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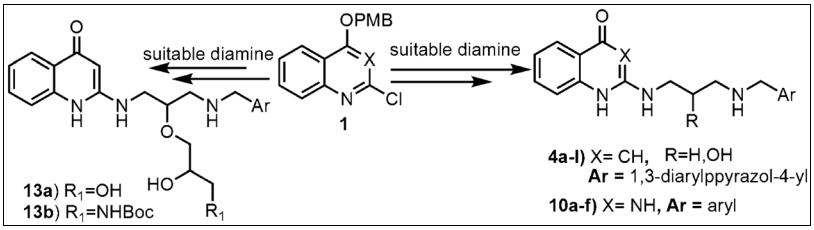
Received April 12, 2011
DOI 10.1002/jhet.1040
View this article online at wileyonlinelibrary.com.



Several new quinolines and quinazolines (**4, 10, 13**) have been synthesized from cheap and readily available chemicals through a series of simple chemical transformations. Most of the synthesized compounds have been evaluated for antibacterial activity against Gram positive and Gram negative strains. Some of the synthesized compounds displayed interesting activity but not very promising for further development.

J. Heterocyclic Chem., **49**, 1391 (2012).

INTRODUCTION

Quinoline being present in the core structure of many natural [1,2] and biologically active products [3,4] has been attracting considerable interests of synthetic and medicinal chemists. Quinoline derivatives particularly containing 4-quinolones (Figure 1) in their molecular structure have been effectively used as antibacterial agents for past 35 years. The antibacterial activity of quinolones having 3-carboxylic acid functionality display by inhibiting nucleic acid synthesis [5] while 2-amino-4-quinolone [6] act by inhibiting protein synthesis [7] in bacteria (Figure 1). The second class of quinolones has recently been discovered [8] as inhibitors of methionyl-tRNA synthetase enzyme which is a promising antibacterial drug target. This class of compounds have also been reported [9,10] to display significant antibacterial activity in the strains of *Staphylococcus areus*, *Entrococcus faecalis* and *Entrococcus faecium*. However, the emergence of drug resistance against existing antibiotics still demands for the synthesis of new antibacterial agents. Herein, we report synthesis and antibacterial activities of pyrazol-4-yl linked quinolones compounds (**4),** aryl quinazolone compounds (**10**), and quinolone-arene **(13)**. We envisioned synthesizing quinolones-pyrazoles hybrid structures because quinazolone [8] and pyrazole [11] are known for antibacterial properties but their hybrid structures have not been evaluated for antibacterial activity.

RESULTS AND DISCUSSION

Chemistry. The targets compounds **4a-l** were synthesized in three step by amination of 2-chloro-4-(4-methoxybenzyloxy) quinoline **1** with excess of 1,3-diaminopropane followed by deprotection of 4-methoxybenzyl group and reductive alkylation of the resulting intermediates 4-quinolones **3** with 1,3-diaryl-1*H*-pyrazole-4-carbaldehydes (Scheme 1). The precursor **1** was prepared by refluxing aniline and malonic acid in phosphorousoxy chloride followed by *para*-methoxybenzyl (PMB) protection in basic condition according to the literature procedures [8], [12]. The other precursor 1,3-diaryl-1*H*-pyrazole-4-carbaldehydes **3'** were prepared [14] in two step from condensation reaction of arylmethylketones and phenylhydrazine in ethanol followed by cyclization of phenylhydrazone with phosphorousoxy chloride in excellent yields.

Quinazolone **10a–f** the other class of target compounds were synthesized from the reaction of 2-chloro-4-quinazolone (**8**) and 1,3-diaminopropane followed by reductive alkylation with suitable aldehydes. The intermediate **8** was synthesized in three steps [13] (Scheme 2).

Quinolone derivative **(13a)** has been synthesized in three steps by nucleophilic substitution reaction of 2-chloro-4-(4-methoxybenzyloxy)quinoline (**1**) with diamine (**18**) followed by deprotection of the 4-methoxybenzyloxy (PMB) group to provide 4-quinolone derivative **12a,** which on reductive alkylation with 3,4-dichlorobenzaldehyde in alkaline medium afforded compound **13a** (Scheme 3). Similarly compound **13b** was obtained from reaction of 2-chloroquinoline **1** and diamine **22** followed by deprotection of PMB group and reductive alkylation with 3,4-dichlorobenzaldehyde (Scheme 3).

Diamine (**18**) required for preparation of compound **13a** has been synthesized from 1,3-dibromopropan-2-ol

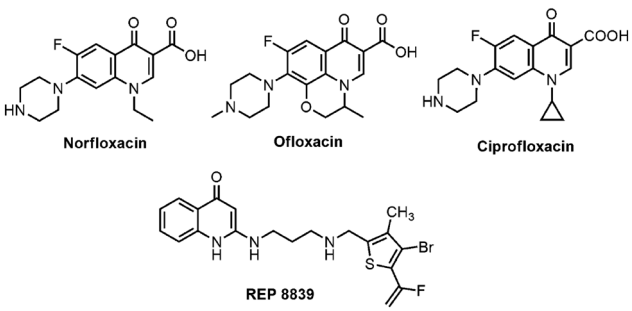
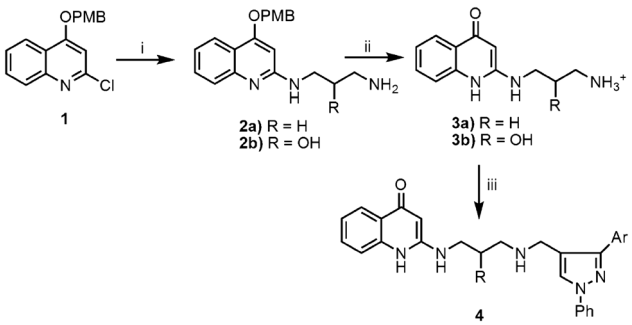


Figure 1. Structure of quinolone drugs.

(Scheme 4). 1,3-Dibromopropan-2-ol (**14**) on treatment with sodium azide in DMF at 80°C provided diazide **15** which on allylation with allyl bromide in presence cesium hydroxide afforded compound **16**. The olefin of compound **16** was conveniently transformed into dihydroxy derivative (**17**) which on azide reduction with 10% Pd-C provided diamine **18** as racemic mixture in overall very good yield (Scheme 4).

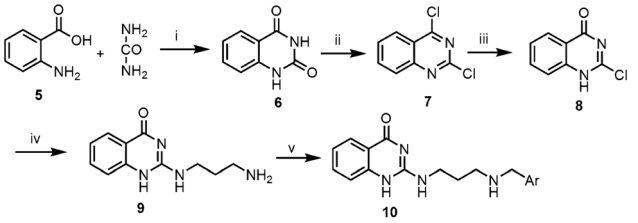
The intermediate **16** was further transformed into the diamine **22** (Scheme 5). Compound **16** was converted to epoxide **19** with mCPBA which on aminolysis with aqueous ammonia followed by Boc-protection afforded intermediate **21**. Compound **21** on Pd-catalyzed hydrogenation in hydrogen atmosphere formed diamine **22** in quantitative yield (Scheme 5).

