

## New building blocks for convenient access to positional isomers of FTY720 and analogues

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Dedicated to Dr. J. S. Yadav on the occasion of his 65<sup>th</sup> anniversary

DOI: <http://dx.doi.org/10.3998/ark.5550190.p009.260>

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### Abstract

Two new Weinreb amide based bifunctional building blocks have been developed starting from *meta* and *ortho*-toluic acid for convenient access to *meta*- and *ortho*- positional isomers of FTY720. Julia olefination and Grignard reaction are the key steps used in the synthesis of **2** and **3**. The bifunctional building blocks **4** and **5** are easy to scale-up and in addition to synthesis of **2** and **3**, these building blocks would be valuable in search of a new amphiphiles, as the functionalities therein allows for change in the nature of polar head-group and lipophilic chain.

**Keywords:** FTY720, olefination, sulfone, synthesis, Weinreb amide

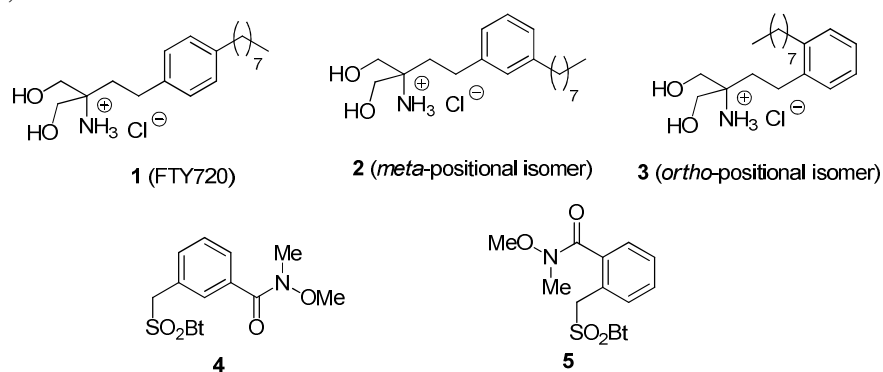
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### Introduction

FTY720, **1**,<sup>1,2</sup> clinically known as fingolimod hydrochloride, is a recently approved drug by the US Food and Drug Administration as a first-line treatment for relapsing forms of multiple sclerosis, which is a common inflammatory disorder of the central nervous system. FTY720, **1** structurally contains a polar hydrophilic group, protonated 2-amino-propane-1,3-diol unit and hydrophobic 4-octylphenethyl carbon chain for its amphipathic nature. Due to the importance of the FTY720, varieties of methods are available for the synthesis of FTY720. The polar head-group of FTY720 has been commonly installed from nitrodiol,<sup>3</sup> benzylamine,<sup>4</sup> diethyl acetamidomalonate,<sup>5-7</sup> or tris(hydroxymethyl)aminomethane (TRIS).<sup>8-10</sup> Whereas the lipophilic alkyl chain traditionally through Friedel–Crafts Acylation followed by Wolff–Kishner reduction.<sup>5</sup> Fürstner et al developed iron catalyzed cross coupling reaction between aryl triflate and alkylmagnesium halide.<sup>6</sup> Kim et al have used palladium-catalyzed Sonogashira coupling reaction to install hydrocarbon chain.<sup>8</sup> Calzavara and McNulty employed Wittig reaction

between 4-hydroxymethylbenzaldehyde and trialkylphosphoniumbromide to incorporate alkyl chain.<sup>9</sup>

The synthetic route reported from our group for the synthesis of FTY720 (**1**) installed polar head-group through Wittig, Horner–Wadsworth–Emmons and Julia reaction whereas alkyl chain incorporated through Weinreb amide functionality.<sup>10</sup> In contrast to FTY720, the synthesis of its positional isomer **2** and **3** has been reported only by one method by Kiuchi et al in 2000 during their initial drug discovery process for novel immunosuppressant.<sup>5</sup> In this direction they have synthesized a series of 2-substituted 2-aminopropane-1,3-diols and studied their immunosuppressive effect on rat skin allograft. They have shown synthesis and SAR of analogues of FTY720. As a result of studies they found that FTY720 can be used as a potent drug for organ transplantation. They observed that potency of various analogues was dependent on position of phenyl ring in the hydrocarbon chain and separation of the quaternary carbon and phenyl ring by two carbon atoms. The *ortho*- and *meta*-positional isomers **2** and **3** showed comparatively less activity than FTY720. These findings gave indication that *para*-substitution at phenyl ring is important for the immunosuppressive activity. The (*pro-S*) hydroxymethyl group is essential for potent immunosuppressive activity of FTY720, whereas (*pro-R*) hydroxymethyl group can be replaced by hydroxyethyl, hydroxypropyl, methyl or ethyl groups. Due to the importance and significance of this drug and in the absence of any report towards understanding its interaction with lipid bilayer membrane, efforts were expended towards this objective using fluorescence spectroscopy. Aggregation studies revealed that FTY720 possess efficient aggregating ability in aqueous solutions. Also FTY720 was found to prevent the partitioning of small molecules like 1-naphthol into the lipid bilayer membrane.<sup>11-12</sup> With these results in hand, a need to study the effect of other positional isomers **2** and **3** of FTY720 on the lipid bilayer membrane became interesting and relevant. In this context there was a genuine need for a good synthetic scheme enabling access to these positional isomers of FTY720. In the light of our immediate requirement for **2** and **3**, for studies towards their interaction with lipid membrane there was a need for a robust synthetic route which would not only provide **2** and **3**, but also enable change in nature of polar head-group and lipophilic part in a search towards novel amphiphile, based on FTY720 architecture.

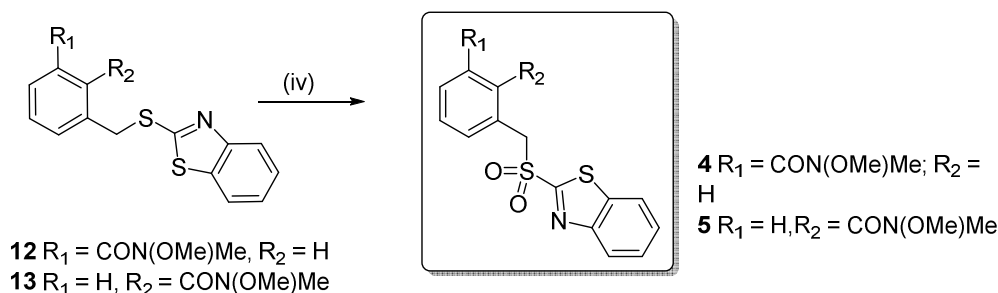
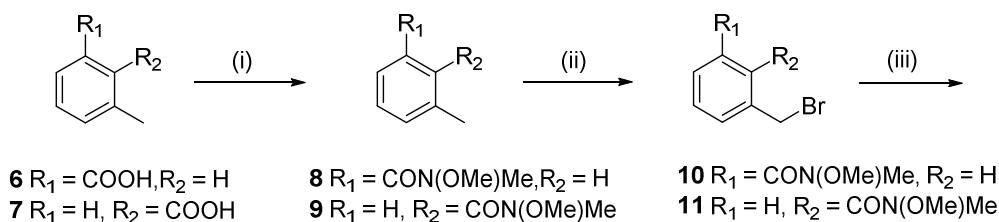


**Figure 1.** Structure of FTY720, positional isomers and building blocks.

The synthesis of positional isomers **2** and **3** was envisaged through building blocks **4** and **5** easily amenable through simple reactions on cheap and commercially available, *meta*- and *ortho*-toluic acids as starting materials. The convenient route developed for the synthesis of **2** and **3** is disclosed herein.

