A new synthesis of amino acid-based enantiomerically pure substituted 2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxalines†‡

Krishnananda Samanta and Gautam Panda*

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A new series of enantiomerically pure 2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxalines were synthesized for the first time in twelve steps from 1-fluoro-2-nitrobenzene and *S*-amino acids with 13–20% overall yields. First use of intramolecular Mitsunobu cyclization for 1,2,3,4-tetrahydroquinoxalines followed by PPh_3/I_2/imidazole mediated 6-*exo-tet* cyclization were the key steps.

Introduction

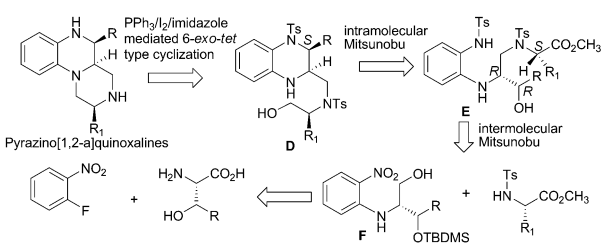
Nitrogen-containing benzo-fused tricycles such as pyrrolo[1,2-*a*]quinoxalines,[1] imidazo[1,5-*a*]quinoxalines,[2,3d] imidazo[1,2-*a*]quinoxalines,[3] [1,2,4]triazolo[4,3-*a*]quinoxalines,[3a,4,5] and 1*H*-imidazo[4,5-*b*]quinoxalines,[6] 2,3,4,4a-tetrahydro-1*H*-pyrazino-[1,2-*a*]quinoxalin-5-(6*H*)-ones[7] have a wide range of biological activities. Among these compounds, 2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxalines and 2,3,4,4a-tetrahydro-1*H*-pyrazino[1,2-*a*]quinoxalin-5-(6*H*)-ones are common structural units that are found in a wide range of biologically important and therapeutically useful agents. They are used as serotonin 5-hydroxytryptamine[7,8] (5-HT) receptor agonists. They are known to exhibit 5-HT_{2C} agonist binding along with antihypertensive activity.[9] 3-Substituted 2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxalines[10] exhibited no anorexigenic or stimulant activity at 60 mg kg^{-1} i. p. dose. 5-HT_{2C} receptor agonists are useful for the treatment of disorders such as obsessive-compulsive disorder, depression, anxiety, schizophrenia, obesity, type II diabetes migraine, sleep and eating disorders.

Mainly two synthetic approaches are known for the construction of 2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxalines. In the first approach,[10] condensation of quinoxaline-2-aldehyde with benzylamine followed by reduction, ring closure with diethyl oxalate, and LAH reduction are the key steps. It suffers from several drawbacks, giving 2-benzylamino-methyl-1,2,3,4-tetrahydroquinoxaline along with 2-methyl-1,2,3,4-tetrahydroquinoxaline when condensation at large scale was performed and the reduction was not stereospecific as well. In the second approach, quinoxalone was prepared from 4-carbobenzyloxypiperazine-2-carboxylic acid[7] and substituted 1-halo-2-nitrobenzene *via* reduction of an aromatic nitro group followed by lactam formation. Finally, reduction of quinoxalone with BH_3·THF furnished 2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxalines. In both approaches, only one ring (either **B** or **C**) of the pyrazino[1,2-*a*]quinoxaline nucleus was constructed on the available precursor.

We have been working on the synthesis and biology of *S*-amino acid-based chiral heterocycles and natural product like molecules.[11] In continuation of our program, we became interested in synthesizing a series of enantiomerically pure substituted 2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxalines following a new synthetic route based on amino acids. In our approach, both **B** and **C** rings were constructed with diversification obtained from different type of amino acids.

Results and discussion

The retrosynthetic strategy for pyrazino[1,2-*a*]quinoxaline is delineated in Scheme 1. We envisioned that the pyrazino[1,2-*a*]quinoxaline nucleus can be constructed by PPh_3/I_2/imidazole-mediated 6-*exo-tet* type cyclization from intermediate **D**, which could be readily obtained by intermolecular Mitsunobu cyclization[12] of **F** with *N*-tosyl amino acids methyl ester followed by intramolecular Mitsunobu cyclization of intermediate **E**. The preparation of the intermediate **F** is outlined in Scheme 2. To begin with, *S*-amino acids **2a–b** were reacted with 1-fluoro-2-nitrobenzene **1** in the presence of K_2CO_3 and dry DMF at 80 °C to furnish 2-nitrobenzene-protected amino acid derivatives, which were converted to their methyl esters **3a–b** in the presence of $SOCl_2$ and MeOH. In addition, it was experimented to know whether any racemization of the amino acids occurred upon nucleophilic aromatic substitution. The chiral HPLC of **3a** and **3b** revealed that the nucleophilic aromatic substitution of amino acid on 2-nitrofluorobenzene took place without any racemization (see the ESI‡). We used reference compound {mixture of *S*-**3b** and its

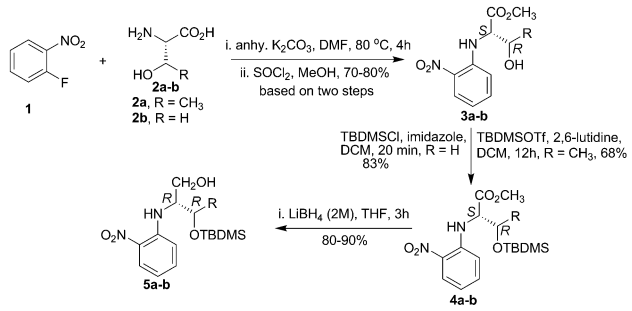


Scheme 1 Retrosyntetic analysis of pyrazino[1,2-*a*]quinoxalines

Medicinal and Process Chemistry Division, Central Drug Research Institute, Lucknow, 226001, UP, India. E-mail: gautam.panda@gmail.com, gautam_panda@cdri.res.in; Fax: 91-522-2623405; Tel: 91-522-2612411-18, Ext. 4385, 4469