Scheme 1. Reagents and conditions: (i) **2a:** 1,3-diaminopropane, 90°C, 48 h, yield 72%; **2b:** 1,3-diaminopropan-2-ol, K_2CO_3, DMSO, 80°C, 48 h, yield 55%; (ii) 20% TFA-DCM, rt, 2 h; (iii) 1,3-diaryl-1*H*-pyrazole-4-carbaldehydes **3'**, MeONa, $NaCNBH_3$, MeOH, 50°C, 6 h.



4	Ar	R	Yield (%)
a	C_6H_5	H	56
b	4-$H_3CC_6H_4$	H	52
c	4-$H_3COC_6H_4$	H	48
d	4-ClC_6H_4	H	56
e	4-BrC_6H_4	H	54
f	2-thienyl	H	50
g	C_6H_5	OH	52
h	4-$H_3CC_6H_4$	OH	55
i	4-$H_3COC_6H_4$	OH	51
j	4-FC_6H_4	OH	53
k	4-ClC_6H_4	OH	57
l	2-thienyl	OH	54

Scheme 2. Reagents and conditions: (i) Fuse, 190°C, 1 h, yield 95%; (ii) $POCl_3$, reflux, 5 h, yield 92%; (iii) 1N NaOH, rt, 3 h, yield 92%; (iv) 1,3-diaminopropane, 70°C, 48 h, yield 80%; (v) suitable aldehyde, MeONa, $NaCNBH_3$, MeOH, 50°C, 6 h.



10	Ar	Yield (%)
a	4-ClC_6H_4	56
b	3,4-$Cl_2C_6H_4$	54
c	4-BrC_6H_4	55
d	4-pyridyl	58
e	2-thienyl	52
f	1-naphthyl	55

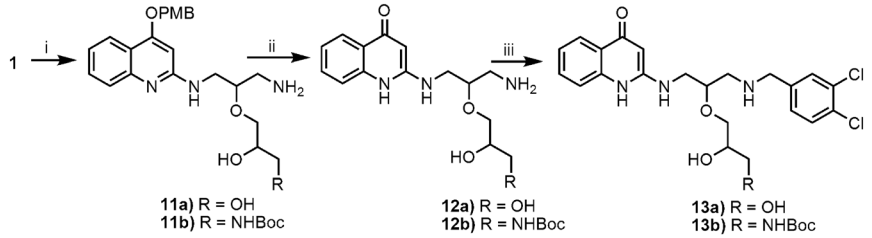
Biology. Antibacterial activity of all the synthesized compounds was performed using microdilution method (CLSI M7-A8 2009) against three Gram positive strains (*S. aureus* ATCC 29213, Methicillin resistant *S. aureus,* Vancomycin resistant *Enterococcus faecalis*), and two Gram negative strains (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853), Table 1. Bacterial suspensions were prepared in sterile normal saline from 24 h grown culture. The Minimum Inhibitory Concentration (MIC) was performed in Muller Hinton Broth (MHB; BD Biosciences). Two-fold serial dilutions of samples were prepared in MHB in 100 μL volume in a 96 well U bottom microtiter plates (Tarson, Mumbai, India). The final concentration of the samples ranged from 0.5 to 256 μg/mL. The turbidity of bacterial suspensions was adjusted to 0.5 McFarland ($\sim 1.5 \times 10^8$ CFU/mL), which was further diluted in MHB and, a 100-μL volume of this diluted inoculum was added to each well of the plate, resulting in a final inoculum of 5×10^6 CFU/mL. The plates were incubated at 37°C for 24 h and were read visually. The minimum concentration of the sample showing no turbidity was recorded as MIC.

These compounds were also evaluated against *Candida albicans* and *Aspergillus fumigatus* for antifungal activity but none of these compounds displayed significant activity.

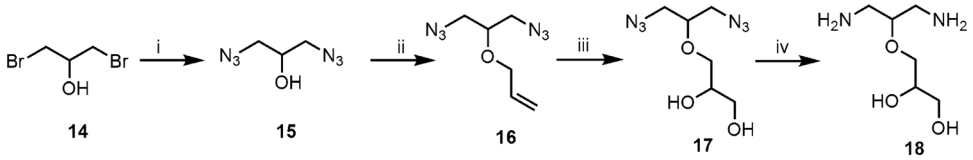
EXPERIMENTAL

***N^1*-(4-(4-Methoxybenzyloxy)quinolin-2-yl)propane-1,3-diamine (2a).** A mixture of **1** (15.0 g, 50 mmol) and 1,3-diaminopropane (20 mL) was stirred at 80–90°C for 48 h. The excess of 1, 3-diaminopropane was evaporated and crude product obtained was purified on silica gel column chromatography using CH_2Cl_2/MeOH/NH_3 sol (90:10:0.5) as eluent. ^{1}H NMR (CD_3OD, 300 MHz) δ 1.84–1.92 (m, 2H, CH_2), 2.79 (t, J = 7.2 Hz, 2H, NCH_2), 3.32 (t, J = 7.2 Hz, 2H, NCH_2), 3.84 (s, 3H, OCH_3), 5.09 (s, 2H, OCH_2),

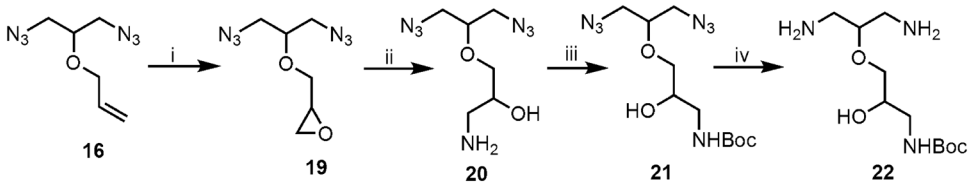
Scheme 3. Reagents and conditions: (i) **11a:** Compound **18**, K_2CO_3, DMSO, 80°C, 48 h; yield 48%; **11b:** Compound **22**, K_2CO_3, DMSO, 80°C, 48 h; yield 52%; (ii) 10% Pd-C, MeOH, rt, 1 h, yield quantitative; (iii) 3,4-Dichlorobenzaldehyde, MeONa, $NaCNBH_3$, MeOH, 50°C, 6 h; yield **11a:** 48%; **11b:** 52%.



Scheme 4. Reagents and condition: (i) NaN_3, DMF, 24 h, 80°C, yield quantitative; (ii) Allyl iodide, $CsOH{\cdot}H_2O$, TBAI, 4Å MS, CH_3CN, 48, rt, yield 80%; (iii) OsO_4, NMO, acetone, H_2O, 16 h, rt, yield 66%; (iv) 10% Pd-C, MeOH, rt, yield quantitative.



Scheme 5. Reagents and condition: (i) mCPBA, DCM, 3 h, rt, yield 80%; (ii) 28% aq. NH_3, $EtOH/H_2O$ (1:1), 2 h, rt, yield 78%; (iii) $(Boc)_2O$, DCM, 2 h/rt, yield 90%; (iv) 10% Pd-C, EtOH, rt, yield quantitative.