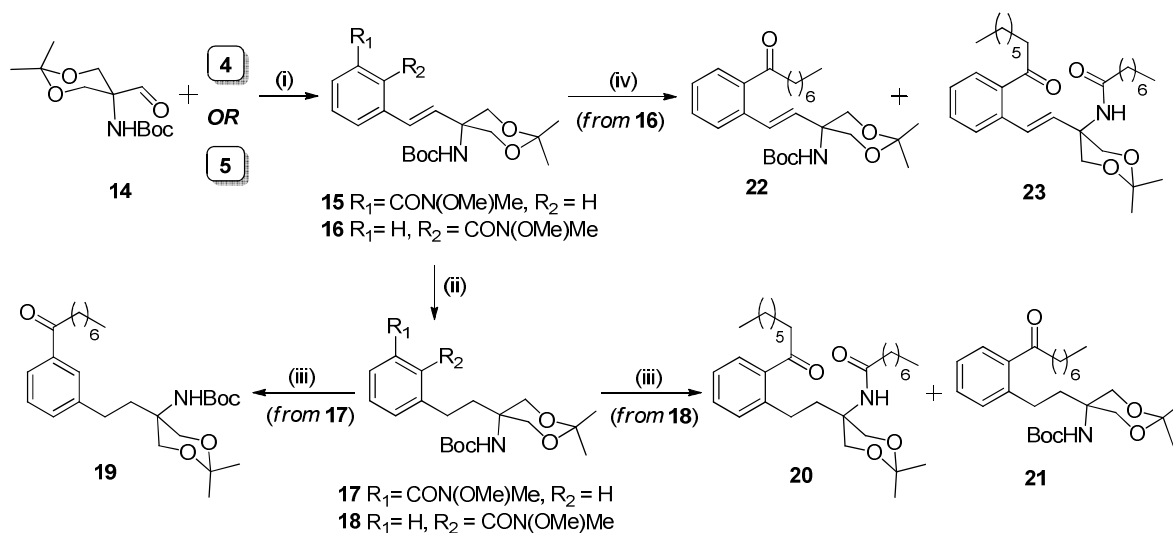
## Results and Discussion

The synthesis of building block **4** and **5** could be easily achieved through simple functional group inter-conversion on toluic acid **6** and **7** respectively (Scheme 1). Synthetic efforts started with conversion of acid **6** and **7** to the corresponding Weinreb amide (WA) **8** and **9** through their acid chloride intermediates in 76% and 70% yield respectively. Reaction of amide **8** and **9** with *N*-bromosuccinimide, resulted in benzylic bromination furnishing the corresponding bromides **10** and **11** in 76 % and 72 % yields respectively. Nucleophilic substitution on the benzylic bromide **10** and **11** with 2-mercaptobenzothiazole afforded sulfide **12** (74%) and **13** (71%), which on oxidation provided the requisite building block **4** and **5** respectively in good yields. Moving towards the projected strategy for the synthesis of **2** and **3**, the known aldehyde **14**<sup>13</sup> was subjected separately to olefination with sulfone **4** and **5** (Scheme 2). To our delight Julia olefination afforded corresponding *E*-alkene products **15** and **16** in 56% and 84% yields respectively. The olefinated products **15** and **16** upon hydrogenation using 10% Pd/C as catalyst in ethyl acetate gave the corresponding alkane WA **17** and **18** in 91-92 % yield. For the incorporation of alkyl chain, the alkane WA **17** and **18** were now treated with heptylmagnesium bromide at 0 °C. In case of **17** as the substrate, the reaction afforded the corresponding ketone **19** in 73% yields, whereas with the isomeric substrate **18**, the anticipated ketone **21** was obtained in 10% yield. Grignard reaction with the substrate **18** afforded an additional product. Careful analysis of the <sup>1</sup>H NMR data for the additional product, particularly the integration values [0.898-0.858 ppm (m, 6H) and 1.26-1.35 ppm (m, 16H)], indicated presence of two alkyl residues. The presence of a signal at 205.6 ppm in <sup>13</sup>C-NMR spectrum, hinted against the over-addition product, on the amide functionality.



**Reagents and conditions :** (i)  $\text{SOCl}_2$  (1.3 eq), dry DCM, reflux, 12h, then  $\text{Me(MeO)NH.HCl}$  (1.3eq),  $\text{Et}_3\text{N}$  (2eq),  $0^\circ\text{C}$  r.t, 6h, **8** (76%), **9** (70%); (ii) NBS(1.3 eq), AIBN,  $\text{CCl}_4$ ,  $70^\circ\text{C}$ , 24h, **10** (76%), **11** (72%); (iii) 2-Mercaptobenzothiazole (1.2 eq), dry DCM,  $\text{Et}_3\text{N}$  (2.5 eq), **12** (74%), **13** (71%); (iv)  $\text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O}$ ,  $\text{H}_2\text{O}_2$  (15 eq), Methanol, r.t, 12h, **4** (81%), **5** (81%)

### Scheme 1. Synthesis of building block **4** and **5**.



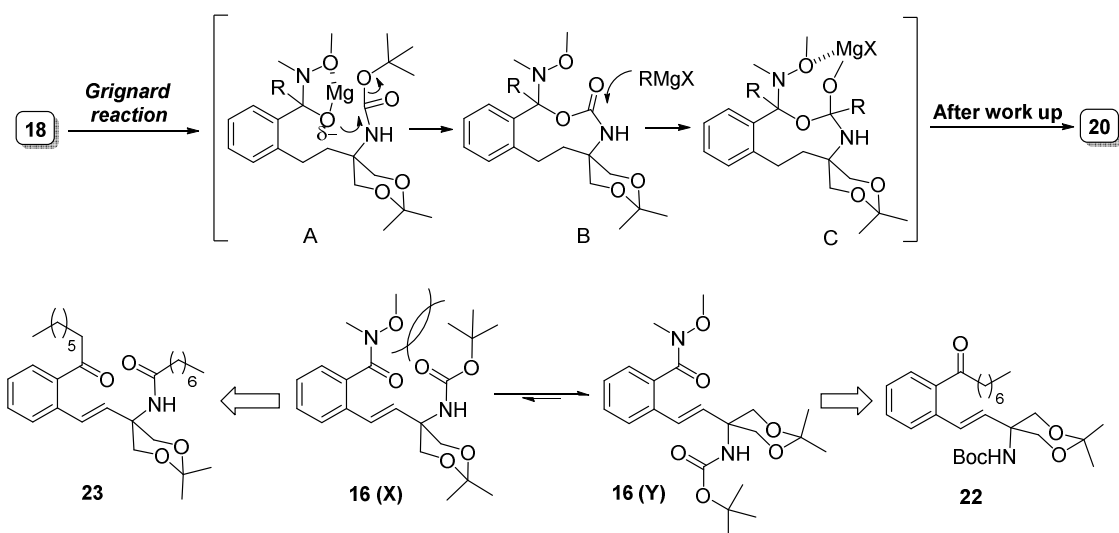
**Reagents and conditions :** (i)  $\text{NaH}$  (60%), dry DMF,  $0^\circ\text{C}$ -r.t, 4-5h, **15** (56%), **16** (84%); (ii)  $\text{H}_2$ , Pd/C,  $\text{EtOAc}$ , r.t, 12h, **17** (92%), **18** (91%); (iii) Heptylmagnesium bromide, Dry THF,  $0^\circ\text{C}$ - $10^\circ\text{C}$ , 3h, **19** (73%), **20** (20%), **21** (10%); (iv) Heptylmagnesium bromide, Dry THF,  $0^\circ\text{C}$ - $10^\circ\text{C}$ , 3h, **22** (48%), **23** (7%).

