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Synthesis and antitubercular activity of substituted phenylmethyl- and pyridylmethyl amines

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Abstract—A total of 42 benzyl- and pyridylmethyl amines were synthesized either by reductive amination of aromatic/heteroaromatic aldehydes with amines or by conjugate addition of amines to the cinnamates followed by reduction of the ester group with lithium aluminium hydride to the respective propanolamines. All the synthesized compounds were evaluated against both avirulent and virulent strains of *Mycobacterium tuberculosis*. Many of the compounds exhibited MIC as low as 1.56 μg/mL. Few of potent compounds were also evaluated against clinical isolates of MDR TB and found to be active at one or other concentrations with MIC as low as 3.12 μg/mL.

1. Introduction

Tuberculosis (TB) an infectious disease caused by different species of mycobacteria represents a major public health and socioeconomic problem in most of the developing countries.[1] One-third of the World's population (2 billion people) is infected with this disease, of which 16 million are active cases with an additional 8 million added every year. Mortality figures have reached 3 million per year, with one-third of all AIDS patients eventually dying of TB. Of the new cases, 22% are from India, 21% from Sub-Saharan Africa and another 21% from other Asian Countries.[2] The coincidence of tuberculosis with the AIDS epidemic is an additional problem.[3] isoniazid, rifampicin, ethambutol, pyrazinamide and many other first and second line agents are known today to treat tuberculosis. Even though in a qualitative manner, the Directly Observed Short Course (DOTS) has been successful, the fact is that only half the patients are diagnosed for treatment in the first place. Second half of the rest do not complete the full course of treatment, leading to emergence of Multi Drug Resistant (MDR) TB. In weak monitoring cases the compliance with treatment drops to as low as 2 months, against the 6 months stipulated. The answer to these problems lies in the discovery of new drugs with novel mode of action and shorter duration of treatment along with better compliance and reduced incidence of adverse reactions to drugs.[4]

The new drugs should also be effective against latent infections of TB, defined as TB that has not manifested as a disease. Although number of new prototype leads are known today and the effort to get the best compound for the treatment of this devastating disease is still on globally, yet no new chemical entity has yet entered into clinics since 1966.[5]

Since the beginning of medical history chemotherapeutic principles of various amine derivatives have been known either as therapeutic agents or as biological tools.[6] It is the lone pair of electrons on nitrogen imparting it the unique feature to act as a proton acceptor, which makes it one of the largest acid scavengers used in the synthesis of pharmaceuticals. Bacteriostatic activity in tertiary amines and quaternary ammonium salts, *p*-toluidine moiety have been reported long back.[7] A number of aromatic and heteroaromatic amines were synthesized and evaluated for their antitubercular efficacy and some of them possess very good antitubercular activities.[8] Structure–activity relationship has been discussed in this class of compounds previously. *N*-Alkyl benzylamines (**A**)

Keywords: Tuberculosis; MDR TB; Phenylmethyl amines; Antitubercular agents; Reductive amination CDRI Communication No. 7035.

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have been reported to be specific antitubercular compounds as they are inactive against a number of Gram-positive, Gram-negative bacteria and fungi.[9] Detailed structure activities in this class of compounds have been reported, some of the compounds of this series viz. bromohexine and ambroxol isolated from Indian shrub *Adhatoda vasicca* widely used as mucolytics have shown pH-dependent growth inhibitory effect on *Mycobacterium tuberculosis*.[10]

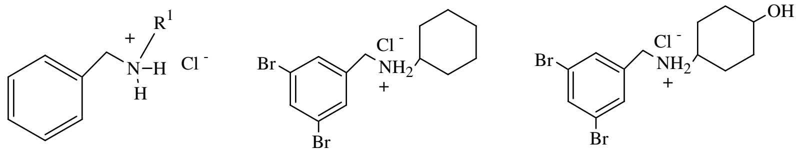
We have recently discovered new prototype amine hybridized molecules as potent antitubercular both from sugars and nonsugars.[11] It has been reported that these compounds are concentrated in macrophages where the mycobacterium resides; they might exert a clinically substantial effect on intracellular tubercle bacilli. Further, it has also been established that such compounds have certain indirect effect on enhancing the antitubercular activities. Such compounds elevate the lysozyme levels in bronchial secretion[12] and levels of rifampicin in lung tissue and sputum and thereby help in clearance of bacilli laden mucus from cavities and bronchi.[13] Thus these compounds may be useful as potential adjunctive in the treatment of tuberculosis (Fig. 1).

Keeping the above facts in mind and in continuation of our work on the development of new antitubercular agents we were interested to synthesize some benzyl amine derivatives, observe the effect of various substituents in the benzene ring and alkyl chain and evaluate them for their antitubercular efficacy.

2. Results and discussion

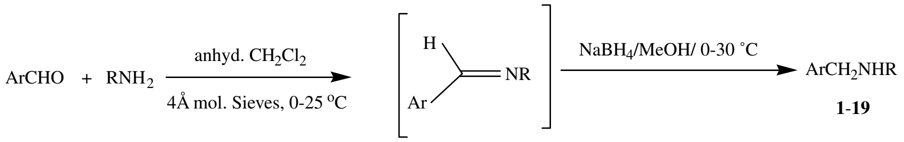
2.1. Chemistry

The first series of compounds without any substituents at the methylene carbon of the phenyl (pyridyl) methyl amine and in the side-chain alkyl moiety at the nitrogen atom were prepared by reductive amination process involving different methods reported so far. Out of all the methods used for this, the reaction of aromatic (heteroaromatic) aldehydes with amines in presence of dehydrating agents (4 Å mol Sieves) followed by reduction of the intermediate imines with sodium borohydride proved to be the best one with respect to economy and yields. Thus reaction of appropriate aromatic aldehydes and selected amines in dichloromethane in presence of 4 Å mol Sieves resulted in the intermediate Schiff's bases, which were reduced in situ either with $NaBH_4$ to give the phenyl (pyridyl) methyl amine derivatives (**1**–**19**) in very good yields (Scheme 1). All of these compounds were



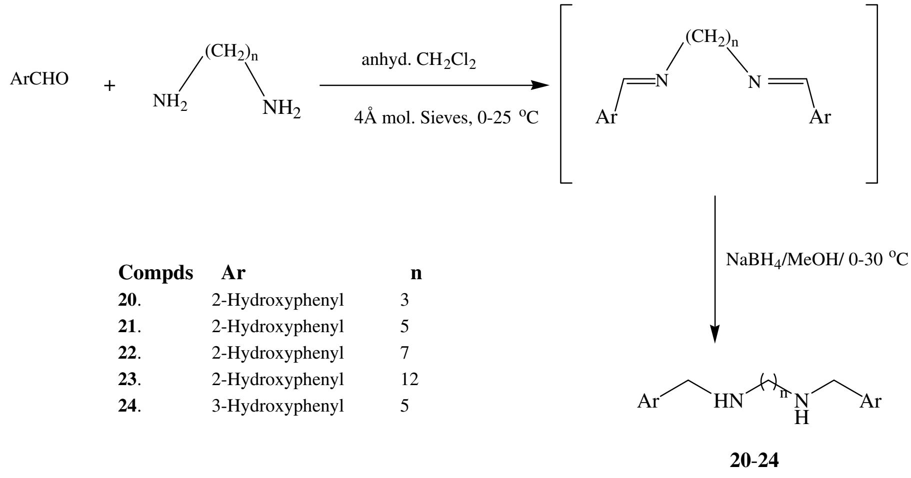
A **Bromhexine** **Amboxol**

Figure 1. Antitubercular benzylamines.



Compds	Ar	R
1.	4-Hydroxy - 3-methoxy phenyl	cycloproyl
2.	4-Hydroxy-3-methoxy phenyl	*n*-Hexadecyl
3.	4-Hydroxy - 3-methoxy phenyl	*n*-Octadec-9-enyl
4.	4-Florophenyl	*n*-Hexdecyl
5.	4-Florophenyl	*n*-Octadec-9-enyl
6.	3,4-Dimethoxyphenyl	*n*-Octadec-9-enyl
7.	2-Hydroxyphenyl	*n*-Dodecyl
8.	2-Hydroxy phenyl	*n*-Octadec-9-enyl
9.	4-Chlorophenyl	*n*-Octyl
10.	4-Chlorophenyl	*n*-Dodecyl
11.	4-Chlorophenyl	*n*-Hexadecyl
12.	4-Chlorophenyl	*n*-Octadec-9-enyl
13.	2-Nitrophenyl	*n*-Octyl
14.	4-Pyridyl	*n*-Octyl
15.	4-Pyridyl	*n*-Hexadecyl
16.	4-Pyridyl	*n*-Octadec-9-enyl
17.	3-Pyridyl	*n*-Hexadecyl
18.	3-Pyridyl	*n*-Octadec-9-enyl
19.	2-Pyridyl	*n*-Dodecyl

Scheme 1. Synthesis of phenyl (pyridyl) methyl amines.



Compds	Ar	n
20.	2-Hydroxyphenyl	3
21.	2-Hydroxyphenyl	5
22.	2-Hydroxyphenyl	7
23.	2-Hydroxyphenyl	12
24.	3-Hydroxyphenyl	5

Scheme 2. Synthesis of diphenyl methyl diamines.