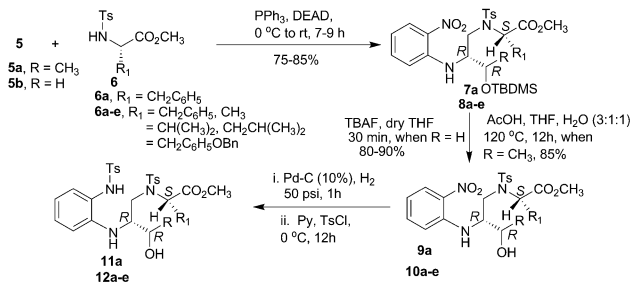
† Dedicated to Dr C. M. Gupta on the completion of his 65th birthday

‡ Electronic supplementary information (ESI) available: NMR and HPLC spectra. See DOI: 10.1039/c000029a



Scheme 2 Syntheses of compounds **5a–b**

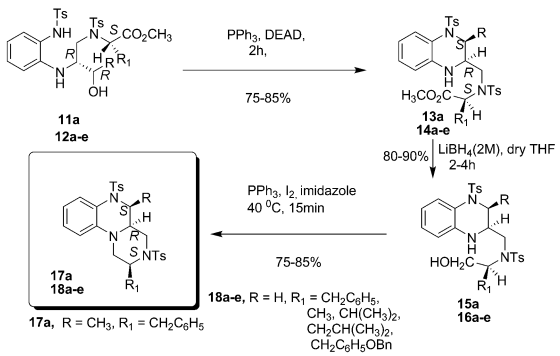
enantiomer *R*-**3b**} to check the condition that was suitable for the separation of racemic compounds. Silylation of **3** was performed under two different conditions. The secondary hydroxy of **4a** (R = CH_3) was protected using TBDMSOTf, 2,6-lutidine in dry DCM at –78 °C with 68% yield. The primary hydroxy of **4b** (R = H) was protected by treatment with TBDMSCl, imidazole in dry DCM with 83% yield. $LiBH_4$ reduction of **4a–b** furnished alcohols **5a–b** in 80–90% yield. The synthesis of intermediate **E** was achieved by treatment of **5a–b** with different *N*-tosyl protected amino acid methyl esters under Mitsunobu conditions to furnish **7a**, **8a–e** in 75–85% yield, Scheme 3.



Scheme 3 Syntheses of compounds **11a**, **12a–e**

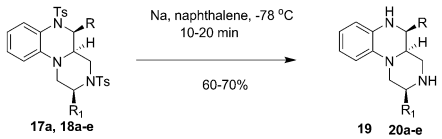
The tosyl derivatives of amino acids were synthesized in two steps; first amino acids were converted to their methyl esters by the treatment with $SOCl_2$ and MeOH, followed by tosylation with *p*-toluenesulfonyl chloride and triethylamine in the presence of dry DCM in good yields.

Desilylation of **7a** in the presence of AcOH–THF–H_2O (3 : 1 : 1) at reflux for 12 h, and **8a–e** by TBAF, gave alcohols **9a** and **10a–e**, respectively, in good yields. It is noted that a successful Mitsunobu displacement reaction is dependent on the pK_a associated with the incoming nucleophile and independent of the nucleophilicity of the nucleophile.[13] Hence, after reduction of the aromatic nitro group by 10% Pd on activated charcoal, the amino functionality was converted to its sulfonamide derivatives by treatment with pyridine and tosyl chloride to afford **11a**, **12a–e** in good yields. To achieve the target pyrazino[1,2-*a*]quinoxalines (Scheme 4), **11a**, **12a–e** were treated with DEAD/PPh_3 under Mitsunobu condition to furnish enantiomerically pure substituted 1,2,3,4-tetrahydroquinoxalines in 75–85% yields. $LiBH_4$ reduction of the ester gave alcohols **15a**, **16a–e**, in 80–90% yields. The targeted pyrazino[1,2-*a*]quinoxalines were obtained by PPh_3/I_2/imidazole-mediated 6-*exo*-*tet* cyclization of **15a**, **16a–e** to provide **17a**, **18a–e** in 75–85% yield.



Scheme 4 Syntheses of pyrazino[1,2-*a*]quinoxalines **17a**, **18a–e**

Both tosyl groups of the final molecules **17a**, **18a–e** were deprotected (Scheme 5) by using sodium naphthalenide[14] in dry THF with 60–70% yields (Table 1). All the final molecules were characterized by 1D NMR, mass, elemental analysis and the enantiomeric purity and overall yields are shown in Table 1.



Scheme 5 Deprotection of the tosyl groups (**17a**, **18a–e**)

Table 1 Yield of the tosyl groups deprotection step

Entry	Comp no.	Yield in deprotection (%)	Overall yield from **1** (%)
1	**17a**	63	13
2	**18a**	62	14
3	**18b**	65	17
4	**18c**	64	20
5	**18d**	68	17
6	**18e**	64	17

In summary, we have reported a twelve step synthesis of substituted 2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxalines with 13–20% overall yield from naturally abundant *S*-amino acids for the first time. Inter and intramolecular Mitsunobu cyclization, and PPh_3/I_2/imidazole-mediated 6-*exo*-*tet* cyclization were the key steps for the construction of the pyrazino[1,2-*a*]quinoxaline nucleus. Each step was operationally simple and high yielding conversion. Both the **B** and **C** ring were constructed with diversification from amino acids unlike the reported procedure.[7,10] Removal of the tosyl group with high yield is generally difficult. We have removed both tosyl groups of all the final molecules **17a**, **18a–e** with 60–70% yield using sodium naphthalenide protocol. Biological evaluations of this series are currently under way.

Experimental

General methods

All chemicals were purchased from Aldrich Milwaukee, WI. Melting points were determined on COMPLAB melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR RXI spectrometer. ^{1}H NMR and ^{13}C NMR

spectra were recorded on a Brucker DPX-200 or DPX-300 spectrometer using $CDCl_3$ as solvent. Tetramethylsilane (0.00 ppm) served as an internal standard in ^{1}H NMR and $CDCl_3$ (77.0 ppm) in ^{13}C NMR. Chemical shifts are expressed in parts per million (ppm). Mass spectra were recorded on JEOL SX 102 spectrometer. Elemental analyses were done on Varian EL-III C H N analyzer (Germany). The enantiomeric excess was determined by Lichro-CART Chiradex column (250 × 4 mm, 5 μm) using water and acetonitrile as eluent at 30 °C.