### Scheme 2. Synthesis of ketone **19** and **22**.

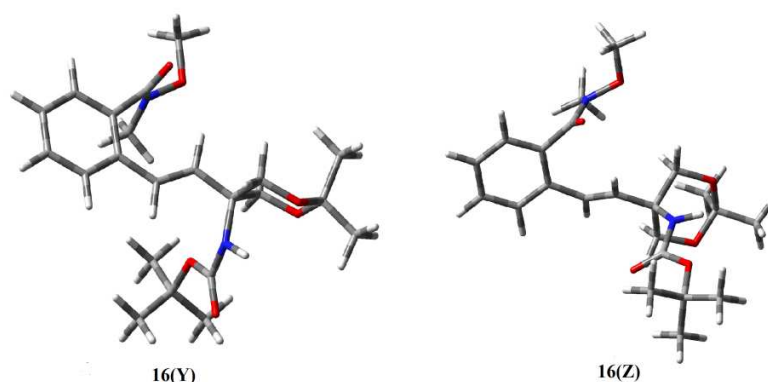
However, the conspicuous absence of the *t*-butoxy residue of the NHBoc functionality, hinted addition of the  $\text{CH}_3(\text{CH}_2)_6\text{MgBr}$  on the carbamate functionality, and this was supported by the presence of a signal at 174.1 ppm in  $^{13}\text{C}$ -NMR spectrum. The DEPT spectrum further confirmed that this signal corresponded to quaternary carbon. Hence the additional product, obtained in 20% yield, besides the desired ketone **21** (10%) was found to be **20**. The ESI mass spectrum also confirmed this understanding.  $m/z$   $[\text{M}+\text{H}]^+$  Calcd. For  $\text{C}_{30}\text{H}_{50}\text{NO}_4$  is 488.3740 found 488.3720. The formation of product **20** resulting from the addition of a second equivalent of Grignard reagent on to carbamate carbonyl functionality was a surprise, because such a process did not occur in the case of *meta*-isomer, substrate **17**. Presuming that the stirring of reaction mixture at room temperature was responsible for the additional addition to carbamate functionality, reaction was conducted at  $-10\text{ }^\circ\text{C}$ . However at this temperature, there was no reaction and starting material was recovered. These results were intriguing, in the light of successful addition of Grignard reagent onto the substrate **17** using same set of reactions and conditions.

This problem was unique to this substrate **18**, wherein the reaction site had another functionality appended in the vicinity at the *ortho*-position. The obtainment of the product **20** implies that the tetrahedral intermediate **A** resulting from the addition of first equivalent of heptylmagnesium bromide onto WA functionality, initiates internal addition onto the proximate carbamate carbonyl group in case of substrate **18**, thereby facilitating the second addition to the carbamate carbonyl through the sequence, **A**  $\rightarrow$  **B**  $\rightarrow$  **C** (Figure 2). With this rationale, we contested to use alkene substrate **16**, as a suitable alternative to **18** for the Grignard addition. The *E*-geometry of the alkene should probably keep the NHBoc containing residue away from the reaction site. The reaction with heptylmagnesium bromide at  $0\text{ }^\circ\text{C}$ , indeed resulted in much better yield of the anticipated ketone **22** (48%), although compound **23** resulting from addition of two heptyl-residues was also obtained as a minor component (7%). The formation of double addition product, **23**, could be due to the presence of conformer **16X**, wherein intramolecular displacement of *t*-butoxy can be envisaged as proposed earlier in the intermediate **A** for substrate **18**.

For validation and further understanding of the arguments presented, the stabilities of conformers **16(X)** and **16(Y)** were evaluated using Gaussian 09 program.<sup>14</sup> The calculated electronic and thermal energies have shown that conformer **16(X)** is unstable. In addition to **16(Y)** there is another conformer possible, **16(Z)** (Figure 3). The sum of electronic and thermal energies for these conformers, **16(Y)** and **16(Z)** are  $-889714.4\text{ kcal/mol}$  and  $-889715.7\text{ kcal/mol}$  respectively. So from this observation we can conclude that formation of product **22** is through the conformers **16(Y)** and/or **16(Z)** collectively.

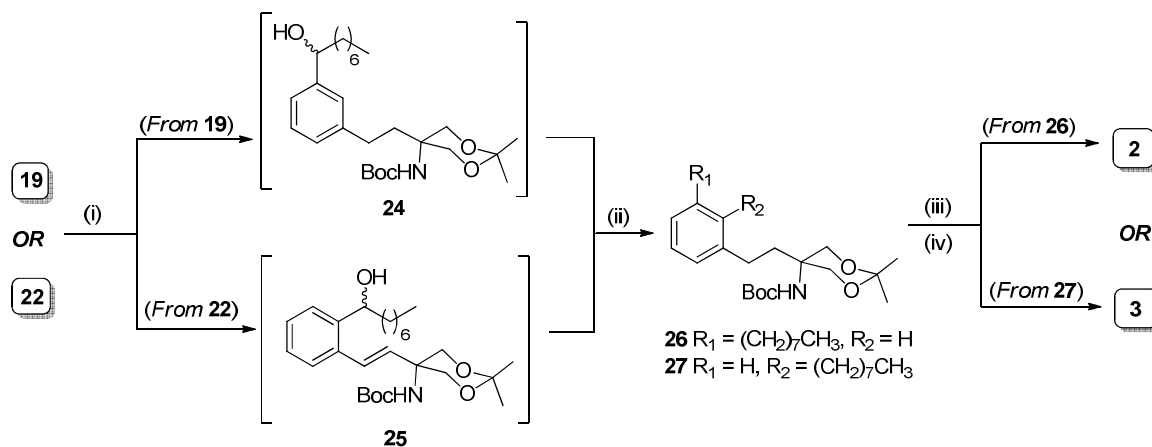


**Figure 2.** Rationalisation for the formation of compounds 20 and 23.



**Figure. 3** Stable conformers of alkene 16.

With ketone **19** and **22** in hand, it paved the way for the targeted synthesis of **2** and **3** (Scheme 3). The ketone functionality of **19** and **22** was reduced by using  $\text{NaBH}_4$  in methanol to give mixture of benzylic alcohols **24** and **25** respectively in good yields. To effect deoxygenation of benzylic alcohol, the compound **24** was subjected to hydrogenation by using 10% Pd/C in EtOAc/Acetic acid (1:1) mixture as solvent to afford deoxygenated compound **26** (*meta*-isomer) in 78% yield. In case of *ortho*-isomer **25** while deoxygenation, double bond also reduced and we isolated compound **27** in 75% yield. Final removal of acetonide and *N*-Boc protection was accomplished in a single step by treatment with TFA/ $\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$  (2:2:1) at room temperature. The free base of **2** and **3** were converted to their hydrochloride salt by treatment with dry HCl-Et<sub>2</sub>O in THF. The <sup>1</sup>H and <sup>13</sup>C NMR spectral data of **2** and **3** was matched with literature reported data.