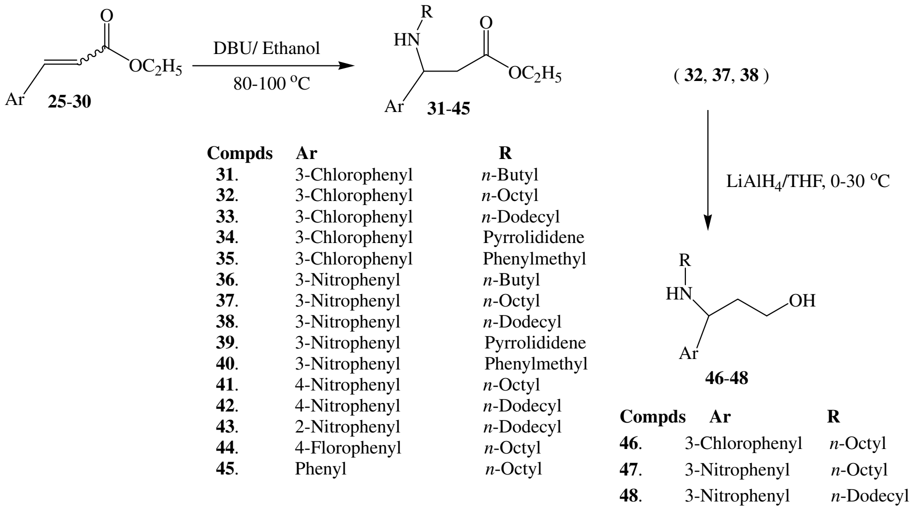
characterized on the basis of spectral data and microanalysis.

Since diamines and polyamines based on the structure of spermine and spermidine are known to have antiparasitic and antimicrobial activities and that the antitubercular activity is enhanced by increase in hydrophobic character, hence in the next attempt diaryl diamines were prepared to see their effect on the bacterium. Thus reaction of two equivalents of aromatic aldehydes with one equivalent of selected diamines separately using the above reductive amination strategy led to the formation of respective N^1,N^n-diarylmethyl-diamines (**20**–**24**) in excellent yields (Scheme 2).

The cinnamates **25**–**30** were prepared by literature methods.[14] Thus conjugate addition of selected amines with the above cinnamates separately led to the formation of respective ethyl 3-amino-3-phenyl propionates **31**–**45** in moderate to good yields (Scheme 3). It is appropriate to mention here that in the above reaction very low yields of the propenamides were also obtained which were not isolated, however characterized in few instances. As the esters were not very active against *M. tuberculosis* we reduced the ester group into alcohols in some selected compounds to see its effect on antitubercular profile. Thus compounds **32**, **37** and **38** on reduction with lithium aluminium hydride in tetrahydrofuran led to the formation of respective alcohols **46**–**48** in good yields (Scheme 3). The structures of all the compounds were established on the basis of spectroscopic analysis and analytical data.

2.2. Biological activity

All the synthesized compounds were evaluated against *M. tuberculosis* H37 Ra and *M. tuberculosis* H37 Rv strains following earlier protocol.[15,16] Among all the 42 compounds screened for anti-TB activity except compounds **11**, **14**, **20**, **21**, **22**, **31**, **33**, **36**, **37**, **39**, **41**, **42**, **43**, **44** and **45** other compounds of the series were found to be active at one or the other concentration ranging from 12.5 to 1.56 μg/mL. By closer look into structure–activity relationship of the compounds, it is evident that

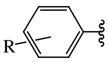
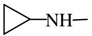
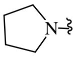
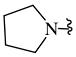


Compds	Ar	R
31.	3-Chlorophenyl	*n*-Butyl
32.	3-Chlorophenyl	*n*-Octyl
33.	3-Chlorophenyl	*n*-Dodecyl
34.	3-Chlorophenyl	Pyrrolididene
35.	3-Chlorophenyl	Phenylmethyl
36.	3-Nitrophenyl	*n*-Butyl
37.	3-Nitrophenyl	*n*-Octyl
38.	3-Nitrophenyl	*n*-Dodecyl
39.	3-Nitrophenyl	Pyrrolididene
40.	3-Nitrophenyl	Phenylmethyl
41.	4-Nitrophenyl	*n*-Octyl
42.	4-Nitrophenyl	*n*-Dodecyl
43.	2-Nitrophenyl	*n*-Dodecyl
44.	4-Florophenyl	*n*-Octyl
45.	Phenyl	*n*-Octyl

Compds	Ar	R
46.	3-Chlorophenyl	*n*-Octyl
47.	3-Nitrophenyl	*n*-Octyl
48.	3-Nitrophenyl	*n*-Dodecyl

Scheme 3. Synthesis of phenylmethyl amino esters and amino alcohols.

Table 1. Antitubercular activities of synthesized phenylmethyl- and pyridylmethyl amines against *M. tuberculosis H37Ra* and *M. tuberculosis H37Rv*

Compound		R^1	NR^2	MIC *H37Ra* (μg/mL)	MIC *H37Rv* (μg/mL)
1	3-Methoxy-4-hydroxyphenyl	H		>25	12.5[a]
2	3-Methoxy-4-hydroxyphenyl	H	*n*-Hexadecyl-NH–	>25	3.12[a]
3	3-Methoxy-4-hydroxyphenyl	H	*n*-(9-Octadecenyl)-NH–	>25	1.56[a] 25[b]
4	4-Fluorophenyl	H	*n*-Hexadecyl-NH–	<25	12.5[a]
5	4-Fluorophenyl	H	*n*-(9-Octadecenyl)-NH–	>25	12.5[a]
6	3,4-Dimethoxyphenyl	H	*n*-(9-Octadecenyl)-NH–	<25	3.12[a] 6.25[b]
7	2-Hydroxyphenyl	H	*n*-Dodecyl-NH–	<25	6.25[a] 25[b]
8	2-Hydroxyphenyl	H	*n*-(9-Octadecenyl)-NH–	<25	1.56[a] 3.12[b]
9	4-Chlorophenyl	H	*n*-Octyl-NH–	<25	12.5[a]
10	4-Chlorophenyl	H	*n*-Dodecyl-NH–	<25	3.12[a]
11	4-Chlorophenyl	H	*n*-Hexadecyl-NH–	>25	25[a]
12	4-Chlorophenyl	H	*n*-(9-Octadecenyl)-NH–	<25	3.12[a] 25[b]
13	2-Nitrophenyl	H	*n*-Octyl-NH–	<25	12.5[a]
14	4-Pyridyl	H	*n*-Octyl-NH–	>25	25[a]
15	4-Pyridyl	H	*n*-Hexadecyl-NH–	<25	3.12[a] 3.12[b]
16	4-Pyridyl	H	*n*-(9-Octadecenyl)-NH–	<25	6.25[a] 50[b]
17	3-Pyridyl	H	*n*-Hexadecyl-NH–	<25	3.12[a] 3.12[b]
18	3-Pyridyl	H	*n*-(9-Octadecenyl)-NH–	<25	3.12[a] 25[b]
19	2-Pyridyl	H	*n*-Dodecyl-NH–	<25	1.56[a]
20	2-Hydroxyphenyl	H	–NH(CH$_2$)$_3$NH–	>25	25[a]
21	2-Hydroxyphenyl	H	–NH(CH$_2$)$_5$NH–	>25	25[a]
22	2-Hydroxyphenyl	H	–NH(CH$_2$)$_7$NH–	<25	25[a]
23	2-Hydroxyphenyl	H	–NH(CH$_2$)$_{12}$NH–	<25	3.12[a]
24	3-Hydroxyphenyl	H	–NH(CH$_2$)$_5$NH–	>25	6.25[a]
31	3-Chlorophenyl	2-Carbethoxymethyl	*n*-Butyl-NH–	>25	25[a]
32	3-Chlorophenyl	2-Carbethoxymethyl	*n*-Octyl-NH–	>25	12.5[a]
33	3-Chlorophenyl	2-Carbethoxymethyl	*n*-Dodecyl-NH–	>25	25[a]
34	3-Chlorophenyl	2-Carbethoxymethyl		>25	12.5[a]
35	3-Chlorophenyl	2-Carbethoxymethyl	C$_6$H$_5$CH$_2$NH–	>25	12.5[a]
36	3-Nitrophenyl	2-Carbethoxymethyl	*n*-Butyl-NH–	>25	25[a]
37	3-Nitrophenyl	2-Carbethoxymethyl	*n*-Octyl-NH–	>25	25[a]
38	3-Nitrophenyl	2-Carbethoxymethyl	*n*-Dodecyl-NH–		6.25[a]
39	3-Nitrophenyl	2-Carbethoxymethyl		>25	25[a]
40	3-Nitrophenyl	2-Carbethoxymethyl	C$_6$H$_5$CH$_2$NH–	>25	12.5[a]
41	4-Nitrophenyl	2-Carbethoxymethyl	*n*-Octyl-NH–	<25	25[a]
42	4-Nitrophenyl	2-Carbethoxymethyl	*n*-Dodecyl-NH–	>25	25[a]
43	2-Nitrophenyl	2-Carbethoxymethyl	*n*-Dodecyl-NH–	<25	25[a]
44	4-Fluorophenyl	2-Carbethoxymethyl	*n*-Octyl-NH–	>25	25[a]
45	Phenyl	2-Carbethoxymethyl	*n*-Octyl-NH–	<25	25[a]
46	3-Chlorophenyl	2-Hydroxyethyl	*n*-Octyl-NH–	<25	12.5[a]
47	3-Nitrophenyl	2-Hydroxyethyl	*n*-Octyl-NH–	<25	12.5[a]
48	3-Nitrophenyl	2-Hydroxyethyl	*n*-Dodecyl-NH–	<25	12.5[a]
INH					0.65[a] >1.56[b]
Rifmp					0.75[a] >40[b]
Ethm					3.25[a]

MIC, Minimum inhibitory concentration, the concentration of the test compound at which complete (>99%) inhibition of the bacterial colonies was observed. INH, isoniazid; Rifmp, rifampicin; Ethm, ethambutol.

[a] MIC against sensitive strains.