Experimental procedures and characterization data of selected examples

General experimental procedure for the synthesis of (3). To a solution of **2a–b** (1.2 eq) in 30 mL of DMF was added K_2CO_3 (3 equiv.) at 25 °C followed by *ortho*-nitro aryl fluorides (1 equiv.) and was stirred for 4 h at 80 °C. K_2CO_3 was filtered off and DMF was removed under vacuum. It was diluted with 30 mL MeOH and followed by $SOCl_2$ (2 equiv.) at 0 °C for 3–4 h. After removal of solvent, it was diluted with water and added excess $NaHCO_3$ to neutralize HCl and extracted with ethyl acetate. Removal of solvent and column chromatography on silica gel with AcOEt–hexane (1.5 : 8.5) as eluent furnished **3**.

(2*S*,3*R*)-Methyl-3-hydroxy-2-(2-nitrophenylamino)butanoate (3a). Yellow oil; yield, 75% (two steps); R_f, 0.54 (6.5 : 3.5), hexane–ethyl acetate); $[\alpha]_D^{30}$ = +121.7 (*c* 0.10, MeOH), HPLC analysis: ee > 99 (t_R = 5.5 min, CH_3CN–H_2O); IR (neat, cm^{-1}): 3539, 3364, 2904, 1740, 1621, 1573, 1432, 742. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, 1H, J = 7.9), 8.20 (dd, 1H, J_1 = 1.4, J_2 = 8.5), 7.47-7.41 (m, 1H), 6.79-6.70 (m, 2H), 4.42-4.40 (m, 1H), 4.21 (q, 1H, J = 3.1), 3.79 (s, 3H), 2.71 (bs, 1H), 1.35 (d, 3H, J = 6.4). ^{13}C NMR (75 MHz, $CDCl_3$) 171.6, 144.4, 136.2, 132.9, 127.0, 116.4, 113.8, 67.8, 61.0, 52.7, 19.9. MS (ESI): m/z 255 [M+H]$^+$.

(2*S*,3*R*)-Methyl-3-(*tert*-butyldimethylsilyloxy)-2-(2-nitrophenylamino)butanoate (4a). To a stirred solution of **3a** (1 g, 3.93 mmol) in anhydrous DCM (15 mL) were added TBDMS-OTf (0.82 ml, 4.72 mmol) and 2,6-lutidine (0.68 ml, 5.89 mmol) at –78 °C and stirred for 12 h. It was diluted with water and extracted with DCM. Removal of solvent and column chromatography on silica gel with AcOEt–hexane (1.0 : 9.0) as eluent furnished **4a** (984 mg, 68%) as a yellow oil. R_f, 0.51 (9.5 : 0.5), hexane–ethyl acetate); IR (neat, cm^{-1}): 3368, 2957, 2367, 1742, 1627, 1579, 1434, 1151, 760.^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (d, 1H, J = 8.6), 8.22 (dd, 1H, J_1 = 1.5, J_2 = 8.5), 7.43-7.37 (m, 1H), 6.71-6.61 (m, 2H), 4.62-4.55 (m, 1H), 4.11-4.08 (m, 1H), 3.73 (s, 3H), 1.32 (d, 3H, J = 6.3), 0.92 (s, 9H), 0.12-0.03 (m, 6H). MS (ESI): m/z 369 [M+H]$^+$.

(2*R*,3*R*)-3-(*tert*-Butyldimethylsilyloxy)-2-(2-nitrophenylamino)-butan-1-ol (5a). To a stirred solution of **4a** (650 mg, 1.76 mmol) in anhydrous THF (10 mL) was added a solution of $LiBH_4$ (2M) (1.05 mL, 2.11 mmol) at 0 °C. It was stirred at RT for 3 h and was quenched by ethyl acetate followed by water at 0 °C. After usual work-up, the crude was chromatographed on silica gel with hexane–ethyl acetate, 8.5 : 1.5 as eluent to furnish **5a** (510 mg, 85%) as a yellow oil. R_f 0.51 (AcOEt–hexane, 2.5 : 7.5); IR (Neat, cm^{-1}): 3543, 3364, 2951, 1622, 1584, 1421, 788. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (d, 1H, J = 8.4), 8.18 (dd, 1H, J_1 = 1.5, J_2 = 8.6), 7.43-7.37 (m, 1H), 6.97 (d, 1H, J = 8.6), 6.65-6.60 (m, 1H), 4.31-4.24 (m, 1H), 3.78-3.75 (m, 2H), 3.68-3.60 (m, 1H), 2.09 (bs, 1H), 1.23 (d, 3H, J = 6.3), 0.95 (s, 9H), 0.13-0.11 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) 145.7, 136.1, 132.1, 127.0, 115.2, 114.1, 66.8, 62.5, 59.1, 25.7, 20.9, 17.9, -4.3, -5.1. MS (ESI): m/z 341 [M+H]$^+$.

(*R*)-3-(*tert*-Butyldimethylsilyloxy)-2-(2-nitrophenylamino) propan-1-ol (5b). Same procedure as for **5a**. Yellow oil. Yield, 87%; R_f, 0.52 (7.0 : 3.0, hexane–ethyl acetate); IR (neat, cm^{-1}): 3548, 3361, 2958, 1621, 1586, 1427, 771.^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (d, 1H, J = 7.8), 8.17 (dd, 1H, J_1 = 1.4, J_2 = 8.6), 7.44-7.38 (m, 1H), 6.93 (d, 1H, J = 8.7), 6.67-6.61 (m, 1H), 3.97-3.75 (m, 5H), 2.29 (bs, 1H), 0.93 (s, 9H), 0.10-0.09 (m, 6H). MS (ESI): m/z 327 [M+H].