6.11 (s, 1H, ArH), 6.90 (d, J = 8.58 Hz, 2H, ArH), 7.14–7.18 (m, 1H, ArH), 7.38 (d, J = 8.58 Hz, 2H, ArH), 7.48–7.54 (m, 1H, ArH), 7.58–7.60 (m, 1H, ArH), 8.01–8.04 (m, 1H, ArH).

1-Amino-3-[4-(4-methoxybenzyloxy) quinolin-2-yl-amino] propan-2-ol (2b). A mixture of **1** (15.0 g, 50 mmol) and 2-hydroxy-1,3-diaminopropane (22.5 g, 250 mmol) was stirred in DMSO (80 mL) at 80°C in presence of potassium carbonate (8.3 g, 60 mmol) for 48 h. The reaction mixture was poured into distilled water (50 mL) and extracted from ethyl acetate (25 mL × 3), dried over sodium sulfate, and evaporated. The solid obtained was purified on silica gel column using $CH_2Cl_2/MeOH/NH_3$ sol (90:10:0.5) as eluent. White solid; mp 133–135°C, IR (KBr) ν 3336 cm^{-1} (OH); MS(FAB) m/z 354 (MH^+, 30%); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.48–3.59 (m, 2H, NCH_2), 3.64–3.69 (m, 2H, NCH_2), 3.73–3.76 (m, 1H, CH), 3.88 (s, 3H, OCH_3), 5.09 (s, 2H, OCH_2), 6.37 (s, 1H, ArH), 6.94 (d, J = 8.70 Hz, 2H, ArH), 7.15–7.20 (m, 1H, ArH), 7.38 (d, J = 8.70 Hz, 2H, ArH), 7.48–7.53 (m, 1H, ArH), 7.58–7.61 (m, 1H, ArH), 7.96–7.99 (m, 1H, ArH).

General procedure for the synthesis of 2-(3-((3-aryl-1-phenyl-1*H*-pyrazol-4-yl)methylamino)propylamino)quinolin-4(1*H*)-one (4a-f). A solution of *N*'-(4-(4-methoxybenzyloxy) quinolin-2-yl) propane-1,3-diamine **2a** (337 mg, 1 mmol) was stirred in 20% TFA-DCM (10 mL) for 2 h at room temperature. TFA was evaporated under reduced pressure and quinolin-4-one (**3a**) thus obtained was dissolved in dry methanol (10 mL), acetic acid (0.1 mL) was added at room temperature followed by 0.5 M MeONa solution in methanol (1.0 mmol). The resulting reaction mixture was stirred for 15 min at room temperature then 1-phenyl-3-aryl-1*H*-pyrazole-4-carbaldehyde **3'** (1.0 mmol) was added, stirred at 50°C for 1 h. A solution of $NaCNBH_3$ (1.5 mmol) in MeOH (5 mL) was added dropwise and stirred again for 6 h at 50°C. Methanol was evaporated under reduced pressure and crude product thus obtained was purified on silica gel column using $DCM/MeOH/NH_3$ sol (95:5:0.5) as eluent.

2-(3-((1,3-Diphenyl-1*H*-pyrazol-4-yl)methylamino)propylamino) quinolin-4(1*H*)-one (4a). Solid; mp 210–212°C; IR (KBr) ν 3340 (NH), 1646 cm^{-1} (CO); MS (FAB) m/z 450 (MH^+, 50), 329 (10), 233 (25); ^1H NMR ($CDCl_3$, 300 MHz), δ 1.66 (m, 2H, CH_2), 2.63 (t, J = 6.4 Hz, 2H, CH_2), 3.16-3.18 (m, 2H, CH_2), 3.72 (s, 2H, CH_2), 5.58 (s, 1H, ArH), 6.79–6.80 (m, 1H, ArH), 7.06–7.20 (m, 3H, ArH), 7.24–7.38 (m, 4H, ArH), 7.63–7.72 (m, 5H, ArH), 7.88 (s, 1H, Pyrazolyl), 8.16 (d, J = 1H, ArH); Anal. Calcd for $C_{28}H_{27}N_5O$: C, 74.81; H, 6.05; N, 15.58. Found: C, 74.94; H, 6.20; N, 15.50.

2-(3-((1-Phenyl-3-p-tolyl-1*H*-pyrazol-4-yl)methylamino) propylamino)quinolin-4(1*H*)-one (4b). Solid; mp 220–222°C; IR (KBr) ν 3350 (NH), 1656 cm^{-1} (CO); MS (FAB) m/z 464 (MH^+, 50), 329 (10), 233 (25); ^1H NMR ($CDCl_3$, 300 MHz), δ 1.64 (m, 2H, CH_2), 2.30 (s, 3H, Me), 2.66 (t, J = 6.4 Hz, 2H, CH_2), 3.18–3.19 (m, 2H, CH_2), 3.72 (s, 2H, NCH_2), 5.56 (s, 1H, ArH), 6.79–6.80 (m, 1H, ArH), 7.06–7.20 (m, 3H, ArH), 7.24–7.38 (m, 3H, ArH), 7.63–7.72 (m, 5H, ArH), 7.88 (s, 1H, Pyrazolyl), 8.16 (d, J = 8.10 Hz, 1H, ArH); Anal. Calcd for

Table 1

Antibacterial activity (MIC) of the synthesized compounds.

S. No	Compounds (4, 10, 13)	MIC (μg/mL)				
		S. aureus ATCC 29213	MRSA 15187	VRE	*E. coli* ATCC 25922	*P. aeruginosa* ATCC 27853
1	**4a**	**32**	**64**	**32**	>256	>256
2	**4b**	**32**	**32**	**32**	>256	>256
3	**4c**	Nil	Nil	Nil	Nil	Nil
4	**4d**	Nil	Nil	Nil	Nil	Nil
5	**4e**	**32**	**32**	**32**	>256	>256
6	**4f**	Nil	Nil	Nil	Nil	Nil
7	**4g**	**128**	**256**	**256**	>256	>256
8	**4h**	Nil	Nil	Nil	Nil	Nil
9	**4i**	**64**	**128**	**128**	>256	>256
10	**4j**	**64**	**128**	**128**	>256	>256
11	**4k**	Nil	Nil	Nil	Nil	Nil
12	**4l**	Nil	Nil	Nil	Nil	Nil
13	**10a**	**128**	**128**	**128**	>256	>256
14	**10b**	**16**	**16**	**16**	>256	>256
15	**10c**	**64**	**64**	**64**	>256	>256
16	**10d**	Nil	Nil	Nil	Nil	Nil
17	**10e**	Nil	Nil	Nil	Nil	Nil
18	**10f**	Nil	Nil	Nil	Nil	Nil
19	**13a**	ND	ND	ND	ND	ND
20	**13b**	ND	ND	ND	ND	ND
21	**Ciprofloxacin**	0.25	16	32	0.03	0.06

Nil, indicates insignificant activity; NT, indicates not determined; Ciprofloxacin, standard drug.

$C_{29}H_{29}N_5O$: C, 75.14; H, 6.31; N, 15.11. Found: C, 75.20; H, 6.19; N, 15.22.