[b] MIC against clinical isolates of MDR TB.

substitution in aromatic ring by any of the group like hydroxy, methoxy, fluoro, chloro and nitro affects the activity profile. Compounds with aromatic ring having fluoro group are more active than the compounds with chloro group. Substitution of the benzylic carbon in these compounds either with carbethoxy or hydroxyl ethyl substituent results in loss of activity. Among the 2-hydroxy phenylmethyl amine derivatives, compound **7** with 12-carbon chain substituent was found to be active as MIC 6.25 µg/mL. Introduction of another 2-hydroxy phenylmethyl amine (compound **23**) moiety leads to an increase in the activity profile of the compounds against *M. tuberculosis H37 Rv* as the MIC was found to be 3.12 µg/mL. In general, hydroxyl substituent in the aromatic ring at position-2 leads to measurable increase in activity profile as compared to substitution at the other positions. Among the disubstituted compounds in benzene ring the best compound is **3** with 4-hydroxy-3-methoxy phenyl ring having MIC 1.56 µg/mL. Substitution of the hydroxyl group with methoxy group in the disubstituted phenyl ring, for example, compound **6** results in deterioration of its activity profile as MIC is higher (3.12 µg/mL). Among the pyridyl methyl amines almost all the compounds displayed activity at one or other concentration ranging from 25 to 1.56 µg/mL. Among the compounds of pyridyl series the activity trend is in the order of 2-pyridyl > 3-pyridyl > 4-pyridyl as evident from the antitubercular activity of compounds **14–18**. It is also evident that most of these compounds are active in infectious strain (*M. tuberculosis H37 Rv*) only and inactive against avirulent strain (*M. tuberculosis H37 Ra*), indicating that they are more specific to the virulent strain. Many compounds having MIC < 6.25 mg/mL were screened against clinical isolates of drug resistant tuberculosis strain also and found to be active either at the same concentration used for *H37Rv* or higher than that shown in Table 1.

3. Conclusion

In conclusion we have synthesized different phenylmethyl and pyridylmethyl amines in a straightforward manner using reductive amination or Michael type 1,4-conjugate addition of amines followed by further desired manipulations. All the compounds were screened against avirulent and virulent strains of *M. tuberculosis*. Most of the compounds displayed high order of activity and the selected compounds were also evaluated against clinical isolates of MDR TB showing potent activity.

4. Experimental

4.1. General methods

Melting points were determined on a Buchi 510 apparatus. Elemental analyses for all compounds were performed on a Carlo Erba Model EA-1108 elemental analyzer and data of C, H and N are within ±0.4% of calculated values. Thin-layer chromatography was used to monitor the reactions. IR (KBr) spectra were recorded using Perkin-Elmer 881 spectrophotometer and the values are expressed as ν_{max} cm^{-1}. Mass spectral data were recorded on a Jeol (Japan) SX 102/DA-6000 Mass Spectrometer/Data system. The ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Spectrospin spectrometer at 200 or 300 and 50 MHz, respectively, using TMS as internal standard. The chemical shift values are on δ scale and the coupling constants (J) are in Hz.

4.2. Synthesis of compounds 1–19

4.2.1. 4-(Cyclopropylaminomethyl)-2-methoxyphenol (1). *Typical procedure*: To a magnetically stirred solution of 4-hydroxy-3-methoxybenzaldehyde (2.0 g, 13.10 mmol) and 4 Å mol Sieves. in dichloromethane (7 mL), cyclopropyl amine (0.90 mL, 13.10 mmol) was added and stirring continued for 3.0 h untill the disappearance of starting material (TLC). The solvent was evaporated under reduced pressure and the residue, so obtained, was dissolved in methanol (5 mL). $NaBH_4$ (0.18 g, 4.98 mmol) was added slowly at 0 °C and stirring continued for additional 4 h. The reaction mixture was quenched with saturated ammonium chloride solution. The reaction mixture was filtered, solvent evaporated under reduced pressure and the residue, so obtained, was dissolved in ethyl acetate (60 mL), washed with water (2 × 20 mL) followed by saturated aqueous NaCl solution (2 × 20 mL) and organic layer dried over anhyd Na_2SO_4. The organic layer was concentrated under reduced pressure to obtain a crude product which was chromatographed over SiO_2 using hexane/ethyl acetate (7:3) to give compound **1** as colourless liquid (yield, 2.31 g, 92%); IR (KBr): ν_{max} 3450, 3276, 2940 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.86–6.79 (m, 3H, ArH), 3.85 (s, 3H, OCH_3), 3.50 (br s, 1H, OH), 3.75 (s, 2H, CH_2Ar), 2.17–2.13 (m, 1H, CH), 0.45–0.40 (m, 4H, 2× CH_2); FABMS *m/z* 194 $[M+H]^+$; Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.39; H, 7.77; N, 7.25. Found: C, 68.42; H, 7.78; N, 7.30.

4.2.2. 4-(Hexadecylaminomethyl)-2-methoxyphenol (2). Obtained by reaction of 4-hydroxy-3-methoxybenzaldehyde (1.68 g, 11.05 mmol) and hexadecylamine (2.58 g, 11.05 mmol) as described above gave (**2**) as colourless solid (3.55 g, 90%); mp 130 °C IR (KBr): ν_{max} 3459, 3287 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.86–6.78 (m, 3H, ArH), 3.89 (br s, 1H, OH), 3.86 (s, 3H, OCH_3), 3.70 (s, 2H, CH_2Ar), 2.62 (t, J = 6.0 Hz, 2H, NCH_2), 1.51 (br s, 1H, NH), 1.26–1.24 (m, 28H, 14× CH_2), 0.88 (t, J = 6.0 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 147.3, 145.4, 132.2, 121.4, 114.9, 111.4, 75.2, 75.0, 56.1, 54.3, 49.8, 32.3, 32.1, 30.2, 30.1, 30.0, 30.0, 30.0, 29.9, 29.7, 27.7, 27.5 23.0, 14.5; FABMS *m/z* 378 $(M+H)^+$; Anal. Calcd for $C_{24}H_{43}NO_2$: C, 76.39; H, 11.40; N, 3.71. Found: C, 76.42; H, 11.48; N, 3.74.

4.2.3. 2-Methoxy-4-(octadec-9-enylamino) phenol (3). Obtained by reaction of 4-hydroxy-3-methoxybenzaldehyde (1.42 g, 9.34 mmol) and octadec-9-enylamine (3.03 mL, 9.34 mmol) as described above. Colourless liquid in (3.37 g, 90%) yield; IR (KBr): ν_{max} 3398, 3020 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.26–6.78

(m, 3H, ArH), 5.36–5.34 (m, 2H, –CH=), 3.86 (s, 3H, OCH_3), 3.70 (s, 2H, CH_2Ar), 3.20 (br s, 1H, OH), 2.62 (t, J = 7.0 Hz, 2H, NCH_2), 2.01–1.99 (m, 4H, 2× CH_2), 1.51 (br s, 1H, NH), 1.27–1.25 (m, 24H, 12× CH_2), 0.87 (t, J = 6.7 Hz, 3H, CH_3), ^{13}C NMR (50 MHz, $CDCl_3$): δ 147.1, 145.2, 132.3, 130.8, 130.3, 130.2, 121.4, 114.7, 111.3, 56.2, 54.3, 49.7, 32.9, 32.3, 31.9, 30.8, 30.2, 30.1, 30.0, 29.9, 29.7, 29.6, 27.7, 27.6, 23.0, 14.4; FABMS *m/z* 404 $[M+H]^+$; Anal. Calcd for $C_{26}H_{45}NO_2$: C, 77.41; H, 11.16; N, 3.47. Found: C, 77.48; H, 11.19; N, 3.41.

4.2.4. (4-Fluorophenylmethyl)hexadecylamine (4). Obtained by reaction of 4-fluorobenzaldehyde (1.50 g, 14.28 mmol) and hexadecylamine (3.54 g, 14.47 mmol) as described above gave **4** as colourless liquid in (4.70 g, 95%) yield; IR (KBr): ν_{max} 3393, 2926 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.29 (d, J = 8.2 Hz, 1H, ArH), 7.25 (d, J = 8.2 Hz, 1H, ArH), 7.04 (d, J = 8.6 Hz, 1H, ArH), 6.97 (d, J = 8.6 Hz, 1H, ArH), 3.74 (s, 2H, CH_2Ar), 2.60 (t, J = 7.1 Hz, 2H, NCH_2), 1.66 (br s, 1H, NH), 1.48–1.49 (m, 2H, CH_2), 1.27–1.22 (m, 26H, 13× CH_2), 0.87 (t, J = 6.6 Hz, 3H, CH_3); FABMS: *m/z* 350 $[M+H]^+$; Anal. Calcd for $C_{23}H_{40}FN$: C, 79.08; H, 11.46; N, 4.01. Found: C, 79.00; H, 11.50; N, 4.08.

4.2.5. (4-Fluorophenylmethyl)-octadeca-9-enyl amine (5). Obtained by reaction of 4-fluorobenzaldehyde (1.50 g, 14.28 mmol) and octadec-9-enylamine (4.67 mL, 14.28 mmol) as described above. Colourless liquid (4.70 g, 90%) yield; IR (KBr): ν_{max} 3400, 3020, 2928 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.27–7.02 (m, 4H, ArH), 5.36–5.32 (m, 2H, –CH=CH–), 3.72 (s, 2H, CH_2Ar), 2.58 (t, J = 7.1 Hz, 2H, NCH_2), 2.02–1.96 (m, 4H, 2× CH_2), 1.48 (br s, 1H, NH), 1.28–1.24 (m, 24H, 12× CH_2), 0.87 (t, J = 6.7 Hz, 3H, CH_3); FABMS: *m/z* 376 $[M+H]^+$; Anal. Calcd for $C_{25}H_{42}FN$: C, 80.00; H, 11.27; N, 3.73. Found: C, 80.05; H, 11.19; N, 3.78.