(*S*)-Methyl-2-(*N*-((2*R*,3*R*)-3-(*tert*-butyldimethylsilyloxy)-2-(2-nitrophenylamino)butyl)-4-methylphenylsulfonamido)-3-phenylpropanoate (7a). To a stirred solution of **5a** (220 mg, 0.64 mmol), **6a** (258 mg, 0.77 mmol) and triphenylphosphine (254 mg, 0.97 mmol) in THF (7 mL) was added DEAD (0.15 mL, 0.97 mmol) in THF drop wise at 0 °C and stirred for 2 h. It was allowed to warm to 25 °C and was stirred for an additional 5 h. It was stirred with 1 : 1 mixture of hexane : diethylether; triphenylphosphine oxide was filtered off. After usual work-up, and concentration of solution, the chromatography (eluent = hexane–ethyl acetate 8.5 : 1.5) of crude over silica gel furnished **7a** (350 mg, 83%) as a yellow oil. R_f 0.51 (8.0 : 2.0, hexane–ethyl acetate); IR (neat, cm^{-1}): 3362, 2953, 1739, 1621, 1513, 1352, 1161, 763. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (d, 1H, J = 9.3), 8.18 (dd, 1H, J_1 = 1.5, J_2 = 8.6), 7.69-7.66 (m, 2H), 7.45-7.40 (m, 1H), 7.26-7.21 (m, 5H), 7.12-7.08 (m, 3H), 6.66-6.61 (m, 1H), 4.60-4.55 (m, 1H), 4.28-4.23 (m, 1H), 4.16-4.09 (m, 1H), 3.59 (dd, 1H, J_1 = 6.1, J_2 = 15.2), 3.43 (dd, 1H, J_1 = 7.1, J_2 = 15.2), 3.31-3.23 (m, 4H), 2.83-2.76 (m, 1H), 2.41 (s, 3H), 1.18 (d, 3H, J = 6.2), 0.99 (s, 9H), 0.15-0.11 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) 170.0, 145.6, 144.0, 136.15, 136.06, 135.9, 132.2, 129.6, 129.0, 128.6, 127.6, 127.0, 126.9, 115.2, 114.7, 67.7, 62.5, 58.0, 51.8, 48.1, 36.2, 25.9, 21.5, 20.9, 18.0, -3.5, -4.8. MS (ESI): m/z 656 [M+H]$^+$. Anal. Calcd. (%) for $C_{33}H_{45}N_3O_7SSi$; C, 60.43; H, 6.92; N, 6.41; Found: C, 60.57; H, 6.98; N, 6.55.

General experimental procedure for the synthesis of 8

Same procedure as for **7a**.

(*S*)-Methyl-2-(*N*-((*R*)-3-(*tert*-butyldimethylsilyloxy)-2-(2-nitrophenylamino)propyl)-4-methylphenylsulfonamido)-3-phenylpropanoate 8a. Yellow oil. Yield, 77%; R_f, 0.52 (9.0 : 1.0, hexane–ethyl acetate); IR (neat, cm^{-1}): 3366, 2954, 1742, 1616, 1509, 1342, 1158, 761. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (d, 1H, J = 8.7), 8.16 (dd, 1H, J_1 = 1.5, J_2 = 8.6), 7.65-7.63 (m, 2H), 7.49-7.45 (m, 1H), 7.26-7.13 (m, 8H), 6.67-6.63 (m, 1H), 4.63 (dd, 1H, J_1 = 1.8, J_2 = 9.6, 4.25 (bs, 1H), 4.09 (dd, 1H, J_1 = 1.8, J_2 = 10.5), 3.73 (dd, 1H, J_1 = 3.3, J_2 = 10.5), 3.57 (dd, 1H, J_1 = 9.4, J_2 = 15.4), 3.32-3.28 (m, 2H), 3.23 (s, 3H), 3.01 (dd, 1H, J_1 = 5.8, J_2 = 13.6), 2.38 (s, 3H), 0.93 (s, 9H), 0.11-0.03 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 144.4, 144.0, 136.3, 136.1, 135.2, 132.2, 129.5, 129.1, 128.6, 127.8, 127.1, 127.0, 115.6, 114.5, 62.5, 60.9, 53.2, 51.7, 45.5, 37.2, 25.9, 21.5, 18.2, -5.5, -5.6. MS (ESI): m/z 642 [M+H], 664 [M+Na]$^+$. Anal. Calcd. (%) for $C_{32}H_{43}N_3O_7SSi$; C, 59.88; H, 6.75; N, 6.55; Found: C, 59.92; H, 6.79; N, 6.69.

(*S*)-Methyl 2-(*N*-((*R*)-3-(*tert*-butyldimethylsilyloxy)-2-(2-nitrophenylamino)propyl)-4-methylphenylsulfonamido)propanoate 8b. Yellow oil. Yield, 80%; R_f, 0.51 (8.5 : 1.5, hexane–ethyl acetate); IR (neat, cm^{-1}): 3361, 2959, 1739, 1616, 1510, 1153, 760. ^1H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 8.36 (d, 1H, J = 8.6), 8.19 (dd, 1H, J_1 = 1.3, J_2 = 8.6), 7.67-7.65 (m, 2H), 7.54-7.50 (m, 1H), 7.34-7.24 (m, 3H), 6.70-6.65 (m, 1H), 4.60 (q, 1H, J = 7.3), 4.32-4.30 (m, 1H), 4.12-4.09 (m, 1H), 3.78 (dd, 1H, J_1 = 3.0, J_2 = 10.4), 3.38 (s, 3H), 3.31-3.29 (m, 2H), 2.42 (s, 3H), 1.52 (d, 3H, J = 7.3), 0.95 (s, 9H), 0.15-0.10 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 144.4, 143.6, 136.2, 135.5, 132.3, 129.5, 127.7, 127.1, 115.5, 114.6, 60.6, 56.6, 53.1, 51.9, 44.8, 26.0, 21.6, 18.3, 16.9, -5.4. MS (ESI): m/z 566 [M+H], 588 $[M+Na]^+$. Anal. Calcd. (%) for $C_{26}H_{39}N_3O_7SSi$; C, 55.20; H, 6.95; N, 7.43; Found: C, 55.29; H, 7.01; N, 7.56.