2-(3-((3-(4-Methoxyphenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylamino)propylamino)quinolin-4(1*H*)-one (4c). Solid; mp 234-236°C; IR (KBr) ν 3431 (NH), 1637 cm^{-1} (CO); MS (FAB) *m/z* 480 (MH^+, 70), 460 (20), 329 (60); ^1H NMR ($CDCl_3$, 300 MHz), δ 1.68 (m, 2H, CH_2), 2.64 (t, *J* = 6.4 Hz, 2H, CH_2), 3.18-3.19 (m, 2H, CH_2), 3.68 (s, 2H, CH_2), 3.70 (s, 3H, OCH_3), 5.61 (s, 1H, ArH), 6.87–6.89 (m, 3H, ArH), 7.06–7.35 (m, 4H, ArH), 7.61–7.67 (m, 4H, ArH), 7.84 (s, 1H, Pyrazolyl), 8.16 (d, *J*=8.1 Hz, 1H, ArH); Anal. Calcd for $C_{29}H_{29}N_5O_2$: C, 72.63; H, 6.10; N, 14.60. Found: C, 72.52; H, 6.22; N, 14.38.

2-(3-((3-(4-Chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylamino)propylamino)quinolin-4 (1*H*)-one (4d). Solid; mp 216–218°C; IR (KBr) ν 3436 (NH), 1639 cm^{-1} (CO); MS (FAB) *m/z* 484 (MH^+, 50), 463 (20), 329 (10); ^1H NMR (DMSO-d_6, 300 MHz), δ 1.75–1.79 (m, 2H, CH_2), 2.71 (t, *J* = 6.4 Hz, 2H, CH_2), 3.28-3.35 (m, 2H, CH_2), 3.74 (s, 2H, CH_2), 5.31 (brs, 1H, NH), 5.76 (s, 1H, ArH), 6.46 (brs, 1H, NH), 7.08–7.13 (m, 1H, ArH), 7.29–7.33 (m, 2H, ArH), 7.40–7.52 (m, 5H, ArH), 7.85–7.96 (m, 5H, ArH), 8.51 (s, 1H, ArH); Anal. Calcd for $C_{29}H_{26}ClN_5O$: C, 69.48; H, 5.41; N, 14.47. Found: C, 69.56; H, 5.58; N, 14.58.

2-(3-((3-(4-Bromophenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylamino) propylamino)quinolin-4(1*H*)-one (4e). Solid; mp 230–232°C; IR (KBr) ν 3432 (NH), 1638 cm^{-1} (CO); MS (FAB) *m/z* 528 (MH^+, 50), 460 (40), 329 (10); ^1H NMR (DMSO-d_6, 300 MHz), δ 1.74–1.79 (m, 2H, CH_2), 2.71 (t, *J* = 6.4 Hz, 2H, CH_2), 3.27–3.35 (m, 2H, CH_2), 3.74 (s, 2H, CH_2), 5.28 (brs, 1H, NH), 5.76 (s, 1H, ArH), 6.43 (brs, 1H, NH), 7.08–7.13 (m, 1H, ArH), 7.28–7.33 (m, 2H, ArH), 7.40–7.52 (m, 3H, ArH), 7.62–7.64 (m, 2H, ArH), 7.85–7.92 (m, 5H, ArH), 8.51 (s, 1H, ArH); Anal. Calcd for $C_{29}H_{26}BrN_5O$: C, 63.64; H, 4.96; N, 13.25. Found: C, 63.50; H, 4.86; N, 13.38.

2-(3-((1-Phenyl-3-(thiophen-2-yl)-1*H*-pyrazol-4-yl)methylamino) propylamino) quinolin-4(1*H*)-one (4f). Solid; mp 205–206°C; IR (KBr) ν 3432 (NH), 1638 cm^{-1} (CO); MS (FAB) *m/z* 456 (MH^+, 50), 294 (10); ^1H NMR ($CDCl_3$, 300 MHz), δ 1.68–1.72 (m, 2H, CH_2), 2.66 (t, *J* = 6.4 Hz, 2H, CH_2), 3.19–3.20 (m, 2H, CH_2), 3.70 (s, 2H, CH_2), 5.62 (s, 1H, ArH), 6.96–6.98 (m, 2H, ArH), 7.07–7.19 (m, 3H, ArH), 7.25–7.37 (m, 3H, ArH), 7.58–7.61 (m, 2H, ArH), 7.81 (s, 1H, Pyrazolyl), 8.17 (d, *J* = 8.10 Hz, 1H, ArH); Anal. Calcd for $C_{26}H_{25}N_5OS$: C, 68.55; H, 5.53; N, 15.37. Found: C, 68.68; H, 5.70; N, 15.48.

General procedure for the synthesis of 2-(3-((1,3-diaryl-1*H*-pyrazol-4-yl)methylamino)-2-hydroxypropylamino)quinolin-4(1*H*)-one (4g-l). A mixture of **2b** (1.0 mmol) was stirred with 20%TFA-DCM (10 mL) for 2 h at room temperature. TFA was evaporated under reduced pressure and quinolin-4-one (**3b**) thus obtained was dissolved in dry methanol (10 mL), acetic acid (0.1 mL) was added at room temperature followed by 0.5 M MeONa solution in methanol (1.0 mmol). The resulting reaction mixture was stirred for 15 min at room temperature then 1-phenyl-3-aryl-1*H*-pyrazole-4-carbaldehyde **3'** (1.0 mmol) was added, stirred at 50°C for 1 h. A solution of $NaCNBH_3$ (1.5 mmol) in MeOH (5 mL) was added dropwise and stirred again for 6 h at 50°C. Methanol was evaporated under reduced pressure and crude product thus obtained was purified on silica gel column using DCM/MeOH/NH_3 sol (95:5:0.5) as eluent.

2-(3-((1,3-Diphenyl-1*H*-pyrazol-4-yl)methylamino)-2-hydroxypropylamino)quinolin-4(1*H*)-one (4g). Solid; mp 203–204°C; IR (KBr) ν 3624 (OH), 3423 (NH), 1638 cm^{-1} (CO); MS (FAB) *m/z* 467 (M^++2, 50), 233 (100); ^1H NMR ($CDCl_3$, 300 MHz), δ 2.48–2.49 (m, 2H, CH_2), 3.08–3.09

(m, 2H, CH_2), 3.60–3.75 (m, 3H, CH_2), 5.62 (s, 1H, ArH), 6.92–6.94 (m, 2H, ArH), 7.12–7.32 (m, 7H, ArH), 7.56–7.83 (m, 4H, ArH), 7.83 (s, 1H, Pyrazolyl), 8.02 (d, J = 7.50 Hz, 1H, ArH); Anal. Calcd for $C_{28}H_{27}N_5O_2$: C, 72.24; H, 5.85; N, 15.04. Found: C, 72.36; H, 5.97; N, 15.18.