4.2.6. (3,4-Dimethoxyphenylmethyl)octadec-9-enyl amine (6). Obtained by reaction of 3,4-dimethoxybenzaldehyde (1.7 g, 10.24 mmol) and octadec-9-enylamine (3.3 mL, 10.24 mmol). Colourless oil (3.90 g, 92%) yield; IR (KBr): ν_{max} 3425, 3002 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.26 (s, 1H, ArH), 6.89 (two d, J = 11.6 Hz, 1.6 Hz, 2H, ArH), 5.36–5.34 (m, 2H, –CH=CH), 3.88, 3.86 (s, 6H, 2× OCH_3), 3.73 (s, 2H, CH_2Ar), 2.62 (t, J = 7.1 Hz, 2H, NCH_2), 2.02–1.97 (m, 4H, 2× CH_2), 1.63 (bs, 1H, NH), 1.26–1.23 (m, 24H, 12× CH_2), 0.87 (t, J = 6.7 Hz, 3H, CH_3), ^{13}C NMR (50 MHz, $CDCl_3$): δ 149.3, 148.4, 133.5, 130.6, 130.1, 120.5, 111.8, 111.4, 56.1, 56.2, 54.2, 49.8, 32.9, 32.2, 32.1, 30.4, 30.2, 30.0, 30.0, 29.9, 29.8, 29.6, 27.9, 27.7, 27.5, 23.0, 14.4; FABMS: *m/z* 418 $[M+H]^+$; Anal. Calcd for $C_{27}H_{47}NO_2$: C, 77.69; H, 11.27; N, 3.35. Found: C, 77.55; H, 11.32; N, 3.41.

4.2.7. 2-(Dodecylaminomethyl)-phenol (7). Obtained by reaction of 2-hydroxybenzaldehyde (2.00 g, 16.3 mmol) and dodecylamine (3.76 mL, 16.2 mmol) as colourless liquid (4.02 g, 85%) yield; IR (KBr): ν_{max} 3266, 2919 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.25–6.75 (m, 5H, OH, ArH), 3.97 (s, 2H, CH_2Ar), 2.66 (t, J = 7.1 Hz, 2H, NCH_2), 1.52 (br s, 1H, NH) 1.35–1.16 (m, 20H, 10× CH_2), 0.88 (t, J = 6.4 Hz, 3H, CH_3), ^{13}C NMR (50 MHz, CDCl3): δ 158.8, 129.0, 128.5, 123.0, 119.2, 116.7, 53.1, 49.2, 32.3, 30.3, 30.3, 30.2, 30.0, 29.7, 29.8, 29.7, 27.5, 23.0, 14.5; FABMS: *m/z* 292 $[M+H]^+$; Anal. Calcd for $C_{19}H_{33}NO$: C, 78.35; H, 11.34; N, 4.81. Found: C, 78.33; H, 11.30; N, 4.81.

4.2.8. 2-(Octadec-9-en-1-yl-amino-methyl)-phenol (8). Obtained by reaction of 2-hydroxybenzaldehyde (1.50 g, 12.2 mmol) and octadec-9-enylamine (4.0 mL, 12.2 mmol), viscous liquid in (4.10 g, 90%); IR (KBr): ν_{max} 3020, 2929 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.30 (s, 1H, OH), 7.25–6.79 (m, 4H, ArH), 5.36–5.34 (m, 2H, –CH=), 3.96 (s, 2H, CH_2Ar), 2.64 (t, J = 6.9 Hz, 2H, NCH_2), 2.02–1.99 (m, 4H, 2× CH_2), 1.54 (br s, 1H, NH), 1.28–1.15 (m, 24H, 12× CH_2), 0.87 (t, J = 6.7 Hz, 3H, CH_3), ^{13}C NMR (50 MHz, $CDCl_3$): δ 158, 131.2, 130.8, 130.7, 128.2, 123.4, 123.0, 116.7, 116.6, 53.1, 49.0, 33.0, 32.2, 30.1, 30.1, 30.0, 30.0, 29.9, 29.8, 29.6, 27.6, 27.6, 27.5, 23.0, 14.5; FABMS: *m/z* 374 $[M+H]^+$; Anal. Calcd for $C_{25}H_{43}NO$: C, 80.42; H, 11.52; N, 3.75. Found: C, 80.48; H, 11.49; N, 3.81.

4.2.9. *N*-(4-Chlorobenzyl)octylamine (9). The reaction of 4-chlorobenzaldehyde (1.8 g, 12.85 mmol) and octylamine (2.16 mL, 12.2 mmol) gave **9** as colourless solid in (2.96 g, 92%) yield; mp 142–143 °C; IR (KBr): ν_{max} 3400, 3020, 2928 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.46 (d, J = 8.4, Hz, 2H, ArH), 7.33 (d, J = 8.4, Hz, 2H, ArH) 3.92 (s, 2H, CH_2Ar), 2.69 (t, J = 8.0 Hz, 2H, NCH_2), 1.74–1.67 (m, 2H, CH_2), 1.26–1.22 (m, 10H, 5× CH_2), 0.87 (t, J = 6.7 Hz, 3H, CH_3). FABMS: *m/z* 254 $[M+H]^+$; Anal. Calcd for $C_{15}H_{24}ClN$: C, 71.14; H, 9.48; N, 5.53. Found: C, 71.18; H, 9.44; N, 5.55.

4.2.10. *N*-(4-Chlorobenzyl)dodecylamine (10). Obtained by reaction of 4-chlorobenzaldehyde (2.00 g, 14.20 mmol) and dodecylamine (3.27 mL, 14.2 mmol). Colourless solid, yield (3.90 g, 90%); mp 150–151 °C; IR (KBr): ν_{max} 3400, 3020, 2928 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.54 (d, J = 8.4, Hz, 2H, ArH), 7.35 (d, J = 8.4 Hz, 2H, ArH), 3.98 (s, 2H, CH_2Ar), 2.72 (t, J = 8.2, Hz, 2H, NCH_2), 1.8–1.79 (m, 2H, CH_2), 1.25–1.16 (m, 18H, 9× CH_2), 0.87 (t, J = 6.7 Hz, 3H, CH_3); FABMS: *m/z* 310 $[M+H]^+$; Anal. Calcd for $C_{19}H_{32}ClN$: C, 73.78; H, 10.35; N, 4.53. Found: C, 73.75; H, 10.29; N, 4.52.

4.2.11. *N*-(4-Chlorobenzyl)-hexadecylamine (11). Obtained by reaction of 4-chlorobenzaldehyde (1.50 g, 10.70 mmol) hexadecylamine (2.58 g, 10.00 mmol). Colourless granules, (3.50 g, 90%); mp 158–159 °C; IR (KBr): ν_{max} 3393, 2926, 1605 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.34–7.24 (m, 4H, ArH), 3.70 (s, 2H, CH_2Ar), 2.60 (t, J = 8.1 Hz, 2H, NCH_2), 1.95–1.92 (m, 2H, CH_2), 1.29–1.19 (m, 26H, 13× CH_2), 0.87 (t, J = 6.6 Hz, 3H, CH_3). FABMS: *m/z* 366 $[M+H]^+$; Anal. Calcd for $C_{23}H_{40}ClN$: C, 75.61; H, 10.95; N, 3.83. Found: C, 75.58; H, 10.98; N, 3.80.

4.2.12. *N*-(4-Chlorobenzyl)-octadec-9-ene-1-yl-amine (12). Obtained by reaction of 4-chlorobenzaldehyde (1.50 g, 10.7 mmol) and octadec-9-enylamine (3.52 mL, 10.4 mmol) as described above as colourless liquid yield (3.83 g, 92%); IR (KBr): ν_{max} 3400, 3020, 2928, 1511 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.0 Hz, 2H, ArH), 7.25 (d, *J* = 8.0 Hz, 2H, ArH), 5.38–5.32 (m, 2H, –CH=CH), 3.74 (s, 2H, CH_2Ar), 2.59 (t, *J* = 6.5 Hz, 2H, NCH_2), 2.01–1.97 (m, 4H, 2× CH_2), 1.37–1.15 (m, 24H, 12× CH_2), 0.87 (t, *J* = 6.7 Hz, 3H, CH_3). FABMS: *m/z* 392 $[M+H]^+$; Anal. Calcd for $C_{25}H_{42}ClN$: C, 76.72; H, 10.74; N, 3.58. Found: C, 76.77; H, 10.70; N, 3.55.

4.2.13. *N*-(2-Nitrobenzyl)octylamine (13). Obtained by reaction of 2-nitrobenzaldehyde (2.0 g, 13.2 mmol) and octylamine (2.1 mL, 13.3 mmol) as colourless liquid, yield (3.12 g, 90%); IR (KBr): ν_{max} 2926, 1529, 1461 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.21 (br s, 1H, ArH), 8.09 (d, *J* = 8.0 Hz, 1H, ArH), 7.70 (d, *J* = 7.6 Hz, 1H, ArH), 7.46 (dd, *J* = 7.9 Hz, 1H, ArH), 3.89 (s, 2H, CH_2Ar), 2.62 (t, *J* = 7.1 Hz, 2H, NCH_2), 1.51 (br s, 1H, NH) 1.34–1.12 (m, 12H, 6× CH_2), 0.87 (t, *J* = 6.7 Hz, 3H, CH_3), ^{13}C NMR (50 MHz, $CDCl_3$): δ 148.7, 143.3, 134.5, 129.5, 123.2, 122.3, 53.5, 49.9, 32.2, 30.4, 29.8, 29.6, 27.6, 23.0, 14.4; FABMS: *m/z* 265 $[M+H]^+$; Anal. Calcd for $C_{15}H_{24}N_2O_2$: C, 68.18: H, 9.09: N, 10.60. Found: C, 68.23: H, 9.15: N, 10.66.

4.2.14. *N*-(4-Pridylmethyl)-octylamine (14). Obtained by reaction of 4-pyridylcarboxaldehyde (2.0 g, 18.6 mmol) and octylamine (3.09 mL, 18.8 mmol) as viscous liquid yield (3.70 g, 92%);; IR (KBr): ν_{max} 3267, 2920, 1578 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.45 (m, 2H, PyH), 7.65 (m, 1H, PyH), 7.20 (m, 1H, PyH) 3.81 (s, 2H, NCH_2), 2.61 (t, *J* = 4.0 Hz, 2H, CH_2), 1.72 (s, 1H, NH), 1.49 (m, 2H, CH_2), 1.35–120 (m, 10H, 5× CH_2), 0.88 (t, *J* = 4.0 Hz, 3H, CH_3). FABMS: *m/z* 221 $(M+H)^+$; Anal. Calcd for $C_{14}H_{24}N_2$: C, 76.36: H, 10.90: N, 12.72. Found: C, 76.35: H, 10.96: N, 12.68.