(*S*)-Methyl-2-(*N*-((2*R*,3*R*)-3-hydroxy-2-(2-nitrophenylamino)-butyl)-4-methylphenylsulfonamido)-3-phenylpropanoate 9a. To a solution of **7a** (350 mg) in 10 mL AcOH–THF–H_2O (3 : 1 : 1, v/v/v) was refluxed at 120 °C for 16 h. It was extracted with EtOAc. The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to afford a yellow oil that was purified by column chromatography on silica gel with AcOEt–hexane (2.5 : 7.5) as eluent to furnish **9a** (245 mg, 85%) as a yellow oil. R_f, 0.51 (7.0 : 3.0, hexane–ethyl acetate); IR (neat, cm^{-1}): 3660, 3361, 1740, 1617, 1509, 1219, 760. ^1H NMR (300 MHz, $CDCl_3$) δ 8.39 (d, 1H, J = 8.9), 8.19 (dd, 1H, J_1 = 1.4, J_2 = 8.6), 7.66-7.62 (m, 2H), 7.53-7.45 (m, 1H), 7.28-7.20 (m, 5H), 7.09-7.02 (m, 3H), 6.69-6.62 (m, 1H), 4.73-4.65 (m, 1H), 4.34-4.33 (m, 1H), 4.00-3.89 (m, 1H), 3.48 (s, 3H), 3.32-3.21 (m, 2H), 2.80-2.70 (m, 2H), 2.41 (s, 3H), 1.21 (d, 3H, J = 6.4). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 145.2, 144.2, 136.4, 135.8, 135.6, 132.4, 129.8, 128.8, 128.7, 127.4, 127.2, 127.0, 115.4, 113.9, 63.7, 61.2, 55.9, 52.3, 45.6, 35.4, 21.5, 20.0. MS (ESI): m/z 542 $[M+H]^+$. Anal. Calcd. (%) for $C_{27}H_{31}N_3O_7S$; C, 59.87; H, 5.77; N, 7.76; Found: C, 59.88; H, 5.81; N, 7.89.

(*S*)-Methyl-2-(*N*-((2*R*,3*R*)-3-hydroxy-2-(2-(4-methylphenylsulfonamido)phenylamino)butyl)-4-methylphenylsulfonamido)-3-phenylpropanoate (11a). To a solution of **9a** (350 mg, 0.64 mmol) in MeOH was added Pd (10% on carbon) and was allowed to run for 1 h under pressure of 50 psi of H_2. After usual work up, the crude (220 mg, 0.43 mmol) was dissolved in 5 mL anhydrous pyridine, followed by addition of *p*- toluenesulfonylchloride (82 mg, 0.43 mmol) and kept in refrigerator for 12 h. The pyridine was removed and usual work up and chromatography on silica gel with eluent EtOAc–hexane (3.5 : 6.5) to afford **11a** (198 mg, 46% in two steps) as a light brown oil. R_f, 0.48 (5.5 : 4.5, hexane–ethylacetate); IR (neat, cm^{-1}): 3516, 3401, 3022, 2928, 1738, 1328, 1154, 753. ^1H NMR (300 MHz, $CDCl_3$) δ 7.71-7.68 (m, 2H), 7.63-7.60 (m, 2H), 7.27-7.18 (m, 7H), 7.08-7.03 (m, 3H), 6.78-6.66 (m, 3H), 6.48-6.43 (m, 1H), 4.89-4.86 (m, 1H), 4.67-4.62 (m, 1H), 4.09-4.07 (m, 1H), 3.69-3.67 (m, 1H), 3.53-3.45 (m, 1H), 3.42 (s, 3H), 3.30-3.21 (m, 2H), 2.86 (bs, 1H), 2.76 (dd, 1H, J_1 = 6.2, J_2 = 13.7), 2.42 (s, 3H), 2.40 (s, 3H), 1.14 (d, 3H, J = 6.4). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 145.2, 143.8, 143.6, 136.5, 136.2, 135.9, 129.6, 129.5, 129.24, 129.19, 128.9, 128.5, 127.6, 127.5, 127.3, 126.8, 120.2, 116.1, 111.4, 65.7, 61.4, 60.3, 56.0, 52.1, 46.3, 21.5, 21.4, 19.8. MS (ESI): m/z 666 $[M+H]^+$. Anal. Calcd. (%) for $C_{34}H_{39}N_3O_7S_2$; C, 61.33; H, 5.90; N, 6.31; Found: C, 61.47; H, 5.98; N, 6.43.

General experimental procedure for the synthesis of 12

To a stirred solution of **8** (1 equiv.) in THF (20 mL) under N_2, was added TBAF (1 M) (1.2 equiv.) at 0 °C and was stirred for 1 h. After removal of solvent and usual work-up, the crude was directly dissolved in MeOH and added Pd (10% on carbon) and was under pressure of 50 psi of H_2 for 1.3 h. After filtration through Celite and removal of solvent, crude was dissolved in 10 mL anhydrous pyridine at 0 °C, followed by addition of *p*- toluenesulfonylchloride (1.1 equiv.). and kept in the refrigerator for 12 h. Removal of pyridine and usual work-up and chromatography afforded the title compound **12**.

(*S*)-Methyl-2-(*N*-((*R*)-3-hydroxy-2-(2-(4-methylphenylsulfonamido)phenylamino)propyl)-4-methylphenylsulfonamido)-3-phenylpropanoate 12a. Light brown oil. Yield, 46% (in three steps); R_f 0.51 (9.8 : 0.2, $CHCl_3$–MeOH). IR (neat, cm^{-1}): 3519, 3398, 3262, 1737, 1159, 761. ^1H NMR (300 MHz, $CDCl_3$) δ 7.67-7.59 (m, 5H), 7.49-7.44 (m, 1H), 7.25-7.17 (m, 8H), 7.10-7.07 (m, 3H), 6.66-6.62 (m, 1H), 6.50-6.45 (m, 1H), 4.99-4.90 (m, 1H), 4.76-4.70 (m, 1H), 4.23-4.15 (m, 1H), 3.78-3.71 (m, 2H), 3.64-3.63 (m, 1H), 3.43 (s, 3H), 3.28 (dd, 1H, J_1 = 8.4, J_2 = 13.8), 2.86 (dd, 1H, J_1 = 6.7, J_2 = 14.0), 2.41 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 144.1, 143.8, 136.4, 136.3, 136.2, 132.2, 132.0, 129.6, 129.5, 129.0, 128.65, 128.59, 127.7, 127.4, 126.9, 121.1, 117.0, 112.2, 61.7, 60.4, 53.4, 52.3, 46.0, 36.0, 21.6, 21.1. MS (ESI): m/z 652$[M+H]^+$. (%) Anal. Calcd. for $C_{33}H_{37}N_3O_7S_2$; C, 60.81; H, 5.72; N, 6.45; Found: C, 60.90; H, 5.79; N, 6.51.