**Reagents and conditions** : (i)  $NaBH_4$ , MeOH,  $0^\circ C-5^\circ C$ , 0.5h, **24** (78%), **25** (84%); (ii)  $H_2$ , Pd/C, EtOAc/AcOH (1:1), r.t., 12h, **26** (78%), **27** (75%); (iii) TFA/DCM/ $H_2O$  (2:2:1), r.t., 12h; (iv) Dry THF, Ethereal HCl, **2** (61%), **3** (68%) over two steps.

**Scheme 3.** Synthesis of positional isomers of FTY720, **2** and **3**.

## Conclusions

Synthesis of two new bifunctional building blocks containing Weinreb amide functionality has been achieved starting from *m*- and *o*-toluic acid. These building blocks are conveniently synthesized on gram scale quantities and have enabled synthesis of positional isomers, **2** and **3** of FTY720. Julia olefination and Grignard reaction are the key steps for the synthesis. This is second synthesis for positional isomers of FTY720. The route has additional inbuilt potential of varying polar head group and lipophilic carbon chain. The aim to study their aggregating ability in aqueous solutions and interaction with lipid bilayer membranes for comparison with FTY720, has been initiated and will be reported elsewhere in due course of time.

## Experimental Section

**General.** High resolution NMR experiments were recorded on BRUKER AV 400 FT NMR and AV 500 FT NMR instrument operating at 400 MHz and 500 MHz respectively using tetramethylsilane (TMS) as the internal standard. Infra-Red spectra were recorded using JASCO FT/IR spectrophotometer. High Resolution Mass Spectra (HRMS) were recorded on a MICRO Q TOF mass spectrometer using ESI technique at 10eV. Melting points were determined and are uncorrected. For the reaction purposes and column chromatography, distilled and dry solvents were used. For column chromatography, 100-200 mesh size silica gels were used. All the reactions were followed up by a TLC analysis. This was done using precoated 'MERCK F<sub>254</sub>' plates. The solvent system used throughout, unless otherwise specified, was ethyl acetate-hexane with various percentage of polarity depending on the nature of the substrate. The spot detection

on TLC was done by exposure of plate under UV light or dipping in to the solution of Hanessian's stain or ninhydrin stain followed by charring on hot plate.

**3-((Benzothiazol-2-ylthio)methyl)-*N*-methoxy-*N*-methylbenzamide (12).** To a solution of bromo compound **10** (4.020 g, 15.58 mmol) in 41 mL dry DCM (10 vol), 2-Mercaptobenzothiazole (3.130 g, 18.69 mmol) was added, followed by drop wise addition of Et<sub>3</sub>N (5.5 mL, 38.95 mmol) at 0 °C, allowed it to attain room temperature gradually and stirred it for 2 h. Then the reaction mixture was quenched by addition of 2 mL water, organic layer was washed with water and dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The crude product was then subjected to column chromatography using hexanes:ethyl acetate (80:20) to give the pure product **12**. Yellowish liquid; Yield: 74%; R<sub>f</sub>: 0.37 (hexanes: ethyl acetate, 7:3); IR (CHCl<sub>3</sub>): 3024, 2405, 2359, 1654, 1524, 1424, 1216, 928, 770 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz]: δ 7.88 (d, 1H, *J* 8 Hz, Ar-H), 7.73 (d, 1H, *J* 7.5 Hz, Ar-H), 7.6 (d, 1H, *J* 7.5 Hz, Ar-H), 7.41 (td, 1H, *J* 7.5 Hz, Ar-H), 7.35 (td, 2H, *J* 7.5 Hz, Ar-H), 7.3 (d, 1H, *J* 7.5 Hz, Ar-H), 7.27 (d, 1H, *J* 7.5 Hz, Ar-H), 4.73 (s, 2H, -CH<sub>2</sub>), 3.55 (s, 3H, -OCH<sub>3</sub>), 3.33 (s, 3H, -NCH<sub>3</sub>); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]: δ 153.2, 135.4, 134.7, 134.66, 130.7, 129.9, 127.5, 126.1, 126.1, 124.4, 121.7, 121.1, 61.2, 35.0, 34.9; HRMS: *m/z* [M+H]<sup>+</sup> Calcd. for C<sub>17</sub>H<sub>17</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub> 345.0731 found 345.0728.

**2-((Benzothiazol-2-ylthio)methyl)-*N*-methoxy-*N*-methylbenzamide (13).** Yellowish liquid; Yield: 71%; R<sub>f</sub>: 0.44 (hexanes: ethyl acetate, 7:3); IR (CHCl<sub>3</sub>): 3020, 2939, 2399, 2354, 1524, 1428, 1214, 924, 760, 672 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz]: δ 7.88 (d, 1H, *J* 8.0 Hz, Ar-H), 7.73 (d, 1H, *J* 8.0 Hz, Ar-H), 7.60 (d, 1H, *J* 7.6 Hz, Ar-H), 7.40-7.43 (m, 1H, Ar-H), 7.34-7.34 (m, 2H, Ar-H), 7.26-7.31 (m, 2H, Ar-H), 4.73 (s, 2H, -CH<sub>2</sub>), 3.56 (s, 3H, -OCH<sub>3</sub>), 3.34 (s, 3H, -NCH<sub>3</sub>); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]: δ 153.1, 135.4, 134.69, 134.61, 130.7, 129.8, 127.5, 126.1, 124.3, 121.6, 121.0, 61.2, 34.9, 32.3, 26.9; HRMS: *m/z* [M+H]<sup>+</sup> Calcd. for C<sub>17</sub>H<sub>17</sub>N<sub>2</sub>O<sub>2</sub>S<sub>2</sub> 345.0731 found 345.0730.

**3-((Benzothiazol-2-ylsulfonyl)methyl)-*N*-methoxy-*N*-methylbenzamide (4).** To a solution of **12** (3.900 g, 11.32 mmol) in 39 mL methanol (10 vol), Sodium tungstate dihydrate (3.730 g, 11.32 mmol) was added, followed by addition of H<sub>2</sub>O<sub>2</sub> (19.2 mL) at room temperature and allowed to stir for 12 h. After completion of reaction, solvent was evaporated and the organic materials were extracted in ethyl acetate, washed with water. The combined organic layer was then dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to get crude compound which was purified by column chromatography to get pure compound **4**. White solid; mp 98-100 °C Yield: 81%; R<sub>f</sub>: 0.14 (hexanes: ethyl acetate, 7:3); IR (CHCl<sub>3</sub>): 3208, 3018, 2355, 1707, 1508, 1335, 1216, 929, 775, 750 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 400 MHz]: δ 8.25 (d, 1H, *J* 8.4 Hz, Ar-H), 7.93 (d, 1H, *J* 8.0 Hz, Ar-H), 7.63-7.67 (m, 3H, Ar-H), 7.58 (td, 1H, *J*<sub>1</sub> 8.0 Hz, *J*<sub>2</sub> 1.2 Hz, Ar-H), 7.38 (d, 1H, *J* 7.6 Hz, Ar-H), 7.33 (t, 1H, *J* 8.0 Hz, Ar-H), 4.79 (s, 2H, -CH<sub>2</sub>), 3.41 (s, 3H, -OCH<sub>3</sub>), 3.27 (s, 3H, -NCH<sub>3</sub>); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 100 MHz] δ 168.8, 165.2, 152.7, 137.1, 135.0, 133.3, 131.1, 129.4, 128.9, 128.3, 127.9, 126.3, 125.7, 122.4, 61.2, 60.8, 33.7; HRMS: *m/z* [M+H]<sup>+</sup> Calcd. for C<sub>17</sub>H<sub>17</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub> 377.0630 found 377.0618.