2-(2-Hydroxy-3-((1-phenyl-3-p-tolyl-1*H*-pyrazol-4-yl) methylamino) propylamino)quinolin-4(1*H*)-one (4h). Solid; mp 208–210°C; IR (KBr) ν 3622 (OH), 3434 (NH), 1638 cm^{-1} (CO); MS (FAB) *m/z* 481 (M^++2, 50), 263 (40); ^1H NMR ($CDCl_3$, 300 MHz), δ 2.32 (s, 3H, Me), 2.48-2.49 (m, 2H, CH_2), 3.08-3.09 (m, 2H, CH_2), 3.60–3.75 (m, 3H, CH_2), 5.62 (s, 1H, ArH), 6.92–6.94 (m, 2H, ArH), 7.12–7.32 (m, 6H, ArH), 7.56–7.83 (m, 4H, ArH), 7.83 (s, 1H, Pyrazolyl), 8.02 (d, J = 8.10 Hz, 1H, ArH); Anal. Calcd for $C_{29}H_{29}N_5O_2$: C, 72.63; H, 6.10; N, 14.60. Found: C, 72.78; H, 6.24; N, 14.74.

2-(2-Hydroxy-3-((3-(4-methoxyphenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylamino) propylamino)quinolin-4(1*H*)-one (4i). Solid; mp 205–206°C; IR (KBr) ν 3622 (OH), 3434 (NH), 1638 cm^{-1} (CO); MS (FAB) *m/z* 496 (MH^+, 50), 263 (40); ^1H NMR (DMSO-d_6, 300 MHz), δ 2.64-2.75 (m, 2H, CH_2), 3.08–3.09 (m, 2H, CH_2), 3.72–3.83 (m, 6H, CH_2 and OMe), 5.38 (brs, 1H, NH), 5.76 (s, 1H, ArH), 6.36 (brs, 1H, NH), 6.98–7.01 (m, 2H, ArH), 7.08–7.13 (m, 1H, ArH), 7.23–7.30 (m, 2H, ArH), 7.40–7.51 (m, 3H, ArH), 7.80–7.92 (m, 5H, ArH and Pyrazolyl), 8.47 (s, 1H, ArH); Anal. Calcd for $C_{29}H_{29}N_5O_3$: C, 70.28; H, 5.90; N, 14.13. Found: C, 70.34; H, 5.82; N, 14.24.

2-(3-((3-(4-Fluorophenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylamino)-2-hydroxypropylamino)quinolin-4(1*H*)-one (4j). Solid; mp 236–237°C; IR (KBr) ν 3622 (OH), 3423 (NH), 1638 cm^{-1} (CO); MS (FAB) *m/z* 484(MH^+, 50), 251 (80); ^1H NMR ($CDCl_3$, 300 MHz), δ 2.48–2.50 (m, 2H, CH_2), 3.08–3.09 (m, 2H, CH_2), 3.49–3.60 (m, 2H, CH_2), 3.78–3.80 (m, 1H, CH), 5.64 (s, 1H, ArH), 6.87–6.98 (m, 4H, ArH), 7.07–7.12 (m, 3H, ArH), 7.21–7.25 (m, 2H, ArH), 7.52–7.61 (m, 3H, ArH), 7.80 (s, 1H, Pyrazolyl), 8.01 (d, J = 7.8 Hz, 1H, ArH); Anal. Calcd for $C_{28}H_{26}FN_5O_2$: C, 69.55; H, 5.42; N, 14.48. Found: C, 69.66; H, 5.56; N, 14.42.

2-(3-((3-(4-Chlorophenyl)-1-phenyl-1*H*-pyrazol-4-yl) methylamino)-2-hydroxypropylamino)quinolin-4(1*H*)-one (4k). Solid; mp 251–252°C; IR (KBr) ν 3622 (OH), 3387 (NH), 1638 cm^{-1} (CO); MS (FAB) *m/z* 500 (MH^+, 50), 267 (60); ^1H NMR (CD_3OD, 300 MHz), δ 2.71–2.83 (m, 2H, CH_2), 3.29–3.33 (m, 2H, CH_2), 3.91–3.95 (m, 3H, CH, CH_2), 5.56 (s, 1H, ArH), 7.21–7.33 (m, 3H, ArH), 7.41–7.52 (m, 5H, ArH), 7.74–7.78 (m, 4H, ArH), 8.08–8.09 (m, 1H, Pyrazolyl), 8.01 (s, 1H, ArH); Anal. Calcd for $C_{28}H_{26}ClN_5O_2$: C, 67.26; H, 5.24; N, 14.01. Found: C, 67.36; H, 5.32; N, 14.14.

2-(2-Hydroxy-3-((1-phenyl-3-(thiophen-2-yl-1*H*-pyrazol-4-yl) methylamino) propylamino)quinolin-4(1*H*)-one (4l). Solid; mp 241–242°C; IR (KBr) ν 3622 (OH), 3421 (NH), 1644 cm^{-1} (CO); MS (FAB) *m/z* 472 (MH^+, 50), 239 (10); ^1H NMR ($CDCl_3$, 300 MHz), δ 2.61–2.64 (m, 2H, CH_2), 3.09–3.12 (m, 2H, CH_2), 3.75–3.89 (m, 3H, CH, CH_2), 5.61 (s, 1H, ArH), 6.92–6.98 (m, 3H, ArH), 7.11–7.13 (m, 3H, ArH), 7.22–7.26 (m, 4H, ArH), 7.52–7.55 (m, 2H, ArH and Pyrazolyl), 7.90–7.92 (m, 1H, ArH); Anal. Calcd for $C_{26}H_{25}N_5O_2S$: C, 66.22; H, 5.34; N, 14.85. Found: C, 66.36; H, 5.32; N, 14.74.

Quinazolin-2,4-dione (6). Anthranilic acid **5** (13.7 g, 0.1 mol) was added in portions to a molten urea (9.0 g, 0.15 mol) at 190°C for 30 min. The temperature of the raction mixture was maintained for 1 h, cooled to room temperature and diluted with water. The solid settled was filtered, washed with water (20 mL) thrice and dried in the air. White solid; mp >250°C; MS (EI) *m/z* 162 (M^+, 86%) [13].

2,4-Dichloroquinazoline (7). A solution of quinazolin-2, 4-dione **6** (2 g) in phosphorousoxychloride ($POCl_3$, 6 mL) was refluxed in presence of *N*,*N*-diethylaniline (0.6 mL) for 5 h. The reaction mixture was allowed to cool to room temperature and poured over crushed ice with vigrourous stirring. Dark brown solid precipitate obtained was filtered, washed with distilled water and finally purified on silica gel column chromatography using hexane/ethyl acetate (40:1) as eluent. White solid; mp 116–117°C; [Lit. [13] mp 116–117°C]; MS (EI) *m/z* 199 (M^+, 78.0).

2-Chloroquinazolin-4(1*H*)-one (8). A suspension of **7** (1.0 mmol) was stirred in 4% aq. sodium hydroxide solution (3 mL) for 3 h. Reaction mixture was diluted with water (6 mL) and filtered to remove unreacted 2,4-dichloroquinazoline. The filtrate was neutralized with dilute acetic acid, white precipitate obtained was filtered and washed with water. White solid; mp 220–221°C [Lit. [13] mp 220–221°C]; MS (EI) *m/z* 180 (M^+, 51.0).