(*S*)-Methyl-2-(*N*-((*R*)-3-hydroxy-2-(2-(4-methylphenylsulfonamido)phenylamino)propyl)-4-methylphenylsulfonamido)propanoate 12b. Same procedure as for **12a**. Brown oil. Yield, 45% (in three steps); R_f 0.48 (9.8 : 0.2, $CHCl_3$–MeOH). IR (neat, cm^{-1}): 3524, 3405, 3025, 1741, 1331, 1159, 765. ^1H NMR (300 MHz, $CDCl_3$) δ 7.66-7.63 (m, 4H), 7.24-7.18 (m, 4H), 7.08-7.03 (m, 1H), 6.85 (bs, 1H), 6.65-6.60 (m, 2H), 6.48-6.43 (m, 1H), 4.99-4.98 (bs, 1H), 4.64 (q, 1H, J = 7.4), 3.79-3.68 (m, 2H), 3.55 (s, 3H), 3.42-3.24 (m, 2H), 2.74 (bs, 1H), 2.41 (s, 3H), 2.38 (s, 3H), 1.38 (d, 3H, J = 7.2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 144.2, 143.5, 143.4, 136.7, 136.6, 129.6, 129.5, 129.4, 129.0, 128.8, 127.8, 127.3, 121.1, 116.8, 112.0, 60.6, 55.9, 53.4, 52.4, 45.5, 21.63, 21.60, 15.9. MS (ESI): m/z 576 [M+H], 598 $[M+Na]^+$. (%)Anal. Calcd. for $C_{27}H_{33}N_3O_7S_2$; C, 56.33; H, 5.78; N, 7.30; Found: C, 56.44; H, 5.87; N, 6.92.

(*S*)-Methyl-2-(4-methyl-*N*-(((2*R*,3*S*)-3-methyl-4-tosyl-1,2,3,4-tetrahydroquinoxalin-2-yl)methyl)phenylsulfonamido)-3-phenylpropanoate 13a. To a stirred solution of **11a** (180 mg, 0.27 mmol), and triphenylphosphine (85 mg, 0.32 mmol) in anhydrous THF (7 mL) under N_2, was added DEAD (0.05 mL, 0.32 mmol) in THF drop wise at 0 °C and stirred for 2 h. Removal of triphenylphosphine oxide and usual procedure furnished **13a** 144 mg, 82%) as a colorless oil. R_f 0.51 (7.5 : 2.5, hexane–ethyl acetate). IR (neat, cm^{-1}): 3392, 3020, 2358, 1739, 1159, 761. ^1H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 7.78-7.75 (m, 2H), 7.66-7.64 (m, 2H), 7.27-7.18 (m, 10H), 6.93-6.90 (m, 2H), 6.67-6.63 (m, 1H), 4.86-4.81 (m, 1H), 4.36-4.29 (m, 2H), 3.51-3.46 (m, 1H), 3.37 (s, 3H), 3.27 (dd, 1H, J_1 = 8.4, J_2 = 13.9), 2.91 (dd, 1H, J_1 = 7.1, J_2 = 13.9), 2.60-2.54 (m, 1H), 2.40 (s, 3H), 1.40 (d, 3H, J = 5.8). ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 170.8, 143.5, 137.4, 136.8,

136.1, 131.4, 129.5, 129.1, 128.7, 127.6, 127.3, 127.0, 124.8, 123.7, 119.7, 119.1, 61.2, 52.0, 43.5, 43.5, 43.4, 41.9, 36.6, 21.6, 14.5. MS (ESI): m/z 648 $[M+H]^+$. Anal. Calcd. (%) for $C_{34}H_{37}N_3O_6S_2$; C, 63.04; H, 5.76; N, 6.49; Found: C, 63.24; H, 5.98; N, 6.43.

(*S*)-Methyl-2-(4-methyl-*N*-(((*R*)-4-tosyl-1,2,3,4-tetrahydroquinoxalin-2-yl)methyl)phenylsulfonamido)-3-phenylpropanoate 14a. Same procedure as for **13a** Colorless oil. Yield, 79%; R_f 0.50 (7.5 : 2.5, hexane–ethyl acetate). IR (neat, cm^{-1}): 3382, 3022, 2362, 1736, 1217, 768. ^1H NMR (300 MHz, $CDCl_3$) δ 7.57-7.55 (m, 2H), 7.49-7.44 (m, 2H), 7.28-7.23 (m, 5H), 7.15-7.13 (m, 2H), 7.09-7.05 (m, 2H), 6.99-6.94 (m, 1H), 6.70-6.64 (m, 1H), 6.43 (dd, 1H, J_1 = 1.2, J_2 = 8.0), 4.85 (bs, 1H), 4.60 (dd, 1H, J_1 = 6.4, J_2 = 9.0), 4.17-4.12 (m, 1H), 3.42 (s, 3H), 3.29-3.20 (m, 1H), 3.11-3.07 (m, 2H), 3.02-2.95 (m, 2H), 2.70 (dd, 1H, J_1 = 6.4, J_2 = 13.54, 2.43 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 144.1, 143.8, 137.2, 136.2, 135.6, 135.5, 129.7, 129.6, 129.0, 128.8, 128.71, 128.67, 127.5, 127.2, 126.5, 125.4, 121.3, 117.0, 114.8, 61.6, 52.1, 48.8, 47.6, 46.7, 37.6, 21.5, 21.3. MS (ESI): m/z 634 $[M+H]^+$. Anal. Calcd.(%) for $C_{33}H_{35}N_3O_6S_2$; C, 62.54; H, 5.57; N, 6.63. Found: C, 62.65; H, 5.66; N, 6.52.

(*S*)-Methyl-3-methyl-2-(4-methyl-*N*-(((*R*)-4-tosyl-1,2,3,4-tetrahydroquinoxalin-2-yl)methyl)phenylsulfonamido)butanoate 14c. Same procedure as for **13a**. Colorless oil. Yield, 84%; R_f 0.45 (7.5 : 2.5, hexane–ethyl acetate). IR (neat, cm^{-1}): 3396, 3022, 2956, 1738, 1156, 761. ^1H NMR (300 MHz, $CDCl_3$) δ 7.66-7.58 (m, 3H), 7.48-7.45 (m, 2H), 7.27-7.19 (m, 4H), 6.99-6.93 (m, 1H), 6.68-6.63 (m, 1H), 6.48 (dd, 1H, J_1 = 1.0, J_2 = 8.0), 5.00 (bs, 1H), 4.36-4.29 (m, 1H), 4.21-4.16 (m, 1H), 4.04-4.00 (m, 1H), 3.51-3.46 (m, 1H), 3.42 (s, 3H), 3.07-2.86 (m, 2H), 2.43 (s, 3H), 2.40 (s, 3H), 1.80-1.72 (m, 1H), 0.89 (d, 3H, J = 6.5), 0.82 (d, 3H, J = 6.5). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 143.7, 143.2, 137.5, 136.9, 136.0, 129.6, 129.5, 127.7, 127.4, 126.6, 125.6, 121.4, 117.0, 114.9, 64.1, 51.5, 48.3, 48.2, 46.9, 29.3, 21.65, 21.58, 19.8, 19.5, MS (ESI): m/z 586 $[M+H]^+$. Anal. Calcd. (%) for $C_{29}H_{35}N_3O_6S_2$; C, 59.47; H, 6.02; N, 7.17. Found: C, 59.58; H, 6.10; N, 7.26.