4.2.15. *N*-(4-Pyridylmethyl)-hexadecylamine (15). Obtained by reaction of 4-pyridylcarboxaldehyde (2.0 g, 18.6 mmol) and hexadecylamine (4.8 g, 18.8 mmol) as colourless solid yield (5.50 g, 90%); mp 143–144 °C; IR (KBr): ν_{max} 3453, 3286, 2919, 1600 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.54 (d, *J* = 6.0 Hz, 2H, PyH), 7.26 (d, *J* = 6.0 Hz, 2H, ArH), 3.81 (s, 2H, NCH_2), 2.61 (t, *J* = 6.0 Hz, 2H, NCH_2), 1.72 (s, 1H, NH), 1.53–1.43 (m, 2H, CH_2), 1.31–1.18 (m, 26H, 13× CH_2), 0.88 (t, *J* = 6.0 Hz, 3H, CH_3); FABMS: *m/z* 334 $[M+H]^+$; Anal. Calcd for $C_{22}H_{40}N_2$: C, 79.51: H, 12.04: N, 8.43. Found: C, 79.45: H, 11.99: N, 8.48.

4.2.16. *N*-(4-Pyridylmethyl)-octadec-9-enylamine (16). Obtained by reaction of 4-pyridylcarboxaldehyde (2.0 g, 18.6 mmol) and octadec-9-enylamine (6.15 mL, 18.5 mmol). Viscous liquid (5.80 g, 90%); IR (KBr): ν_{max} 3265, 2929 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.52 (dd, *J* = 8.7 Hz, 4.7 Hz, 2H, PyH), 7.67 (d, *J* = 7.7 Hz, 1H, PyH), 7.28–7.24 (m, *J* = 7.7 Hz, 1H, PyH), 5.36–5.32 (m, 2H, 2× –CH=) 3.81 (s, 2H, NCH_2), 2.61 (t, *J* = 4.0 Hz, 2H, NCH_2), 1.72 (s, 1H, NH), 1.49–1.46 (m, 2H, CH_2), 1.40–1.18 (m, 26H, 13× CH_2), 0.88 (t, *J* = 5.8 Hz, 3H, CH_3); FABMS: *m/z* 358 $(M+H)^+$; Anal. Calcd for $C_{24}H_{42}N_2$: C, 80.44: H, 11.73: N, 7.82. Found: C, 80.40: H, 11.69: N, 7.85.

4.2.17. *N*-(3-Pyridylmethyl)hexadecylamine (17). Obtained by reaction of 3-pyridylcarboxaldehyde (2.0 g, 18.6 mmol) and hexadecylamine (4.48 g, 18.8 mmol). Colourless solid, yield (5.55 g, 90%); mp 89–90 °C; IR (KBr): ν_{max} 3267, 2920, 1578 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.61 (m, 2H, PyH), 7.61 (m, 1H, PyH), 7.30 (m, 1H, PyH), 3.81 (s, 2H, NCH_2), 2.61 (t, *J* = 4.0 Hz, 2H, CH_2), 1.72 (s, 1H, NH), 1.49 (m, 2H, CH_2), 1.35–120 (m, 26H, 13× CH_2), 0.88 (t, *J* = 4.0 Hz, 3H, CH_3). FABMS: *m/z* 333 $(M+H)^+$; Anal. Calcd for $C_{22}H_{40}N_2$: C, 79.51: H, 12.04: N, 8.43. Found: C, 79.45: H, 11.99: N, 8.48.

4.2.18. *N*-(3-Pyridylmethyl)octadec-9-ene-1-ylamine (18). Obtained by reaction of 3-pyridylcarboxaldehyde (2.0 g, 18.6 mmol) and hexadecylamine (6.13 mL, 18.6 mmol). Viscous oil, yield (5.90 g, 90%); IR (KBr): ν_{max} 3267, 2920, 1578 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.53 (two d, *J* = 8.7 and 4.0 Hz, 2H, PyH), 7.68 (d, *J* = 7.7 Hz, 1H, PyH), 7.26 (two d, *J* = 7.7 and 3.4 Hz, 1H, PyH), 5.34 (m, 2H, –CH=CH–), 3.78 (s, 2H, NCH_2), 2.61 (t, *J* = 4.0 Hz, 2H, NCH_2), 1.72 (s, 1H, NH), 1.49–1.46 (m, 2H, CH_2), 1.35–1.18 (m, 26H, 13× CH_2), 0.88 (t, *J* = 4.0 Hz, 3H, CH_3); FABMS: *m/z* 358 $(M+H)^+$; Anal. Calcd for $C_{24}H_{42}N_2$: C, 80.44; H, 11.73; N, 7.82. Found: C, 79.99: H, 11.99: N, 7.88.

4.2.19. *N*-(2-Pyridylmethyl)dodecylamine (19). Obtained by reaction of 2-pyridylcarboxaldehyde (2.0 g, 18.6 mmol) and dodecylamine (4.3 mL, 18.8 mmol). Colourless oil, yield (4.60 g, 90%); (KBr): ν_{max} 3266, 2930 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.53 (d, *J* = 4.8 Hz, 1H, PyH), 7.67 (dd, *J* = 7.4 Hz, 1.4 Hz, 1H, PyH), 7.28 (d, *J* = 7.7 Hz, 1H, PyH), 7.16 (m, 1H, PyH), 4.75 (s, 2H, $PyCH_2$), 3.89 (s, 2H,CH_2), 3.10 (br s, 1H, NH), 2.63 (t, *J* = 7.2 Hz, 2H, NCH_2), 1.35–115 (m, 20H, 10× CH_2), 0.88 (t, *J* = 5.6 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 150.0, 148.7, 136.1, 136.0, 123.6, 51.7, 49.9, 32.3, 30.4, 30.3, 30.2, 30.1, 30.0, 29.7, 29.6, 27.7, 23.0, 14.5; FABMS: *m/z* 277 $(M+H)^+$; Anal. Calcd for $C_{18}H_{32}N_2$: C, 78.26: H, 11.59: N, 10.14. Found: C, 78.22: H, 11.62: N, 10.20.

4.3. Synthesis of compounds 20–24

4.3.1. *N*,*N*(Bis-2-hydroxybenzyl)-1,3-diaminopropane (20). The reaction of 2-hydroxybenzaldehyde (3.0 g, 24.5 mmol) and 1,3 diaminopropane (1.0 mL, 12.2 mmol) as above gave **20** as light yellow granules, yield (5.90 g, 85%); mp 65–66 °C; IR (KBr): ν_{max} 3481, 3274, 2925, 1593 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$), 7.18–6.67 (m, 8H, ArH), 3.95 (s, 4H, CH_2Ar), 2.71 (m, 4H, NCH_2), 1.78–1.71 (m, 2H, CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 158.5, 157.9, 129.1, 128.8, 123.0, 122.8, 119.8, 119.5, 119.1, 118.8, 116.7, 53.1, 52.7, 46.7, 30.0; FABMS: *m/z* 287 $[M+H]^+$; Anal. Calcd for $C_{17}H_{22}N_2O_2$: C, 71.32: H, 7.69: N, 9.79. Found: C, 71.36: H, 7.72,: N, 9.74.

4.3.2. N^1,N^5(Bis-2-hydroxybenzyl)-1,5-diaminopentane (21). Obtained by reaction of 2-hydroxybenzaldehyde (3.0 g, 24.5 mmol) and 1,5 diaminopentane (1.4 mL, 12.2 mmol). Colourless powder yield (6.13 g, 80%); mp 105–106 °C; IR (KBr): ν_{max} 3481, 3274, 2925, 1593 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$), 7.25–6.72 (m, 8H, ArH), 6.25 (br s, 2H, OH) 3.97–3.87 (m, 4H, CH_2Ar), 2.69–2.56 (m, 4H, NCH_2), 1.76–1.70 (m, 2H, CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 158.5, 157.9, 129.1, 128.8, 123.0, 122.8, 119.8, 119.5, 119.1, 118.8, 116.7, 53.1, 52.7, 46.7, 30.0. FABMS: *m/z* 314 $[M+H]^+$; Anal. Calcd for $C_{19}H_{26}N_2O_2$: C, 72.61; H, 8.28; N, 8.91. Found: C, 72.66; H, 8.22; N, 8.94.

4.3.3. N^1,N^7(Bis-2-hydroxybenzyl)-1,7-diaminoheptane (22). Obtained by reaction of 2-hydroxybenzaldehyde (3.0 g, 24.5 mmol) and 1,7 diaminoheptane (1.59 g, 12.2 mmol). Colourless granules yield (7.1 g, 85%); mp 108–109 °C; IR (KBr): ν_{max} 3266, 2919, 1603 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.15 (two d, $J = 7.5$ Hz, 2H, ArH), 7.15 (two d, $J = 7.7$ Hz, 4H, ArH), 4.86 (br s, 2H, OH) 3.95 (s, 4H, CH_2Ar), 2.63 (t, $J = 6.7$ Hz, 4H, NCH_2), 1.48 (m, 4H, 2× CH_2) 1.30 (m, 6H, 3× CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 158.2, 129.1, 128.5, 128.1, 127.7, 125.0, 122.5, 119.7, 118.8, 116.2, 64.2, 52.6, 48.5, 29.3, 29.0, 26.9. FABMS: *m/z* 343 $[M+H]^+$; Anal. Calcd for $C_{21}H_{30}N_2O_2$: C, 73.68; H, 8.77; N, 8.18. Found: C, 73.62; H, 8.75; N, 8.22.