2-(3-Aminopropylamino)quinazolin-4(1*H*)-one (9). A mixture of **8** (0.1 mol) and 1,3-diaminopropane (8 mL) was heated to 70°C for 48 h. At the end of the reaction 1,3-diaminopropane was evaporated under reduced pressure and washed with dichloromethane (10 mL × 2) to reveal desired compound (**9**). White solid; mp 145–147°C (decomposed); MS (FAB) *m/z* 219 (MH^+, 100%); ^1H NMR (CD_3OD, 300 MHz), δ 1.72–1.75 (m, 2H, CH_2), 2.89–2.91 (m, 2H, CH_2), 3.53–3.56 (m, 2H, CH_2), 7.16–7.20 (m, 1H, ArH), 7.30–7.32 (m, 1H, ArH), 7.57–7.61 (m, 1H, ArH), 8.00–8.01 (m, 1H, ArH).

General procedure for the synthesis of 2-(3-(substituted benzylamino)propylamino)quinazolin-4(1*H*)-one (10a-f). A solution of **9** (1.0 mmol) in dry methanol (10 mL), acetic acid (0.1 mL) was added at room temperature followed by 0.5 M MeONa solution in methanol (1.0 mmol). The resulting reaction mixture was stirred for 15 min at room temperature then suitable aldehyde (1.0 mmol) was added, stirred at 50°C for 1 h. A solution of $NaCNBH_3$ (1.5 mmol) in MeOH (5 mL) was added dropwise and stirred again for 6 h at 50°C. Methanol was evaporated under reduced pressure and crude product thus obtained was purified on silica gel column using DCM/MeOH/NH_3 sol (95:5:0.5) as eluent.

2-(3-(4-Chlorobenzylamino)propylamino)quinazolin-4(1*H*)-one (10a). Solid; mp 84–85°C; IR (KBr) ν 3464 (NH), 1641 cm^{-1} (CO); MS (FAB) *m/z* 343 (MH^+, 100), 202 (10); ^1H NMR (CD_3OD, 300 MHz), δ 1.66–1.70 (m, 2H, CH_2), 2.48–2.50 (m, 2H, CH_2), 3.31–3.33 (m, 2H, CH, CH_2), 3.57 (s, 2H, CH_2), 7.08–7.12 (m, 6H, ArH), 7.39–7.41 (m, 1H, ArH), 7.82–7.84 (m, 1H, ArH); Anal. Calcd for $C_{18}H_{19}ClN_4O$: C, 63.06; H, 5.59; N, 16.34. Found: C, 63.14; H, 5.66; N, 16.48.

2-(3-(3,4-Dichlorobenzylamino)propylamino)quinazolin-4 (1*H*)-one (10b). Solid; mp 105–107°C; IR (KBr) ν 3470 (NH), 1690 cm^{-1} (CO); MS (FAB) *m/z* 377 (MH^+, 80), 202 (10); ^1H NMR (CD_3OD, 300 MHz), δ 1.82–1.87 (m, 2H, CH_2), 2.64–2.67 (m, 2H, CH_2), 3.48–3.51 (m, 2H, CH, CH_2), 3.71 (s, 2H, CH_2), 7.14–7.24 (m, 3H, ArH), 7.34–7.36 (m, 1H, ArH), 7.47–7.48 (m, 1H, ArH), 7.54–7.57 (m, 1H, ArH), 7.97–7.98 (m, 1H, ArH); Anal. Calcd for $C_{18}H_{18}Cl_2N_4O$: C, 57.30; H, 4.81; N, 14.85. Found: C, 57.38; H, 4.92; N, 14.98.

2-(3-(4-Bromobenzylamino) propylamino) quinazolin-4(1*H*)-one (10c). Solid; mp 88–89°C; IR (KBr) ν 3472 (NH), 1637 cm^{-1} (CO); MS (FAB) *m/z* 387 (MH^+, 100), 202 (10); ^1H NMR (CD_3OD, 300 MHz), δ 1.65–1.70 (m, 2H, CH_2), 2.47–2.52 (m, 2H, CH_2), 3.31–3.36 (m, 2H, CH, CH_2), 3.57 (s, 2H, CH_2),

6.99–7.08 (m, 4H, ArH), 7.23–7.25 (m, 2H, ArH), 7.39–7.41 (m, 1H, ArH), 7.82–7.84 (m, 1H, ArH); Anal. Calcd for $C_{18}H_{19}BrN_4O$: C, 55.82; H, 4.95; N, 14.47. Found: C, 55.70; H, 4.88; N, 14.56.

2-(3-(Pyridin-4-ylmethylamino) propylamino)quinazolin-4 (1*H*)-one (10d). Solid; mp 110–112°C; IR (KBr) ν 3474 (NH), 1640 cm^{-1} (CO); MS (FAB) *m/z* 310 (MH^+, 60), 202 (10); ^1H NMR (CD_3OD, 300 MHz), δ 1.88–1.92 (m, 2H, CH_2), 2.69–2.74 (m, 2H, CH_2), 3.52–3.57 (m, 2H, CH_2), 3.84 (s, 2H, CH_2), 7.18–7.29 (m, 2H, ArH), 7.41–7.43 (m, 2H, ArH), 7.57–7.63 (m, 1H, ArH), 8.01–8.03 (m, 1H, ArH), 8.42–8.44 (m, 2H, ArH); Anal. Calcd for $C_{17}H_{19}N_5O$: C, 66.00; H, 6.19; N, 22.64. Found: C, 66.14; H, 6.28; N, 22.56.

2-(3-(Thiophen-2-ylmethylamino)propylamino)quinazolin-4(1*H*)-one (10e). Solid; mp 114–116°C; IR (KBr) ν 3470 (NH), 1642 cm^{-1} (CO); MS (FAB) *m/z* 315 (MH^+, 100), 202 (10); ^1H NMR (CD_3OD, 300 MHz), δ 1.85–1.89 (m, 2H, CH_2), 2.71–2.76 (m, 2H, CH_2), 3.50–3.52 (m, 2H, CH_2), 3.99 (s, 2H, CH_2), 6.92–6.99 (m, 2H, ArH), 7.18–7.29 (m, 3H, ArH), 7.57–7.62 (m, 1H, ArH), 8.01–8.03 (m, 1H, ArH); Anal. Calcd for $C_{16}H_{18}N_4OS$: C, 61.12; H, 5.77; N, 17.82. Found: C, 61.18; H, 5.88; N, 17.96.

2-(3-(Naphthalen-1-ylmethylamino)propylamino)quinazolin-4(1*H*)-one (10f). Solid; mp 145–146°C; IR (KBr) ν 3480 (NH), 1644 cm^{-1} (CO); MS (FAB) *m/z* 315 (MH^+, 100), 202 (10); ^1H NMR ($CDCl_3$, 300 MHz), δ 1.88–1.90 (m, 2H, CH_2), 2.82–2.84 (m, 2H, CH_2), 3.24–3.27 (m, 2H, CH_2), 3.78 (s, 2H, CH_2), 7.40–7.58 (m, 6H, ArH), 7.86–7.89 (m, 3H, ArH), 7.98–7.99 (m, 1H, ArH), 8.56–8.58 (m, 1H, ArH); Anal. Calcd for $C_{22}H_{22}N_4O$: C, 73.72; H, 6.19; N, 15.63. Found: C, 73.88; H, 6.10; N, 15.56.