**3-((Benzo[d]thiazol-2-ylsulfonyl)methyl)-N-methoxy-N-methylbenzamide (5).** White solid; mp : 92-94 °C; Yield : 81%  $R_f$  0.14 (hexanes: ethyl acetate, 7:3); IR (CHCl<sub>3</sub>): 3210, 3018, 2359, 1651, 1335, 1213, 1017, 925, 869, 760 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz]:  $\delta$  8.24 (dt, 1H,  $J_1$  8.0 Hz,  $J_2$  1.0 Hz, Ar-H), 7.96 (dd, 1H,  $J_1$  7.5 Hz,  $J_2$  0.5 Hz, Ar-H), 7.64 (td, 1H,  $J_1$  8.0 Hz,  $J_2$  1.0 Hz, Ar-H), 7.58 (td, 1H,  $J_1$  8.0 Hz,  $J_2$  1.0 Hz, Ar-H), 7.47 (s, 1H, Ar-H), 7.31-7.39 (m, 3H, Ar-H), 5.14 (s, 2H, -CH<sub>2</sub>), 3.62 (bs, 3H, -OCH<sub>3</sub>), 3.34 (s, 3H, -NCH<sub>3</sub>); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]:  $\delta$  165.6, 152.8, 137.1, 133.3, 1130.2, 28.8, 128.2, 127.8, 126.3, 125.72, 125.66, 124.96, 122.43, 122.38, 61.2, 57.6, 29.8; HRMS:  $m/z$  [M+H]<sup>+</sup> Calcd. for C<sub>17</sub>H<sub>17</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub> 377.0630 found 377.0624.

**(E)-tert-Butyl(5-(3-(methoxy(methyl)carbamoyl)styryl)-2,2-dimethyl-1,3-dioxan-5-yl)carbamate (15).** To a suspension of NaH (0.248 g, 4.14 mmol) in dry DMF, a solution of sulfone **4** (1.560 g, 4.14 mmol) was added at 0 °C. Immediately colour of the reaction mixture changes to yellow. After 5-10 mins, a solution of aldehyde **14** (1.500 g, 5.79 mmol) in dry DMF was added to the reaction mixture. Then reaction mixture was allowed to warm at room temperature and stirred for 4 h. After that reaction mixture was quenched by adding 5 mL saturated NH<sub>4</sub>Cl solution. The aqueous layer was extracted with 50 mL ethyl acetate, washed with brine (2 times). The combined organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to get crude product, which was subjected to column chromatography to get pure compound **15**. Yellowish gummy; Yield: 56%;  $R_f$ : 0.37 (hexanes: ethyl acetate, 1:1); IR (CHCl<sub>3</sub>): 3018, 2955, 2404, 2359, 1651, 1521, 1213, 764, 670 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz],  $\delta$  7.65 (s, 1H, Ar-H), 7.51 (d, 1H,  $J$  7.5 Hz, Ar-H), 7.43 (d, 1H,  $J$  8.0 Hz, Ar-H), 7.32 (t, 1H,  $J$  8.0 Hz, Ar-H), 6.54 (d, 1H,  $J$  16.5 Hz, olefin-H), 6.24 (d, 1H,  $J$  16.5 Hz, olefin-H), 5.27 (s, 1H, N-H), 3.97 (d, 2H,  $J$  11.5 Hz, equatorial-H), 3.90 (d, 2H,  $J$  11.5 Hz, axial-H), 3.53 (s, 3H, -OCH<sub>3</sub>), 3.34 (s, 3H, -NCH<sub>3</sub>), 1.48 (s, 3H), 1.46 (s, 3H), 1.43 (s, 9H); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]:  $\delta$  169.8, 155.0, 136.6, 134.5, 129.8, 129.2, 128.6, 128.3, 127.4, 126.4, 98.5, 66.2, 61.2, 53.2, 33.9, 28.5, 27.8, 19.5; HRMS:  $m/z$  [M+H]<sup>+</sup> Calcd. for C<sub>22</sub>H<sub>33</sub>N<sub>2</sub>O<sub>6</sub> 421.2339 found 421.2350.

**(E)-tert-butyl(5-(2-(methoxy(methyl)carbamoyl)styryl)-2,2-dimethyl-1,3-dioxan-5-yl)carbamate (16).** White solid; mp 68-70 °C; Yield : 84%;  $R_f$  0.64 (hexanes: ethyl acetate, 5:5); IR (CHCl<sub>3</sub>): 3210, 3021, 2931, 2359, 1707, 1508, 1213, 1017, 925, 764 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz]:  $\delta$  7.51 (d, 1H,  $J$  8.0 Hz, Ar-H), 7.33 (t, 1H,  $J$  8.0 Hz, Ar-H), 7.23-7.27 (m, 2H, Ar-H), 6.62 (d, 1H,  $J$  16.5 Hz, olefin-H), 6.21 (d, 1H,  $J$  16.0 Hz, olefin-H), 5.21 (s, 1H, N-H), 3.95 (d, 2H,  $J$  11.5 Hz, equatorial-H), 3.86 (d, 2H,  $J$  11.5 Hz, axial-H), 3.46 (s, 3H, -OCH<sub>3</sub>), 3.26 (s, 3H, -NCH<sub>3</sub>), 1.45 (s, 3H), 1.44 (s, 3H) 1.42 (s, 9H); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]:  $\delta$  154.8, 134.2, 133.95, 130.9, 129.5, 127.5, 126.9, 125.9, 125.1, 98.4, 66.1, 61.2, 53.1, 29.8, 29.7, 27.8, 19.5; HRMS:  $m/z$  [M+H]<sup>+</sup> Calcd. for C<sub>22</sub>H<sub>33</sub>N<sub>2</sub>O<sub>6</sub> 421.2339 found 421.2318.

**tert-Butyl(5-(3-(methoxy(methyl)carbamoyl)phenylethyl)-2,2-dimethyl-1,3-dioxan-5-yl)carbamate (17).** To a solution of compound **15** (1.210 g, 2.89 mmol) in 8.7 mL ethyl acetate, Pd/C (0.243 g, 20 wt%) was added and reaction mixture was stirred under H<sub>2</sub> atmosphere for 12 h at room temperature. Then reaction mixture filtered through celite pad, concentrated under vacuum to get pure compound **17**. White solid; mp 78-80 °C; Yield: 92%;  $R_f$  : 0.37 (hexanes:

ethyl acetate, 1:1); IR (CHCl<sub>3</sub>): 3208, 3015, 2363, 1707, 1508, 1420, 1328, 1213, 1017, 925, 768 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz]: δ 7.45-7.46 (m, 2H, Ar-H), 7.26-7.30 (m, 2H, Ar-H), 5.01 (s, 1H, N-H), 3.89 (d, 2H, *J* 12.0 Hz, equatorial-H), 3.68 (d, 2H, *J* 11.5 Hz, axial-H), 3.55 (s, 3H, -OCH<sub>3</sub>), 3.33 (s, 3H, -NCH<sub>3</sub>), 2.57-2.61 (m, 2H, -CH<sub>2</sub>), 1.97-2.00 (m, 2H, -CH<sub>2</sub>), 1.46 (s, 9H), 1.43 (s, 3H), 1.41 (s, 3H); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]: δ 170.2, 142.0, 134.4, 130.1, 128.24, 128.18, 125.8, 98.6, 66.4, 61.2, 51.1, 60.5, 33.6, 32.1, 29.8, 29.1, 28.6; HRMS: *m/z* [M+H]<sup>+</sup> Calcd. for C<sub>22</sub>H<sub>35</sub>N<sub>2</sub>O<sub>6</sub> 423.2495 found 423.2486.

