dissolving in physiological saline. Lidocaine (lidocaine hydrochloride) was used as a solution (Xylocaine 2%). Test compounds, were dissolved in physiological saline and the pH of the solutions was adjusted to neutrality by using 0.1 M sodium hydroxide solution. Fresh drug solutions were prepared on the day of experiment.

Infiltration anaesthesia in guinea pigs

The test solution (0.25 ml) was injected i.c. (Intracutaneously) in previously shaved backs of male guinea pigs (300-400 g). Blockade of the skin contraction around the injected area to pin pricking with a relatively blunt end of a disposable needle was taken as the criterion of sensory anaesthesia. The sensitivity to pin pricking at six different sites within the wheal was tested by presence or absence of skin-twitch accompanied by squeaking sound at regular intervals after the administration of the drug. The time of onset was calculated as the time from the injection until the animal felt three out of six pricks. The duration of anaesthesia was calculated as the time from the onset of

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anaesthesia until three out of six pricks were distinctly felt during recovery from the local anaesthetic effect. Each concentration was tested in six animals.388

Sciatic nerve block in rats

The test solution (0.2 ml) was injected at mid thigh level in male rats of the Sprague-Dawley strain (150-200 g). The period of motor block was taken from the onset of loss of weight support from the hind leg to the ability to walk normally. Each concentration was tested in six animals.389

Corneal anaesthesia in rabbits

The test solution (0.25 ml) was instilled into one eye of New Zealand white rabbits (2.0-3.5 kg) and into the other eye isotonic saline solution was instilled, which served as control. The corneal reflex is tested to stimuli from a cotton wick. The time of onset and duration of local anaesthesia were measured. Each concentration was tested in six animals.390

DETERMINATION OF PARTITION COEFFICIENT

Partitioning experiment:

Partition coefficients of the compounds were determined378-380 by partitioning the drug between 1-octanol and 7.4 pH phosphate buffer. The drug was dissolved first in 1-octanol (presaturated with buffer) (1mg/1ml) and then 2 ml of 1-octanol and 2 ml of phosphate buffer transferred to a 25 ml conical flask and allowed to partition in a thermostatic shaker water bath which oscillates at 200 rpm at 37°C for 2 h. After the completion of partitioning, the 1-octanol layer was
separated from buffer layer, centrifuged for 10 min., at 3000 rpm. The 1-octanol layer (1 ml) diluted with methanol so as to obtain absorbance in the range of 1.0. The λ<sub>max</sub> at which absorbance has to be measured was determined by plotting UV absorbance spectrum of the compound. The absorbance of the compound in 1-octanol layers before partitioning and after partitioning was determined, which were used for the calculation of partition coefficient of the compound.

**Preparation of 1-octanol stock solution:**

The partition coefficient of base of all the aryloxypropanolamines synthesized was determined. When the compound for which partition coefficient (log P) is to be calculated was solid (147, 167, 168, 169, 172, 177, 178, 181 and 182), it was dissolved in 1-octanol with the help of shaking or with the help of gentle warming. If the base compound is not solid (142, 143, 145, 146, 149, 150, 152, 153, 154, 156, 158, 159, 162, 163, 164, 173 and 174), the base compounds were first liberated from their respective oxalates. Liberation of base were done as follows: The oxalate (10 mg) was dissolved in 5 ml of distilled water, added a few drops of ammonia solution to make the solution basic and then extracted with chloroform (3 x 5 ml). Distillation of chloroform gave the required base (oil), which was dissolved in 1-octanol to prepare the stock solution and used for the partitioning studies as mentioned above. Propranolol (24) was liberated from propranolol hydrochloride in a similar fashion and the free base used for the determination of partition coefficient.

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