3-(1-Amino-3-(4-(4-methoxybenzyloxy)quinolin-2-ylamino) propan-yloxy)propane-1,2-diol (11a). A mixture of **1** (1.50 g, 5.0 mmol) and compound **18** (4.10 g, 25.0 mmol) was stirred in DMSO (30 mL) at 80°C in presence of potassium carbonate (0.83 g, 6.0 mmol) for 48 h. The reaction mixture was poured into distilled water (50 mL) and extracted from ethyl acetate (25 mL × 3), dried over sodium sulfate, and evaporated. The solid obtained was purified on silica gel column using CH_2Cl_2/ MeOH/ NH_3 sol (90:10:0.5) as eluent. White solid; IR (KBr) ν 3660 cm^{-1} (OH); MS(FAB) *m/z* 428 (MH^+, 100%); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.48–3.59 (m, 2H, NCH_2), 3.64–3.69 (m, 2H, NCH_2), 3.73–3.76 (m, 1H, CH), 3.80–3.82 (m, 4H, CH_2), 3.88 (s, 3H, OCH_3), 3.95–3.96 (m, 1H, CH), 5.10 (s, 2H, OCH_2), 6.40 (s, 1H, ArH), 6.96 (d, *J* = 8.70 Hz, 2H, ArH), 7.15–7.20 (m, 1H, ArH), 7.40 (d, *J* = 8.70 Hz, 2H, ArH), 7.48–7.53 (m, 1H, ArH), 7.58–7.61 (m, 1H, ArH), 7.96–7.99 (m, 1H, ArH).

***tert*-Butyl 3-(1-Amino-3-(4-(4-methoxybenzyloxy)quinolin-2-ylamino)propan-2-yloxy)-2-hydroxypropylcarbamate (11b).** This compound was synthesized from compound **1** and compound **22** by following the procedure of preparation of compound **11a.** White solid, IR (KBr) ν 3420 (NH), 3640 cm^{-1} (OH); MS(FAB) *m/z* 527 (MH^+, 100%); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.41 (s, 9H, Boc), 3.48–3.59 (m, 2H, NCH_2), 3.64–3.65 (m, 2H, NCH_2), 3.68–3.96 (m, 2H, CH_2), 3.73–3.76 (m, 1H, CH), 3.82–3.84 (m, 2H, CH_2), 3.90 (s, 3H, OCH_3), 3.92–3.93 (m, 1H, CH), 5.10 (s, 2H, OCH_2), 6.50 (s, 1H, ArH), 6.94 (d, *J* = 8.70 Hz, 2H, ArH), 7.16–7.18 (m, 1H, ArH), 7.42 (d, *J* = 8.70 Hz, 2H, ArH), 7.50–7.51 (m, 1H, ArH), 7.59–7.61 (m, 1H, ArH), 7.94–7.96 (m, 1H, ArH).

2-(3-Amino-2-(2,3-dihydroxypropoxy)propylamino)quinolin-4(1*H*)-one (12a). A solution of compound **11a** (500 mg) in methanol (50 mL) was stirred with 10%Pd-C (100 mg) under H_2 gas balloon for 1h at room temperature. The reaction mixture was passed through celite pad. Filtrate was evaporated under vacuum to get compound **12a** in good purity. White solid; IR (KBr) ν 1710 (CO), 3660 cm^{-1} (OH); MS(FAB) *m/z* 308 (MH^+, 100%); ^1H NMR (CD_3OD, 300 MHz) δ 3.48–3.59 (m, 2H, NCH_2), 3.68–3.70 (m, 2H, NCH_2), 3.74–3.75 (m, 1H, CH), 3.80–3.82 (m, 4H, CH_2), 3.95–3.96 (m, 1H, CH), 5.68 (s, 1H, ArH), 7.23–7.30 (m, 2H, ArH), 7.40 (d, *J* = 8.70 Hz, 1H, ArH), 8.06 (d, *J* = 8.10 Hz, 1H, ArH).

***tert*-Butyl 3-(1-amino-3-(4-oxo-1,4-dihydroquinolin-2-ylamino) propan-2-yloxy)-2-hydroxypropylcarbamate (12b).** Compound **12b** was synthesized from compound **11b** according to the procedure for preparation of compound **12a**. White solid, IR (KBr) ν 1710 (CO), 3430 (NH), 3650 cm^{-1} (OH); MS(FAB) *m/z* 407 (MH^+, 100%); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.41 (s, 9H, Boc), 3.48–3.59 (m, 2H, NCH_2), 3.64–3.65 (m, 2H, NCH_2), 3.68–3.96 (m, 2H, CH_2), 3.73–3.76 (m, 1H, CH), 3.82–3.84 (m, 2H, CH_2), 3.92–3.93 (m, 1H, CH), 5.68 (s, 1H, ArH), 7.23–7.30 (m, 2H, ArH), 7.40 (d, *J* = 8.70 Hz, 1H, ArH), 8.06 (d, *J* = 8.10 Hz, 1H, ArH).

2-(3-(3,4-Dichlorobenzylamino)-2-(2,3-dihydroxypropoxy) propylamino)quinolin-4(1*H*)-one (13a). To a stirred solution of **12a** (123 mg, 0.40 mmol) in methanol (5 mL) was added 0.5 M methanolic solution of MeONa (1 mL, 0.43 mmol). Additional amount of 0.5 M MeONa solution was added to maintain pH 12 of the reaction mixture and stirred for 10 min at room temperature. 3,4-Dichlorobenzaldehyde (70 mg, 0.40 mmol) was added and resultant reaction mixture was stirred at 50°C for 1 h. To this $NaCNBH_3$ (38 mg, 0.60 mmol) in methanol (2 mL) was added dropwise and stirring continued for additional 6 h. Solvent was evaporated under reduced pressure and residue obtained was purified on silica gel column chromatography using DCM/MeOH/ NH_3 solution (95:5:1) as eluent. White solid; mp 152–154°C; IR (KBr) ν 1710 (CO), 3660 cm^{-1} (OH), MS (FAB) 467 (MH^+); ^1H NMR (CD_3OD, 300 MHz) δ 3.48–3.59 (m, 2H, NCH_2), 3.68–3.70 (m, 2H, NCH_2), 3.74–3.75 (m, 3H, CH and CH_2), 3.80–3.82 (m, 4H, CH_2), 3.95–3.96 (m, 1H, CH), 5.67 (s, 1H, ArH), 7.24–7.28 (m, 1H, ArH), 7.34–7.39 (m, 2H, ArH), 7.52–7.56 (m, 2H, ArH), 7.63–7.65 (m, 1H, ArH), 8.06 (d, *J* = 8.10 Hz, 1H, ArH). Anal. Calcd for $C_{22}H_{25}Cl_2N_3O_4$: C, 56.66; H, 5.40; N, 9.01. Found: C, 56.78; H, 5.54; N, 9.18.