***N*-((*S*)-1-Hydroxy-3-phenylpropan-2-yl)-4-methyl-*N*-(((2*R*,3*S*)-3-methyl-4-tosyl-1,2,3,4-tetrahydroquinoxalin-2-yl)methyl)-benzenesulfonamide 15a.** Same procedure as for **5**. Colorless oil. Yield, 83%; R_f 0.52 (6.0 : 4.0, hexane–ethyl acetate). IR (neat, cm^{-1}): 3534, 3401, 2959, 1498, 1159, 761. ^1H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 7.80-7.74 (m, 3H), 7.35-7.32 (m, 2H), 7.26-7.13 (m, 8H), 7.06-7.01 (m, 2H), 6.97-6.93 (m, 2H), 4.14-4.07 (m, 2H), 3.91-3.77 (m, 2H), 3.62-3.58 (m, 1H), 3.39-3.18 (m, 3H), 3.02-2.91 (m, 1H), 2.45 (s, 3H), 2.40 (s, 3H), 1.55 (d, 3H, J = 5.9). ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 143.6, 137.6, 137.5, 137.2, 130.7, 129.9, 129.6, 129.2, 128.6, 127.4, 127.2, 126.5, 125.9, 124.4, 121.2, 120.6, 62.1, 61.2, 46.0, 43.1, 42.7, 33.5, 21.6, 14.5. MS (ESI): m/z 620 $[M+H]^+$. Anal. Calcd. (%) for $C_{33}H_{37}N_3O_5S_2$; C, 63.95; H, 6.02; N, 6.78;. Found: C, 63.79; H, 6.18; N, 7.61.

***N*-((*S*)-1-Hydroxy-3-phenylpropan-2-yl)-4-methyl-*N*-(((*R*)-4-tosyl-1,2,3,4-tetrahydroquinoxalin-2-yl)methyl)benzene sulfonamide 16a.** Same procedure as for **5**. Colorless oil. Yield, 84%; R_f 0.53 (6.0 : 4.0, hexane–ethyl acetate). IR (neat, cm^{-1}): 3525, 3398, 2958, 1498, 1160, 771. ^1H NMR (300 MHz, $CDCl_3$) δ 7.63-7.53 (m, 5H), 7.30-7.21 (m, 7H), 6.99-6.95 (m, 3H), 6.70-6.64 (m, 1H), 6.50 (dd, 1H, J_1 = 1.0, J_2 = 8.1), 4.25-4.18 (m, 1H), 4.15-4.10 (m, 1H), 3.98-3.91 (m, 1H), 3.55-3.50 (m, 2H), 3.39-3.33 (m, 2H), 3.30-3.21 (m, 1H), 2.99-2.91 (m, 1H), 2.46-2.43 (m, 4H), 2.35 (s, 3H). MS (ESI): m/z 606 $[M+H]^+$. Anal. Calcd. (%) for $C_{32}H_{35}N_3O_5S_2$; C, 63.45; H, 5.82; N, 6.94. Found: C, 63.59; H, 5.94; N, 7.10.

***N*-((*S*)-1-Hydroxypropan-2-yl)-4-methyl-*N*-(((*R*)-4-tosyl-1,2,3,4-tetrahydroquinoxalin-2-yl)methyl)benzenesulfon amide 16b.** Same procedure like for **5**. Colorless oil. yield, 81%; R_f 0.51 (6.0 : 4.0, hexane–ethylacetate). IR (neat, cm^{-1}): 3522, 3396, 2959, 1499, 1161, 761.^1H NMR (300 MHz, $CDCl_3$) δ 7.66-7.64 (m, 2H), 7.56-7.45 (m, 3H), 7.31-7.19 (m, 4H), 6.98-6.88 (m, 1H), 6.69-6.59 (m, 1H), 6.51 (d, 1H J = 8.1), 4.19-4.06 (m, 2H), 3.97-3.90 (m, 1H), 3.49-3.43 (m, 1H), 3.29-3.20 (m, 2H), 3.03-3.01 (m, 1H), 2.69 (dd, 1H, J_1 = 10.0, J_2 = 14.6), 2.45 (s, 3H), 2.37 (s, 3H), 0.66 (d, 3H, J = 6.8). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 137.2, 136.8, 129.9, 129.83, 129.77, 127.4, 127.3, 127.2, 126.6, 126.3, 125.4, 124.4, 117.3, 115.4, 115.3, 63.7, 55.9, 51.0, 48.2, 46.9, 21.6, 13.4. MS (ESI): m/z 530 $[M+H]^+$. Anal. Calcd. (%) for $C_{26}H_{31}N_3O_5S_2$; C, 58.96; H, 5.90; N, 7.93. Found: C, 58.91; H, 5.98; N, 7.78.