**tert-Butyl(5-(2-(methoxy(methyl)carbamoyl)phenylethyl)-2,2-dimethyl-1,3-dioxan-5-yl)-carbamate (18).** Gummy liquid, Yield : 91%; R<sub>f</sub>: 0.67 (hexanes: ethyl acetate, 1:1); IR (CHCl<sub>3</sub>): 3716, 3025, 2359, 1710, 1662, 1508, 1216, 1024, 929, 768 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz]: δ 7.17-7.32 (m, 4H, Ar-H) 5.14 (s, 1H, N-H), 3.98 (d, 2H, *J* 9.5 Hz, equatorial-H), 3.63 (d, 2H, *J* 11.5 Hz, axial-H), 3.51 (s, 3H, -OCH<sub>3</sub>), 3.29 (s, 3H, -NCH<sub>3</sub>), 2.54 (t, 2H, *J* 8.5 Hz, -CH<sub>2</sub>), 1.98-2.01 (m, 2H, -CH<sub>2</sub>), 1.42-1.44 (m, 12H), 1.39 (s, 3H); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]: δ 157.1, 155.0, 139.3, 134.7, 129.6, 126.4, 125.8, 98.4, 97.4, 79.2, 66.0, 62.5, 61.2, 51.8, 33.6, 28.4, 26.7, 26.5, 21.0 14.2; HRMS: *m/z* [M+H]<sup>+</sup> Calcd. for C<sub>22</sub>H<sub>35</sub>N<sub>2</sub>O<sub>6</sub> 423.2495 found 423.2515.

**tert-Butyl(2,2-Dimethyl-5-(3-octanoylphenylethyl)-1,3-dioxan-5-yl)carbamate (19).** The Grignard reagent was prepared by heating Mg turnings with a piece of I<sub>2</sub> under vacuum. Then dry THF was added to it followed by heptyl bromide (1.2 mL, 7.60 mmol). Then this mixture was heated at 60 °C for 15-20 min till Mg dissolved. To this solution a solution of amide **17** (0.640 g, 1.52 mmol) was added at 0 °C in inert atmosphere. Then reaction mixture was warmed to room temperature and stirred for 3 h. Subsequent quenching of the reaction mixture was achieved by addition of saturated solution of ammonium chloride. The aqueous layer was extracted with ethyl acetate (20 mL × 3). Combined organic layer was washed with water (20 mL × 2), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to get crude product. Then the crude product was subjected to column chromatography using hexanes: ethyl acetate (92:8) mixture to get pure compound **19**. White solid; mp 54-56 °C Yield: 73%; R<sub>f</sub>: 0.74 (hexanes: ethyl acetate, 7:3); IR (CHCl<sub>3</sub>): 3015, 2398, 1703, 1525, 1420, 1206, 929, 760, 673 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 400 MHz]: δ 7.74-7.76 (m, 2H, Ar-H), 7.32-7.38 (m, 2H, Ar-H), 5.02 (s, 1H, N-H), 3.89 (d, 2H, *J* 11.6 Hz, equatorial-H), 3.69 (d, 2H, *J* 11.6 Hz, axial-H), 2.93 (t, 2H, *J* 7.6 Hz, -COCH<sub>2</sub>) 2.62 (t, 2H, *J* 8.4 Hz, -CH<sub>2</sub>), 1.99 (t, 2H, *J* 8.0 Hz, -CH<sub>2</sub>), 1.71 (t, 2H, *J* 7.2 Hz, -CH<sub>2</sub>), 1.47 (s, 9H), 1.43 (s, 3H, -CH<sub>3</sub>), 1.41 (s, 3H, -CH<sub>3</sub>), 1.25-1.33 (m, 8H), 0.86-0.89 (m, 3H); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 100 MHz]: δ 200.9, 155.05, 142.7, 137.4, 133.1, 128.8, 128.0, 126.0, 98.6, 79.6, 66.5, 63.2, 51.8, 38.8, 33.7, 31.8, 29.5, 29.3, 29.1, 28.6, 25.8, 24.5, 22.7, 19.9, 14.2; HRMS: *m/z* [M+H]<sup>+</sup> Calcd. for C<sub>27</sub>H<sub>44</sub>NO<sub>5</sub> 462.3219 found 462.3237.

**N-(2,2-Dimethyl-5-(2-octanoylphenethyl)-1,3-dioxan-5-yl)octanamide (20).** Gummy liquid; Yield: 20%; R<sub>f</sub>: 0.5 (hexanes: ethyl acetate, 8:2); IR (CHCl<sub>3</sub>): 3019, 2966, 2401, 2360, 1653, 1520, 1424, 1215, 928, 752 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz]: δ 7.69 (dd, 1H, *J*<sub>1</sub> 7.5 Hz, *J*<sub>2</sub> 1.0 Hz, Ar-H), 7.41 (td, 1H, *J*<sub>1</sub> 7.5 Hz, *J*<sub>2</sub> 1.0 Hz, Ar-H), 7.26-7.32 (m, 2H, Ar-H), 6.62 (s, 1H, N-H), 4.45 (d, 2H, *J* 11.5 Hz, equatorial-H), 3.58 (d, 2H, *J* 11.5 Hz, axial-H), 2.92 (t, 2H, *J* 7.5 Hz, -COCH<sub>2</sub>), 2.74 (t, 2H, *J* 8.5 Hz, -CH<sub>2</sub>), 2.28 (t, 2H, *J* 8.0 Hz, -CH<sub>2</sub>), 2.04 (t, 2H, *J* 8.0 Hz, -CH<sub>2</sub>),

1.65-1.72 (m, 4H, -CH<sub>2</sub>), 1.52 (s, 3H, -CH<sub>3</sub>), 1.43 (s, 3H, -CH<sub>3</sub>), 1.25-1.38 (m, 16H), 0.86-0.90 (m, 6H, -CH<sub>3</sub> terminal); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]: δ 205.4, 174.1, 142.5, 137.0, 131.91, 131.88, 129.2, 126.2, 98.4, 64.6, 53.0, 41.7, 37.7, 34.8, 31.8, 29.34, 29.3, 29.2, 27.9, 26.0, 24.6, 24.5, 23.4, 22.7, 14.2; HRMS: *m/z* [M+H]<sup>+</sup> Calcd. for C<sub>30</sub>H<sub>50</sub>NO<sub>4</sub> 488.3740 found 488.3720.