***tert*-Butyl 3-(1-(3,4-Dichlorobenzylamino)-3-(4-oxo-1,4-dihydroquinolin-2-ylamino)propan-2-yloxy)-2-hydroxypropylcarbamate (13b).** This compound was synthesized from the reaction of compound **12b** and 3,4-dichlorobenzaldehyde according to the procedure described for compound **13a.** White solid, IR (KBr) ν 1710 (CO), 3430 (NH), 3650 cm^{-1} (OH); MS (FAB) *m/z* 566 (MH^+, 100%); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.41 (s, 9H, Boc), 3.48–3.59 (m, 2H, NCH_2), 3.64–3.65 (m, 2H, NCH_2), 3.68–3.96 (m, 2H, CH_2), 3.73–3.76 (m, 3H, CH and CH_2), 3.82–3.84 (m, 2H, CH_2), 3.92–3.93 (m, 1H, CH), 5.67 (s, 1H, ArH), 7.24–7.28 (m, 1H, ArH), 7.34–7.39 (m, 2H, ArH), 7.52–7.56 (m, 2H, ArH), 7.63–7.65 (m, 1H, ArH), 8.06 (d, *J*=8.10 Hz, 1H, ArH). Anal. Calcd for $C_{27}H_{34}Cl_2N_4O_5$: C, 57.35; H, 6.06; N, 9.91. Found: C, 57.48; H, 6.20; N, 9.84.

1,3-Diazidopropan-2-ol (15). A mixture of **14** (10.85 g, 50.0 mmol) and sodium azide (9.75 g, 150.0 mmol) in DMF was heated at 80°C for 24 h. The reaction mixture was allowed to cool to room temperature, diluted with water and extracted with ethyl acetate (25 mL × 3). Organic layer was collected, washed with excess of water and dried under vacuum. The

residue obtained was purified by silica gel column using Hexane: EtOAc (9:1). Colorless oil; MS (FAB) 143 (MH^+); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.36–3.37 (m, 4H, CH), 3.66–3.68 (m, 1H, CH).

3-(2-Azido-1-azidomethylethoxy)-propene (16). A mixture of **15** (5.0 g, 35.2 mmol), 4Å molecular sieves (20 g) and $CsOH{\cdot}H_2O$ (11.8 g, 70.4 mmol) in acetonitrile (30 mL) was stirred at room temperature for 20 min under nitrogen atmosphere. *n*-tetrabutylammonium iodide (12.98 g, 35.2 mmol) and allyl iodide (9.58 mL, 105.6 mmol) were added sequentially and resultant mixture stirred for 48 h at room temperature. Solid insoluble was filtered and solvent evaporated under reduced pressure. The crude product was purified on silica gel column using hexane: EtOAc (19:1) as eluent. Colorless oil; MS (FAB) 183 (MH^+); ^1H NMR ($CDCl_3$, 300 MHz) δ 3.37–3.39 (m, 4H, CH), 3.68–3.69 (m, 1H, CH), 4.13–4.15 (m, 2H, allyl), 5.21–5.36 (m, 2H, allyl), 5.87–6.00 (m, 1H, allyl).

3-(1,3-Diazidopropan-2-yloxy)propane-1,2-diol (17). A mixture of compound **16** (1.82 g, 10.0 mmol) and *N*-methylmorpholine *N*-oxide (NMO) (1.755 g, 15.0 mmol) in acetone/water (10:1; 22 mL) was added osmium tetraoxide (2.5% wt solution in *tert*-butanol; 100 μL, 0.10 mmol) and allowed to stir at room temperature for 16 h. The solvent of the reaction mixture was evaporated and extracted with ethyl acetate (15 mL × 2). The ethyl acetate layers were separated, dried (Na_2SO_4), evaporated under reduced pressure and crude obtained was purified by silica gel chromatography using hexane: ethyl acetate (1:1) as eluent to get compound **17**. Colorless oil; MS (FAB) 217 (MH^+); ^1H NMR (CD_3Cl_3, 300 MHz) δ 3.36–3.37 (m, 4H, CH_2), 3.66–3.68 (m, 1H, CH), 3.80–3.82 (m, 4H, CH_2), 3.95–4.01 (m, 1H, CH).

3-(1,3-Diaminopropan-2-yloxy)propane-1,2-diol (18). A mixture compound **17** (1.0 g) and 10% $Pd(OH)_2$ (50 mg), under hydrogen atmosphere in methanol at room temperature for 20 h. The reaction mixture was filtered through celite powder and evaporated under vacuum. The product obtained was directly used for next stage without purification.

2-((1,3-Diazidopropan-2-yloxy)methyl)oxirane (19). A mixture of compound **16** (1.82 g, 10.0 mmol) and 3-chloroperoxybenzoic acid (2.5 g, 15.0 mmol) in DCM (20 mL) was stirred at room temperature for 1.5 h. DCM was evaporated and residue obtained was purified on silica gel column using ethyl acetate: hexane (1:4) as eluent. Colorless oil; MS (FAB) 199 (MH^+); ^1H NMR (CD_3Cl_3, 300 MHz) δ 3.38–3.39 (m, 4H, CH_2), 3.68–3.69 (m, 1H, CH), 3.80–3.82 (m, 2H, CH_2), 4.10–4.12 (m, 1H, CH), 4.20–4.22 (m, 2H, CH_2).

1-Amino-3-(1,3-diazidopropan-2-yloxy)propan-2-ol (20). A solution of compound **19** (1.99 g, 10.0 mmol) in ethanol (15 mL) was added 28% aq. solution NH_3 (1.2 mL, 20.0 mmol) dropwise and stirred at room temperature for 3 h. ethanol was evaporated and residue obtained was purified on silica gel column using ethyl acetate: hexane (1:1) as eluent. Colorless oil; MS (FAB) 216 (MH^+); ^1H NMR (CD_3Cl_3, 300 MHz) δ 3.32–3.34 (m, 2H, CH_2), 3.36–3.38 (m, 4H, CH_2), 3.60–3.62 (m, 1H, CH), 3.68–3.69 (m, 2H, CH_2), 3.72–3.74 (m, 1H, CH).

***tert*-Butyl 3-(1,3-diazidopropan-2-yloxy)-2-hydroxypropylcarbamate (21).** A solution of compound **20** (2.0 g, 9.26 mmol) in DCM (15 mL) was added $(Boc)_2O$ (2.22 g, 10.24 mmol) and stirred at room temperature for 1 h. DCM was evaporated and residue obtained was purified on silica gel column using ethyl acetate: hexane (1:9) as eluent. Colorless oil; MS (FAB) 316 (MH^+); ^1H NMR (CD_3Cl_3, 300 MHz) δ 1.41 (s, 9H, Boc), 3.30–3.32 (m, 2H, CH_2), 3.35–3.36 (m, 4H, CH_2), 3.60–3.61 (m, 1H, CH), 3.66–3.68 (m, 2H, CH_2), 3.72–3.74 (m, 1H, CH).

***tert*-Butyl 3-(1,3-diaminopropan-2-yloxy)-2-hydroxypropylcarbamate (22).** A mixture compound **21** (2.0 g) and 10% $Pd(OH)_2$ (100 mg), under hydrogen atmosphere in methanol at room temperature for 20 h. The reaction mixture was filtered through celite powder and evaporated under vacuum. The product obtained was directly used for next stage without purification.

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