4.3.4. N^1,N^{12}(Bis-2-hydroxybenzyl)-1,12-diaminododecane (23). Obtained by reaction of 2-hydroxybenzaldehyde (2.0 g, 16.3 mmol) and 1,12 diaminododecane (1.62 g, 8.0 mmol). Colourless crystalline solid, yield (5.70 g, 85%); mp 131–132 °C; IR (KBr): ν_{max} 3481 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.19 (dd, $J = 7.4$ Hz, 1.5 Hz, 2H, ArH), 6.94 (d, $J = 6.8$ Hz, 2H, ArH), 4.53 (br s, 2H, OH), 3.98 (s, 4H, CH_2Ar), 2.66 (t, $J = 6.9$ Hz, 4H, NCH_2), 1.52 (m, 4H, $CH_{2's}$), 1.27–1.23 (m, 16H, $CH_{2's}$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 158.7, 129.0, 128.6, 128.2, 123.0, 120.2, 119.3, 116.7, 64.8, 53.1, 49.1, 29.9, 27.5; FABMS: *m/z* 413 $[M+H]^+$; Anal. Calcd for $C_{26}H_{40}N_2O_2$: C, 75.72; H, 9.70; N, 6.79. Found: C, 75.76; H, 9.77; N, 6.79.

4.3.5. N^1,N^5(Bis-3-hydroxybenzyl)-1,5-diaminopentane (24). Obtained by reaction of 3-hydroxybenzaldehyde (2.0 g, 16.3 mmol) and 1,5 diaminopentane (0.9 mL, 8.00 mmol). Viscous oil, yield (4.30 g, 85%); IR (KBr): ν_{max} 3481, 3274 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.19 (m, 3H, ArH), 6.94 (m, 3H, ArH), 6.83 (m, 2H, ArH), 4.53 (br s, 2H, OH), 3.95 (s, 4H, CH_2Ar), 2.78 (t, $J = 7.5$ Hz, 4H, NCH_2), 1.64 (m, 4H, 2× CH_2), 1.35 (m, 2H, CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 160.9, 157.8, 135.0, 129.8, 120.4 119.5, 117.1, 116.9, 115.8, 114.1, 60.7, 50.6, 50.5, 46.7, 46.6, 30.6, 25.7, 25.6, 23.7; FABMS: *m/z* 315 $[M+H]^+$; Anal. Calcd for $C_{19}H_{26}N_2O_2$: C, 72.61: H, 8.28: N, 8.91. Found: C, 72.60: H, 8.26: N, 8.82.

4.4. Synthesis of compounds 31–45

4.4.1. Ethyl-3-butylamino-3-(3-chlorophenyl)-propionate (31). *Typical procedure*: To a magnetically stirred solution of 3-(3-chloro-phenyl)-acrylic acid ethyl ester (**25**, 2.0 g, 9.50 mmol) in ethanol was added butylamine (0.9 mL, 9.50 mmol) followed by the addition of DBU 20 mol%. The reaction mixture was stirred for 8 h at 80 °C, cooled and the solvent was evaporated under reduced pressure to give a crude mass.The latter was dissolved in ethyl acetate (65 mL) and washed with brine (2 × 20 mL) followed by water (2 × 25 mL). The organic layer dried (anhyd Na_2SO_4) was evaporated under reduced pressure to give a brown gum, which was chromatographed over SiO_2 column, using hexane/ethyl acetate (7:1) as eluent to give desired product **31** as viscous liquid. Yield (1.6 g, 60%); IR (KBr): ν_{max} 3338, 1731 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.33 (s, 1H, ArH); 7.23 (m, 3H, ArH), 4.07 (m, 3H, ArCH and OCH_2), 2.60 (t, $J = 6.02$ Hz, 2H, CH_2), 2.40 (m, 2H, NCH_2), 1.79 (s, 1H, NH), 1.40 (m, 4H, 2× CH_2); 1.24 (t, $J = 7.1$ Hz, 3H, OCH_2CH_3), 0.86 (t, $J = 6.9$ Hz, 3H, CH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.9, 145.6, 134.7, 130.7, 127.9, 127.6, 125.6, 60.9, 59.7, 47.6, 43.2, 32.5, 20.7, 14.5, 14.3; FABMS: *m/z* 284 $(M+H)^+$; Anal. Calcd for $C_{15}H_{22}ClNO_2$: C, 63.60; H, 7.77; N, 4.94. Found: C, 63.65; H, 7.80; N, 4.90.

4.4.2. Ethyl 3-octylamino-3-(3-chlorophenyl)-propionate (32). Obtained by reaction of 3-(3-chlorophenyl)acrylic acid ethyl ester (**25**, 2.00 g, 9.50 mmol) and octylamine (1.57 mL, 9.5 mmol) as above. Colourless oil, yield (2.24 g, 70%); IR (KBr): ν_{max} 3336, 1731 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30 (m, 4H, ArH), 4.08 (m, 3H, ArCH and OCH_2), 2.66 (m, 2H, NCH_2), 2.40 (m, 2H, CH_2CO–), 1.68 (br s, 1H, NH), 1.24 (m, 15H, 6× CH_2 and CH_3), 0.86 (t, $J = 6.9$ Hz, 3H, CH_3); ^{13}CNMR (50 MHz, $CDCl_3$): δ 171.9, 145.6, 134.7, 130.1, 127.9, 127.6, 125.6, 60.9, 59.7, 47.9, 43.3, 32.2, 31.3, 30.4, 29.8, 29.6, 27.6, 23.0, 14.5; FABMS: *m/z* 341 $(M+H)^+$; Anal. Calcd for $C_{19}H_{30}ClNO_2$: C, 67.25; H, 8.84; N, 4.12. Found: C, 67.27; H, 8.88; N, 4.10.

4.4.3. Ethyl 3-(3-chlorophenyl)-3-dodecylamino-propionate (33). Obtained by reaction of 3-(3-chlorophenyl)acrylic acid ethyl ester (**25**, 2.0 g, 9.50 mmol) and dodecylamine (2.18 mL, 9.5 mmol) gave compound **33** as colourless liquid, yield (2.6 g, 70%); IR (KBr): ν_{max} 3335, 1733 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.26 (m, 4H, ArH), 4.11 (m, 3H, ArCH and OCH_2), 2.61 (m, 2H, CH_2CO–), 2.41 (m, 2H, NCH_2), 1.73 (br s, 1H, NH), 1.24 (m, 23H, 10× CH_2 and CH_3), 0.87 (t, $J = 6.9$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.9, 145.6, 134.7, 130.1, 128.5, 127.9, 127.6, 125.6, 60.9, 59.7, 56.1, 47.9, 43.2, 41.4, 32.3, 30.4, 30.3, 30.2, 30.0, 29.7, 27.6, 23.0, 14.5; FABMS: *m/z* 396 $(M+H)^+$; Anal. Calcd for $C_{23}H_{38}Cl\ NO_2$: C, 69.87; H, 9.62; N, 3.54. Found: C, 69.82; H, 9.59; N, 3.59.

4.4.4. Ethyl 3-(3-chlorophenyl)-3-(pyrrolidin-1-yl)-propionate (34). Obtained by reaction of 3-(3-chloro-phenyl)-acrylic acid ethyl ester (**25**, 2.0 g, 9.50 mmol) and pyrrolidine (0.79 mL, 9.5 mmol). Colourless oil, yield (1.72 g, 65%); IR (KBr): ν_{max} 3447, 1732 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.22 (d, $J = 1.4$ Hz, 1H, ArH), 8.14 (dd, $J = 7.8$, 1.4 Hz, 1H, ArH), 7.70 (d, $J = 6.8$, 1H, ArH), 8.22 (two d, $J = 7.4$ Hz, 1H, ArH), 3.99 (q,

$J = 7.1$ Hz, 2H, OCH_2), 3.82 (dd, $J = 5.4$ Hz, 1H, ArCH), 3.07–2.37 (m, 6H, NCH_2, CH_2CO–), 1.85 (m, 5H, 2× CH_2, NH), 1.09 (t, $J = 7.0$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.6, 144.3, 134.4, 129.8, 127.9, 127.2, 66.3, 60.7, 52.5, 52.1, 41.9, 30.0, 23.6, 23.5, 14.3; FABMS *m/z* 282 $(M+H)^+$; Anal. Calcd for $C_{15}H_{20}$ Cl NO_2: C, 64.05; H, 7.11; N, 4.98. Found: C, 64.10; H, 7.06; N, 4.98.

4.4.5. Ethyl 3-benzylamino-3-(3-nitrophenyl)-propionate (35). Obtained by reaction of 3-(3-chloro-phenyl)-acrylic acid ethyl ester (**25**, 2.5 g, 1.19 mmol) and benzylamine (1.29 mL, 1.19 mmol). Viscous liquid, yield (2.50 g, 68%); IR (KBr): ν_{max} 3336, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.37–7.20 (m, 9H, ArH), 4.14–4.04 (m, 3H, ArCH and O–CH_2), 3.69–3.49 (m, 2H, ArCH_2), 2.75–2.55 (m, 2H, OCH_2), 1.89 (br s, 1H, NH), 1.65 (t, $J = 6.9$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.9, 145.6, 142.2, 134.7, 130.7, 129.5, 127.9, 127.6, 125.6, 122.6, 60.9, 59.7, 47.6, 43.2, 32.5, 20.7, 14.5, 14.3; FABMS: *m/z* 318 $(M+H)^+$; Anal. Calcd for $C_{18}H_{20}$ Cl NO_2: C, 68.13; H, 6.30; N, 4.41. Found: C, 68.17; H, 6.32; N, 4.44.