***tert*-Butyl(2,2-Dimethyl -5-(2-octanoylphenylethyl)-1,3-dioxan-5-yl)carbamate (21).** White solid; mp 116 °C; Yield : 10%; R<sub>f</sub> : 0.80 (hexanes: ethyl acetate, 8:2); IR (CHCl<sub>3</sub>): 3709, 3593, 3204, 3015, 2927, 2398, 2359, 1707, 1518, 1213, 1017, 929, 754, 670 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz]: δ 7.61 (dd, 1H, J<sub>1</sub> 7.7 Hz, J<sub>2</sub> 0.85 Hz, Ar-H), 7.38 (td, 1H, J<sub>1</sub> 7.5 Hz, J<sub>2</sub> 1.2 Hz, Ar-H), 7.23-7.29 (m, 2H, Ar-H), 5.37 (s, 1H, N-H), 4.08 (d, 2H, J 10.8 Hz, equatorial-H), 3.69 (d, 2H, J 12.0 Hz, axial-H), 2.88 (t, 2H, J 7.5 Hz, -COCH<sub>2</sub>), 2.72 (t, J 8.4 Hz, 2H, -CH<sub>2</sub>), 1.96 (t, 2H, J 8.3 Hz, -CH<sub>2</sub>), 1.66-1.72 (m, 2H, -CH<sub>2</sub>), 1.48 (s, 9H), 1.47 (s, 3H, -CH<sub>3</sub>), 1.43 (s, 3H, -CH<sub>3</sub>), 1.25-1.34 (m, 8H), 0.88 (t, 3H, J 7.0 Hz, -CH<sub>3</sub> terminal); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]: δ 205.1, 155.1, 142.3, 137.9, 134.4, 131.6, 128.7, 126.0, 98.4, 65.9, 63.2, 62.2, 51.9, 41.9, 34.4, 32.9, 31.8, 29.4, 29.3, 28.6, 27.6, 26.5, 24.7, 22.7, 21.2, 14.2; HRMS: *m/z* [M+Na]<sup>+</sup> Calcd. for C<sub>27</sub>H<sub>43</sub>NO<sub>5</sub>Na 484.3039 found 484.3026.

**(*E*)-*tert*-Butyl (2,2-dimethyl-5-(2-octanoylstyryl)-1,3-dioxan-5-yl)carbamate (22).** White solid; mp 68 °C; Yield : 48%; R<sub>f</sub> : 0.63 (hexanes: ethyl acetate, 8:2); IR (CHCl<sub>3</sub>): 3210, 3018, 2938, 2359, 1701, 1510, 1213, 1020, 925, 775 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 400 MHz]: δ 7.56 (dd, 1H, J<sub>1</sub> 7.6 Hz, J<sub>2</sub> 0.8 Hz, Ar-H), 7.52 (d, 1H, J 8.0 Hz, Ar-H), 7.40 (td, 1H, J<sub>1</sub> 7.6 Hz, J<sub>2</sub> 0.8 Hz, Ar-H), 7.29 (td, 1H, J<sub>1</sub> 7.6 Hz, J<sub>2</sub> 0.8 Hz, Ar-H), 6.97 (d, 1H, J 16.4 Hz, olefin-H), 6.13 (d, 1H, J 16.4 Hz, olefin-H), 5.26 (s, 1H, N-H), 3.91-4.01 (m, 4H, -CH<sub>2</sub>), 2.86 (t, 2H, J 7.6 Hz, -COCH<sub>2</sub>), 1.64-1.71 (m, 2H, -CH<sub>2</sub>), 1.49 (s, 3H, -CH<sub>3</sub>), 1.46 (s, 3H, -CH<sub>3</sub>), 1.44 (s, 9H), 1.26-1.35 (m, 8H, -CH<sub>2</sub>), 0.87 (t, 3H, J 7.2 Hz, -CH<sub>3</sub> terminal); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 100 MHz]: δ 205.2, 154.96, 137.8, 136.6, 131.3, 131.2, 129.4, 128.2, 127.9, 127.5, 98.4, 79.7, 66.3, 53.1, 42.2, 31.8, 29.4, 29.3, 28.6, 28.1, 24.7, 22.7, 19.4, 14.2; HRMS: *m/z* [M+Na]<sup>+</sup> Calcd for C<sub>27</sub>H<sub>41</sub>NO<sub>5</sub>Na 482.2882 found 482.2873.

**(*E*)-*N*-(2,2-Dimethyl-5-(2-octanoylstyryl)-1,3-dioxan-5-yl)octanamide (23).** Gummy liquid; Yield: 7%; R<sub>f</sub> : 0.42 (hexanes: ethyl acetate, 8:2); IR (CHCl<sub>3</sub>): 3204, 3021, 2361, 1700, 1509, 1215, 925, 781 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 400 MHz]: δ 7.57 (dd, 1H, J<sub>1</sub> 7.6 Hz, J<sub>2</sub> 1.2 Hz, Ar-H); 7.53 (d, 1H, J 7.6 Hz, Ar-H), 7.39 (td, 1H, J<sub>1</sub> 8.0 Hz, J<sub>2</sub> 1.2 Hz, Ar-H), 7.28 (td, 1H, J<sub>1</sub> 7.6 Hz, J<sub>2</sub> 1.2 Hz, Ar-H), 6.92 (d, 1H, J 16.4 Hz, olefin-H), 6.18 (d, 1H, J 16.4 Hz, olefin-H), 6.08 (s, 1H, N-H), 4.08 (d, 2H, J 12.0 Hz, equatorial-H), 3.93 (d, 2H, J 12.0 Hz, axial-H), 2.86 (t, 2H, J 7.6 Hz, -CH<sub>2</sub>), 2.23 (t, 2H, J 8.0 Hz, -CH<sub>2</sub>), 1.61-1.71 (m, 4H, -CH<sub>2</sub>), 1.49 (s, 3H, -CH<sub>3</sub>), 1.44 (s, 3H, -CH<sub>3</sub>), 1.26-1.33 (m, 16H), 0.86-0.89 (m, 6H, -CH<sub>3</sub> terminal); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 100 MHz]: δ 205.2, 173.3, 137.5, 136.7, 131.5, 130.5, 129.3, 128.3, 128.1, 127.5, 98.5, 66.0, 53.7, 42.0, 37.4, 31.8, 29.4, 29.27, 29.17, 28.5, 25.95, 24.7, 22.7, 19.0, 14.2; HRMS: *m/z* [M+H]<sup>+</sup> Calcd. for C<sub>30</sub>H<sub>48</sub>NO<sub>4</sub> 486.3583 found 486.3594.

***tert*-Butyl (5-(3-octyl)phenylethyl)-2,2-dimethyl-1,3-dioxan-5-yl)carbamate (26).** The mixture of alcohol **24** (0.200 g, 0.43 mmol) was dissolved in mixture of acetic acid and ethyl acetate 2 mL (1:1). Then Pd/C (0.046 g, 10 mol%) was added to it, and reaction mixture was

stirred for 12 h in H<sub>2</sub> atmosphere at room temperature. Then reaction mixture was filtered through celite pad, concentrated under vacuum to get crude product. Then the crude product was subjected to column chromatography using hexanes: ethyl acetate (94:6) as eluent to get pure compound **26**. White solid; mp 42-44 °C; Yield : 78%; R<sub>f</sub> : 0.77 (hexanes: ethyl acetate, 8:2); IR (CHCl<sub>3</sub>): 3018, 2398, 1525, 1423, 1213, 1020, 925, 764, 663 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 400 MHz]: δ 7.17 (t, 1H, *J* 8.0 Hz, Ar-H), 6.98-6.99 (m, 3H, Ar-H), 4.99 (s, 1H, N-H), 3.91(d, 2H, *J* 11.6 Hz, equatorial-H), 3.68 (d, 2H, *J* 12.0 Hz, axial-H), 2.52-2.58 (m, 4H, -CH<sub>2</sub> benzylic), 1.98 (t, 2H, *J* 8.4 Hz, -CH<sub>2</sub>), 1.56-1.61 (m, 2H, -CH<sub>2</sub>), 1.48 (s, 9H), 1.44 (s, 3H, -CH<sub>3</sub>), 1.42 (s, 3H, -CH<sub>3</sub>), 1.26-1.30 (m, 10H), 0.881 (t, 3H, *J* 6.4 Hz, -CH<sub>3</sub> terminal); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 100 MHz]: δ 155.1, 143.3, 142.0, 128.6, 128.4, 126.1, 125.7, 98.5, 66.5, 51.9, 36.8, 36.1, 32.0, 31.7, 29.6, 29.4, 29.2, 28.6, 24.8, 22.8, 19.9, 14.2; HRMS: *m/z* [M+H]<sup>+</sup> Calcd. for C<sub>27</sub>H<sub>46</sub>NO<sub>4</sub> 448.3427 found 448.3414.

**tert-Butyl (5-(2-octyl)phenylethyl)-2,2-dimethyl-1,3-dioxan-5-yl)carbamate (27)**. Gummy liquid; Yield: 75%; R<sub>f</sub> : 0.70 (hexanes: ethyl acetate, 8:2); IR (CHCl<sub>3</sub>): 3025, 2401, 1521, 1423, 1216, 929, 757, 663 cm<sup>-1</sup>; <sup>1</sup>H NMR [CDCl<sub>3</sub>, 500 MHz]: δ 7.09-7.13 (bs, 4H, Ar-H), 5.02 (s, 1H, -NH), 3.95 (d, 2H, *J* 11.5 Hz, equatorial-H), 3.70 (d, 2H, *J* 11.5 Hz, axial-H), 2.55-2.62 (m, 4H, -CH<sub>2</sub> benzylic), 1.91-1.94 (m, 2H, -CH<sub>2</sub>), 1.54-1.59 (m, 2H, -CH<sub>2</sub>) 1.49 (s, 9H), 1.45 (s, 3H, -CH<sub>3</sub>), 1.43 (s, 3H, -CH<sub>3</sub>), 1.27-1.37 (m, 10H), 0.89 (t, 3H, *J* 7.0 Hz, -CH<sub>3</sub> terminal); <sup>13</sup>C NMR [CDCl<sub>3</sub>, 125 MHz]: δ 155.1, 140.7, 139.6, 129.4, 126.2, 126.1, 98.6, 66.5, 51.8, 33.7, 32.7, 32.0, 31.6, 29.9, 29.7, 29.4, 28.6, 27.6, 25.9, 22.8, 19.9, 14.2; HRMS: *m/z* [M+Na]<sup>+</sup> Calcd. for C<sub>27</sub>H<sub>45</sub>NO<sub>4</sub>Na 470.3246 found 470.3239.

**2-Aminohydrochloride-2-[2-(3-octylphenyl)ethyl]propane-1,3-diol (2)**. The compound **26** (0.170 g, 0.38 mmol) was dissolved in 1.14 mL (2:2:1) mixture of DCM, TFA and H<sub>2</sub>O respectively. Then reaction mixture was stirred for 12 h at room temperature. Then reaction mixture was quenched by saturated solution NaHCO<sub>3</sub> until the effervescence stopped. After that compound was extracted with 30 mL ethyl acetate and washed with 30 mL brine. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, evaporated under vacuum to get free amine as yellowish residue. Finally the residue was washed with hexanes to remove minor non-polar impurities. To a solution of amine in 2 mL THF, approximately 0.02 mL ethereal HCl was added at 0 °C and the mixture was allowed to stir at room temperature for 3 h. Then THF was evaporated under vacuum to get yellow residue, which was washed with hexanes (2-3 times) to get white solid compound **2**. White solid; mp 88-90 °C; Yield: 61%; IR (KBr): 3418, 3263, 3049, 2927, 2850, 2355, 1998, 1605, 1518, 1458, 1066, 778, 701 cm<sup>-1</sup>; <sup>1</sup>H NMR [DMSO-d<sub>6</sub>, 500 MHz]: δ 7.91(s, 3H, -NH<sub>3</sub>), 7.18 (t, 1H, *J* 7.5 Hz, Ar-H), 7.00-7.02 (m, 3H, Ar-H), 5.39 (s, 2H, -OH), 3.523-3.529 (bs, 4H), 2.50-2.59 (m, 4H, -CH<sub>2</sub> benzylic), 1.77-1.80 (m, 2H, -CH<sub>2</sub>), 1.54 (s, 2H, -CH<sub>2</sub>), 1.24-1.27 (m, 10H), 0.85 (t, 3H, *J* 7.0 Hz, -CH<sub>3</sub> terminal); <sup>13</sup>C NMR [DMSO, 125 MHz]: δ 142.4, 141.6, 128.2, 128.1, 125.8, 125.5, 60.98, 60.3, 35.2, 33.2, 31.3, 31.1, 28.8, 28.7, 28.6, 28.3, 22.1, 14.0; MS (ESI): *m/z* [M]<sup>+</sup> base peak found at 308 which corresponds to cation part of the compound **2**, Molecular formula C<sub>19</sub>H<sub>34</sub>NO<sub>2</sub>.

**2-Aminohydrochloride-2-[2-(2-octylphenyl)ethyl]propane-1,3-diol (3).** White solid; mp 142-144 °C; Yield: 68%; IR (KBr): 3390, 3281, 3039, 2920, 1602, 1510, 1458, 1058, 754 cm<sup>-1</sup>; <sup>1</sup>H NMR [DMSO, 500 MHz]:  $\delta$  7.93 (s, 3H, -NH<sub>3</sub>), 7.09-7.15 (m, 4H, Ar-H), 5.40 (s, 2H, -OH), 3.53-3.59 (m, 4H), 2.56-2.63 (m, 4H, -CH<sub>2</sub>), 1.72-1.75 (m, 2H, -CH<sub>2</sub>), 1.47-1.53 (m, 2H, -CH<sub>2</sub>), 1.25-1.31 (m, 10H), 0.86 (t, 3H, *J* 7.0 Hz, -CH<sub>3</sub> terminal); <sup>13</sup>C NMR [DMSO-d<sub>6</sub>, 125 MHz]:  $\delta$  140.1, 139.3, 129.1, 128.9, 126.0, 125.9, 61.0, 60.2, 32.9, 31.8, 31.3, 31.0, 29.1, 28.9, 28.7, 25.2, 22.1, 14.0; MS (ESI): *m/z* [M]<sup>+</sup> base peak found at 308 which corresponds to cation part of the compound **3**, Molecular formula C<sub>19</sub>H<sub>34</sub>NO<sub>2</sub>.

## Acknowledgements

The authors thank DST New Delhi for funding toward the 400 MHz and 500 MHz NMR spectrometer to the Department of Chemistry, IIT Madras under the IRPHA scheme and ESI-MS facility under FIST program. S.R.B. is thankful to IIT-Madras for HTRA fellowship.

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