4.4.6. Ethyl 3-butylamino-3-(3-nitrophenyl)-propionate (36). Obtained by reaction of 3-(3-nitro-phenyl)-acrylic acid ethyl ester (**26**, 2.0 g, 9.04 mmol) and pyrrolidine (0.9 mL, 9.05 mmol) to give **36** as colourless oil. Yield (1.90 g, 65%); IR (KBr): ν_{max} cm^{-1}3338, 1731; ^1H NMR (200 MHz, $CDCl_3$): δ 8.24 (d, $J = 1.8$ Hz, 1H, ArH), δ 8.11 (dd, $J = 8.0$, 1.0 Hz, 1H, ArH), δ 7.70 (d, $J = 7.6$ Hz, 1H, ArH), δ 7.50 (dd, $J = 7.9$ Hz, 1H, ArH), 4.12–4.05 (m, 3H, ArCH and O–CH_2), 2.62–2.60 (m, 2H, OCH_2), 2.40–2.38 (m, 2H, NCH_2), 1.74 (br s, 1H, NH), 1.29–1.19 (m, 7H, 2× CH_2 and CH_3), 0.86 (t, $J = 6.9$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.9, 145.6, 134.7, 130.7, 127.9, 127.6, 125.6, 60.9, 59.7, 47.6, 43.2, 32.5, 20.7, 14.5, 14.3; FAB-MS: *m/z* 284 $(M+H)^+$; Anal. Calcd for $C_{15}H_{22}$Cl N_2O_4: C, 54.71; H, 6.68; N, 8.51. Found: C, 54.73; H, 6.69; N, 8.49.

4.4.7. Ethyl 3-(3-nitrophenyl)-3-octylamino-propionate (37). Obtained by reaction of 3-(3-nitro-phenyl)-acrylic acid ethyl ester (**26**, 2.00 g, 9.09 mmol) and octylamine (1.5 mL, 9.05 mmol). Viscous oil, yield (2.04 g, 70%); IR (KBr): ν_{max} cm^{-1}3336, 1731; ^1H NMR (200 MHz, $CDCl_3$): δ 8.23 (s, 1H, ArH), 8.10 (d, $J = 9.1$ Hz, 1H, ArH), 7.70 (d, $J = 7.7$ Hz, 1H, ArH), 7.50 (two d, $J = 7.8$ Hz, 1H, ArH), 4.21–4.05 (m, 3H, ArCH and O–CH_2), 2.69–2.61 (m, 2H, OCH_2), 2.42–2.38 (m, 2H, NCH_2), 1.74 (br s, 1H, NH), 1.30–1.18 (m, 15H, 6× CH_2 and CH_3), 0.86 (t, $J = 6.7$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, CDCl3): δ 171.5, 148.9, 146.6, 133.8, 129.8, 122.8, 122.5, 61.1, 59.5, 48.0, 43.1, 32.1, 30.4, 29.8, 29.6, 27.5, 23.0, 14.5, 14.4; FABMS: *m/z* 351 $(M+H)^+$; Anal. Calcd for $C_{19}H_{30}N_2O_4$: C, 65.14; H, 8.57; N, 8.00. Found: C, 65.19; H, 8.51; N, 8.00.

4.4.8. Ethyl 3-dodecylamino-3-(3-nitrophenyl)-propionate (38). Obtained by reaction of 3-(3-nitro-phenyl)-acrylic acid ethyl ester (**26**, 2.0 g, 9.0 mmol) and dodecylamine (2.08 mL, 9.05 mmol). Colourless oil, yield (2.45 g, 70%); IR (KBr): ν_{max} cm^{-1}3310, 1732; ^1H NMR (200 MHz, $CDCl_3$): δ 8.18 (m, 2H, ArH), 7.66 (m, 2H, ArH), 7.70 (d, $J = 7.6$ Hz, 1H, ArH), 7.48 (two d, $J = 7.8$ Hz, 1H, ArH), 3.97 (q, $J = 7.1$ Hz, 2H, OCH_2), 8.11 (two d, $J = 5.4$ Hz, 1H, ArC*H*), 3.07–2.37 (m, 6H, NCH_2, –CH_2CO–), 1.77 (m, 5H, NH, pyrroldine CH_2), 1.09 (t, $J = 7.1$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, CDCl3): δ 171.9, 148.9, 145.9, 133.7, 129.7, 122.8, 122.5, 61.0, 59.6, 48.0, 43.1, 39.8, 37.3, 32.2, 31.2, 30.4, 29.9, 29.7, 27.5, 27.3, 26.2, 23.0, 14.4; FABMS *m/z* 407 $(M+H)^+$; Anal. Calcd for $C_{23}H_{38}N_2O_4$: C, 67.98; H, 9.35; N, 6.89. Found: C, 67.82; H, 9.33; N, 6.82.

4.4.9. Ethyl 3-(3-nitrophenyl)-3-(pyrrolidin-1-yl)-propionate (39). Obtained by reaction of 3-(3-nitro-phenyl)-acrylic acid ethyl ester (**26**, 2.0 g, 9.0 mmol) and pyrrolidine (0.75 mL, 9.05 mmol) gave compound **39** as colourless liquid yield (1.70 g, 65%); IR (KBr): ν_{max} cm^{-1}3450, 1669; ^1H NMR (200 MHz, $CDCl_3$): δ 8.22 (s, 1H, ArH), 8.11 (d, $J = 8.1$ Hz, 1H, ArH), 7.70 (d, $J = 7.6$ Hz, 1H, ArH), 7.48 (two d, $J = 7.8$ Hz, 1H, ArH), 3.97 (q, $J = 7.1$ Hz, 2H, OCH_2), 8.11 (two d, $J = 5.4$ Hz, 1H, ArC*H*), 3.07–2.37 (m, 6 H, NCH_2, –CH_2CO–), 1.77 (m, 5H, NH, pyrroldine CH_2), 1.09 (t, $J = 7.1$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.9, 145.6, 134.7, 130.7, 127.9, 127.6, 125.6, 60.9, 59.7, 47.6, 43.2, 32.5, 20.7, 14.5, 14.3; FABMS *m/z* 293 $(M+H)^+$; Anal. Calcd for $C_{15}H_{20}N_2O_4$: C, 61.64; H, 6.84; N, 9.58. Found: C, 61.59; H, 6.80; N, 9.60.

4.4.10. Ethyl 3-benzylamino-3-(3-nitrophenyl)-propionate (40). Obtained by reaction of 3-(3-nitro-phenyl)-acrylic acid ethyl ester (**26**, 2.00 g, 9.0 mmol) and benzylamine (1.00 mL, 9.09 mmol) gave compound **40** as colourless liquid in (2.0 g, 68%) yield; IR (KBr): ν_{max} cm^{-1}3336, 1730; ^1H NMR (200 MHz, $CDCl_3$): δ 8.27 (d, $J = 1.4$ Hz, 1H, ArH), 8.13 (dd, $J = 1.0$ Hz, 8.1 Hz, 1H, ArH), 7.73 (d, $J = 7.7$ Hz, 1H, ArH), 7.33 (m, 6H, ArH), 4.23 (two d, $J = 5.6$ Hz, 1H, ArC*H*), 4.11 (q, $J = 7.1$ Hz, 2H, OCH_2), 3.64 and 3.59 (d, $J = 13.1$ Hz, 2H, NHC*H*$_2$Ph), 2.72 (m, 2H, –CH_2CO–), 1.95 (br s, 1H, NH); 1.23 (t, $J = 7.1$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, CDCl3): δ 171.9, 145.6, 140.0, 133.9, 129.9, 128.8, 128.4, 127.5, 127.4, 125.2, 125.3, 123.0, 122.7, 61.1, 58.7, 51.8, 43.1, 14.5; FABMS: *m/z* 329 $(M+H)^+$; Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.85; H, 6.09; N, 8.53. Found: C, 65.80; H, 6.11; N, 8.55.

4.4.11. Ethyl 3-(4-nitrophenyl)-3-octylamino-propionate (41). Obtained by reaction of 3-(4-nitro-phenyl)-acrylic acid ethyl ester (**27**, 2.0 g, 9.09 mmol) and octylamine (1.5 mL, 9.05 mmol) as colourless oil. yield (2.0 g, 65%); IR (KBr): ν_{max} cm^{-1}3336, 1731; ^1H NMR (200 MHz, $CDCl_3$): δ 8.18 and 7.54 (d, $J = 8.7$ Hz, e 4H, ArH), 4.20–4.05 (m, 3H, ArCH and O–CH_2), 2.67–2.30 (m, 4H, NCH_2, and –CH_2CO–), 1.70 (br s, 1H, NH), 1.25 (m, 15H, 6× CH_2 and OCH_2CH_3), 0.86 (t, $J = 6.6$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.9, 145.6, 134.7, 130.7, 127.9, 127.6, 125.6, 60.96, 59.7, 47.6, 43.2, 32.5, 31.8, 31.0, 30.2, 23.5, 20.7, 14.5, 14.3; FABMS: *m/z* 351 $(M+H)^+$; Anal. Calcd for $C_{19}H_{30}N_2O_4$: C, 65.14; H, 8.57; N, 8.00. Found: C, 65.19; H, 8.51; N, 8.00.

4.4.12. Ethyl 3-dodecylamino-3-(4-nitrophenyl)-propionate (42). Obtained by reaction of 3-(4-nitro-phenyl)-acrylic acid ethyl ester (**27**, 2.00 g, 9.0 mmol) and dodecylamine (2.08 mL, 9.05 mmol) as colourless oil, yield (2.45 g, 70%); IR (KBr): $v_{\max}$ cm^{-1}3335, 1733; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.21–7.51 (m, 4H, ArH), 4.18–4.09 (m, 3H, ArCH and O–CH_2), 2.66–2.61 (m, 2H, OCH_2), 2.41–2.35 (m, 2H, NCH_2), 1.72 (br s, 1H, NH), 1.33–1.15 (m, 23H, 10× CH_2 and CH_3), 0.87 (t, $J = 6.7$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.5, 151.2, 147.7, 130.5, 128.4, 124.1, 123.8, 115.2, 61.1, 59.6, 48.5, 48.1, 43.0, 32.2, 31.5, 30.4, 30.0, 29.9, 29.7, 27.5, 23.0, 14.5, 14.4; FABMS: *m/z* 407 $(M+H)^+$; Anal. Calcd for $C_{23}H_{38}N_2O_4$: C, 67.98; H, 9.35; N, 6.89. Found: C, 67.82; H, 9.33; N, 6.82.

4.4.13. Ethyl 3-dodecylamino-3-(2-nitrophenyl)]-propionate (43). Obtained by reaction of 3-(2-nitro-phenyl)-acrylic acid ethyl ester (**28**, 2.0 g, 9.0 mmol) and dodecylamine (2.08 mL, 9.05 mmol) as colourless oil, yield (2.50 g, 70%); IR (KBr): $v_{\max}$ cm^{-1}3344, 1729; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.82–7.42 (m, 4H, ArH), 4.31–4.11 (m, 3H, ArCH and O–CH_2), 2.74–2.79 (m, 2H, OCH_2), 2.54–2.52 (m, 2H, NCH_2), 1.85 (br s, 1H, NH), 1.32–1.16 (m, 23H, 10× CH_2 and CH_3), 0.87 (t, $J = 6.6$ Hz, 3H, CH_3); δ; FABMS: *m/z* 407 $(M+H)^+$; Anal. Calcd for $C_{23}H_{38}N_2O_4$: C, 67.98; H, 9.35; N, 6.89. Found: C, 67.82; H, 9.33; N, 6.82.

4.4.14. Ethyl 3-(4-fluorophenyl)-3-octylamino-propionate (44). Obtained by reaction of 3-(4-floro-phenyl)-acrylic acid ethyl ester (**29**, 2.0 g, 1.03 mmol) and octylamine (1.7 mL, 1.03 mmol). Colourless oil yield (2.3 g, 70%); IR (KBr): $v_{\max}$ cm^{-1}3453, 1727; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.30 (dd, $J = 6.5$ Hz, 2.0 Hz, 2H, ArH), 7.03 (dd, $J = 2.0$ Hz, 8.7 Hz, 2H, ArH), 4.14–4.01 (m, 3H, ArCH and O–CH_2), 2.66–2.57 (m, 2H, OCH_2), 2.37–2.25 (m, 2H, NCH_2), 1.75 (br s, 1H, NH), 1.31–1.12 (m, 15H, 6× CH_2 and OCH_2CH_3), 0.86 (t, $J = 6.7$ Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.1, 164.8, 159.9, 139.0, 129.0, 128.8, 115.8, 60.8, 59.4, 47.9, 43.4, 32.2, 30.4, 29.8, 29.6, 27.6, 23.0, 14.5, 14.4; FABMS: *m/z* 323 $(M+H)^+$ Anal. Calcd for $C_{19}H_{30}FNO_2$: C, 70.80; H, 9.31; N, 4.34. Found: C, 70.75; H, 9.39; N, 4.39.

4.4.15. Ethyl 3-octylamino-3-phenyl-propionate (45). Obtained by reaction of 3-(phenyl)-acrylic acid ethyl ester (**30**, 2.0 g, 1.13 mmol) and octylamine (1.8 mL, 1.13 mmol). Colourless oil, yield (2.3 g, 70%), IR (KBr): $v_{\max}$ 3335, 1733 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.31 (m, 5H, ArH), 4.05 (m, 3H, ArC*H* and O–CH_2), 2.63 (m, 2H, NCH_2), 2.44–2.36 (m, 2H, –CH_2CO–), 1.68 (br s, 1H, NH), 1.23 (m, 15H, CH_2 and CH_3), 0.86 (t, $J = 6.7$ Hz, 3H, CH_2CH_3), ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.0, 143.3, 128.8, 127.6, 127.3, 123.2, 122.8, 115.6, 60.4, 60.1, 47.9, 43.4, 32.2, 30.5, 30.0, 29.9, 29.6, 28.5, 27.6, 23.0, 14.3, 14.2; FABMS: *m/z* 306 $(M+H)^+$; Anal. Calcd for $C_{19}H_{31}NO_2$: C, 75.00; H, 9.86; N, 4.60. Found: C, 75.09; H, 9.88; N, 4.55.

4.5. Synthesis of compounds 46–48

4.5.1. 3-(3-Chlorophenyl)-3-octylaminopropan-1-ol (46). *Typical procedure*: To a magnetically stirred slurry of $LiAlH_4$ (0.030 g, 0.81 mmol) in anhyd THF (10 mL) at 0 °C, the above compound **32** (0.20 g, 0.58 mmol) dissolved in THF (5 mL) was slowly added and stirring continued for 4 h at ambient temperature. Reaction mixture was neutralized by saturated aq solution of Na_2SO_4 at 0 °C and filtered over Celite pad. The filtrate, so obtained, was evaporated under reduced pressure to give a crude mass. The latter was dissolved in chloroform (65 mL) and washed with saturated solution of NaCl (2 × 20 mL) followed by water (2 × 25 mL), dried (anhyd Na_2SO_4). The organic layer was evaporated under reduced pressure to get a crude product, which was chromatographed over SiO_2 column using chloroform: methanol, (98:2) as eluent to afford **46** as viscous oil, yield (0.104 g, 60%); IR (KBr): $v_{\max}$ 3679, 3405 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.23 (m, 4H, ArH), 3.79 (m, 3H, ArC*H* and C*H*$_2$OH), 2.47 (br s, 1H, OH), 2.44 (t, $J = 7.0$ Hz, 2H, NCH_2), 1.84 (m, 2H, CH_2), 1.54–1.23 (m, 12H, 6 xCH_2), 0.86 (t, $J = 6.4$ Hz, 3H, CH_3); FABMS: *m/z* 298 $(M+H)^+$; Anal. Calcd for $C_{17}H_{28}ClNO$: C, 68.68; H, 9.42; N, 4.71 Found: C, 68.70; H, 9.46; N, 4.77.

4.5.2. 3-(3-Nitrophenyl)-3-octylamino-propan-1-ol (47). Obtained by reduction of the above compound **37** (0.20 g, 0.58 mmol) with $LiAlH_4$ (0.030 g, 0.81 mmol) as colourless oil. Yield (0.113 g, 65%); IR (KBr): $v_{\max}$ 3428, 1530 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.15 (m, 2H, ArH), 7.60 (m, 2H, ArH), 3.97 (m, H, ArC*H*), 3.79 (m, 2H, OC*H*$_2$), 2.77 (br s, 1H, OH), 2.40 (m, 2H, NCH_2), 1.68 (br s, 1H, NH), 1.23 (s, 12H, CH_2's), 0.79 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (50 MHz, CDCl3): δ 148.9, 146.0, 133.1, 130.0, 122.7, 121.9, 63.5, 62.3, 47.7, 39.1, 32.1, 30.3, 29.7, 29.5, 27.5, 23.0, 15.6, 14.4; FABMS: *m/z* 309 $(M+H)^+$; Anal. Calcd for $C_{17}H_{28}N_2O_3$: C, 66.23; H, 9.09; N, 9.09. Found: C, 66.28; H, 9.11; N, 9.15.

4.5.3. 3-Dodecylamino-3-(3-nitrophenyl)]-propan-1-ol (48). Obtained by reduction of compound **38** (0.20 g, 0.49 mmol) with $LiAlH_4$ (0.025 g, 0.67 mmol) as above. Colourless gum, yield (0.105 g, 60%);; IR (KBr): $v_{\max}$ cm^{-1}3402, 1531; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.18 (m, 2H, ArH), 7.68–7.28 (m, 2H, ArH), 4.13–3.82 (m, 3H, ArCH, O–CH_2), 3.39 (m, 2H, NHC*H*$_2$), 2.91 (br s, 1H, OH), 2.44 (m, 2H, CH_2), 1.40–1.12 (m, 23H, NH, 11× CH_2), 0.87 (t, $J = 6.3$ Hz, 3H, CH_3); FABMS: *m/z* 365 $(M+H)^+$; Anal. Calcd for $C_{21}H_{36}N_2O_3$: C, 69.23; H, 9.89; N, 7.69. Found: C, 69.21; H, 9.88; N, 7.69.

5. Biological activity

5.1. Activity against *M. tuberculosis H$_{37}$Ra* strain[14]

All the compounds synthesized were evaluated for their efficacy against *M. tuberculosis H$_{37}$Ra* at concentration ranging from 100 μg/mL to 1.56 μg/mL using twofold dilutions in the initial screen. Log phase culture of *M. tuberculosis* H_{37}*Ra* is diluted so as to give final $OD_{550\ nm}$ of 0.05 in Sauton's medium. In 96-well white plate 190 µl of culture is dispensed in each well. A dimethyl-sulfoxide (DMSO) solution of test compounds is dispensed to 96-well plates so as to make final test concentration 25 µg/mL (5 µg test compound is dispensed in 10 µl DMSO). Then the plate is incubated at 37 °C/5% CO_2 for 5 days. On fifth day 15 µl Alamar blue solution is added to the each well of plate. The plate is again incubated overnight at 37 °C/5% CO_2 incubator. The fluorescence is read on BMG polar star with excitation frequency at 544 nm and emission frequency at 590 nm. The compounds, which were found active (>90% inhibition as compared with control) at this concentration, are then tested at 6 serial dilutions starting from 50 to 1.56 µg/mL.

5.2. Activity against *M. tuberculosis $H_{37}Rv$* strain[15]

Drug susceptibility and determination of MIC of the test compounds/drugs against *M. tuberculosis $H_{37}Rv$* was performed by agar microdilution method where twofold dilutions of each test compound were added into 7H10 agar supplemented with OADC and organism. A culture of *M. tuberculosis $H_{37}Rv$* growing on L-J medium was harvested in 0.85% saline with 0.05% Tween 80. A suspension of 1 µg/mL concentration of extracts/compounds was prepared in DMSO. This suspension was added to (in tubes) 7H10 Middle brook's medium (containing 1.7 mL medium and 0.2 mL OADC supplement) at different concentrations of compound keeping the volume constant, that is, 0.1 mL. Medium was allowed to cool keeping the tubes in slanting position. These tubes were then incubated at 37 °C for 24 h followed by streaking of *M. tuberculosis $H_{37}Rv$* (5×10^4 bacilli per tube). These tubes were then incubated at 37 °C. Growth of bacilli was seen after 30 days of incubation. Tubes having the compounds were compared with control tubes where medium alone was incubated with *$H_{37}Rv$*. The concentration at which complete inhibition of colonies occurred was taken as minimum inhibitory concentration (MIC) of test compound.

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