(2*S*,4a*R*,5*S*)-2-Benzyl-5-methyl-3,6-ditosyl-2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxaline 17a. A stirred solution of **15a** (120 mg, 0.19 mmol), triphenylphosphine (76 mg, 0.29 mmol), imidazole (39 mg, 0.57 mmol) and iodine (73 mg, 0.29 mmol) in anhydrous toluene (7 mL) at 40 °C was stirred. After 20 min, 10% aqueous $Na_2S_2O_3$ (20 mL) was added and stirring was continued for another 10 min and was extracted with EtOAc. After usual work up and column chromatography (eluent = hexane–ethyl acetate, 9.0 : 1.0) afforded **17a** (90 mg, 78%) as a colorless oil. $[\alpha]_D^{30}$ = +151.8 (c 0.11, MeOH), HPLC analysis: ee > 99 (t_R = 13.5 min, CH_3CN–H_2O); IR (neat, cm^{-1}): 3454, 2925, 1607, 1348, 1159, 761. ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, 1H, J = 8.2), 7.66-7.58 (m, 2H), 7.34-7.24 (m, 9H), 7.17-7.10 (m, 3H), 7.01-6.92 (m, 2H), 4.33-4.32 (m, 1H), 4.22-4.10 (m, 1H), 3.96-3.93 (m, 1H), 3.50-3.41 (m, 1H), 3.30-3.27 (m, 1H), 3.11-3.04 (m, 2H), 2.98-2.90 (m, 1H), 2.71-2.66 (m, 1H), 2.44 (s, 3H), 2.41 (s, 3H), 1.52 (d, 3H, J = 7.2). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2, 143.5, 137.2, 137.1, 136.8, 136.6, 134.1, 129.75, 129.68, 129.1, 128.7, 127.3, 127.2, 127.1, 127.05, 127.03, 126.7, 123.8, 123.2, 119.1, 63.0, 56.7, 54.2, 50.2, 42.5, 36.1, 21.4, 14.0. MS (ESI): m/z 602 $[M+H]^+$. Anal. Calcd. (%) for $C_{33}H_{35}N_3O_4S_2$; C, 65.86; H, 5.86; N, 6.98 ;Found: C, 65.66; H, 5.75; N, 7.17.

(2*S*,4a*R*)-2-Benzyl-3,6-ditosyl-2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxaline 18a. Same procedure as for **17a**. Colorless oil. Yield, 83%; $[\alpha]_D^{30}$ = −30.4 (c 0.13, MeOH), HPLC analysis: ee > 99 (t_R = 14.8 min, CH_3CN–H_2O); R_f 0.45 (9.0 : 1.0, hexane–ethyl acetate). IR (neat, cm^{-1}): 3456, 2925, 1606, 1342, 1162, 756. ^1H NMR (300 MHz, $CDCl_3$) δ 7.60-7.58 (m, 3H), 7.37-7.35 (m, 2H), 7.30-7.26 (m, 5H), 7.16-7.14 (m, 2H), 7.07-7.04 (m, 3H), 6.82-6.79 (m, 1H), 6.45 (d, 1H, J = 7.9), 4.20-4.12 (m, 2H), 3.55 (dd, 1H, J_1 = 2.6, J_2 = 12.7), 3.40-3.28 (m, 2H), 2.80-2.70 (m, 2H), 2.58-2.52 (m, 2H), 2.46 (s, 3H), 2.34 (s, 3H), 2.24-2.18 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 143.3, 140.1, 137.75, 137.69, 136.2, 129.9, 129.8, 129.5, 129.3, 128.8, 128.7, 127.4, 127.25, 127.20, 127.0, 126.8, 125.0, 118.8, 113.1, 54.9, 52.1, 47.8, 46.9, 43.5, 34.5, 21.6, 21.5. MS (ESI): m/z 588 $[M+H]^+$, 610 $[M+Na]^+$. Anal. Calcd. (%) for $C_{32}H_{33}N_3O_4S_2$; C, 65.39; H, 5.66; N, 7.15; Found: C, 65.51; H, 5.75; N, 7.10.

(2*S*,4a*R*)-2-Methyl-3,6-ditosyl-2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxaline 18b. Same procedure like for **17a**. Colorless oil. Yield, 80%; $[\alpha]_D^{30}$ = +171.5 (*c* 0.10, MeOH), HPLC analysis: ee > 99 (t_R = 9.6 min, CH_3CN–H_2O); R_f 0.51 (7.5 : 2.5, hexane–ethylacetate). IR (neat, cm^{-1}): 3461, 3024, 2927, 1600, 1344, 1162, 759. ^1H NMR (300 MHz, $CDCl_3$) δ 7.65-7.62 (m, 2H), 7.55 (dd, 1H, J_1 = 1.3, J_2 = 8.1), 7.38-7.29 (m, 4H), 7.19-7.15 (m, 2H), 7.07-7.01 (m, 1H), 6.76-6.71 (m, 1H), 6.57 (d, 1H, J = 8.1), 4.20-4.08 (m, 2H), 3.55-3.52 (m, 1H), 3.38-3.34 (m, 1H), 3.19 (dd, 1H, J_1 = 9.5, J_2 = 14.1), 3.09-3.00 (m, 1H), 2.62-2.58 (m, 2H), 2.46 (s, 3H), 2.39 (s, 3H), 0.96 (d, 3H, J = 6.6). ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.6, 143.2, 140.1, 137.7, 136.3, 129.7, 129.4, 127.4, 127.2, 127.1, 126.9, 124.8, 118.4, 112.8, 52.2, 51.5, 48.7, 47.0, 42.7, 21.6, 21.5, 14.3. MS (ESI): *m*/*z* 512 $[M+H]^+$, 534 $[M+Na]^+$. Anal. Calcd. (%) for $C_{26}H_{29}N_3O_4S_2$; C, 61.03; H, 5.71; N, 8.21; Found: C, 61.27; H, 5.79; N, 8.35.

General experimental procedure for the synthesis of 19, 20a–e. Sodium metal (20 equiv.) and naphthalene (22 equiv.) were dissolved in 10 mL dry THF and stirred for 2 h, until a dark green colour appeared. The desired THF solution of **17a**, **18a–e** (1 equiv.) was cooled to −78 °C and then Na–napthalenide solution was added dropwise *via* a syringe, until a dark green colour persisted and stirred for 10–20 min at −78 °C. It was quenched by adding 1–2 drops water and usual work up followed by chromatography (eluent = methanol–chloroform 1.0 : 9.0) of crude over silica gel furnished **19**, **20a–e** in 60–70% yield.

(2*S*,4a*R*,5*S*)-2-Benzyl-5-methyl-2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]quinoxaline (19). Light brown oil. Yield, 63%; R_f, 0.52 (8.8 : 1.2, chloroform–methanol); IR (neat, cm^{-1}): 3447, 3022, 2362, 1649, 1216, 765. ^1H NMR (300 MHz, $CDCl_3$) δ 7.24-7.16 (m, 5H), 6.81-6.78 (m, 4H), 3.59-3.56 (m, 1H), 3.32 (bs, 1H), 3.17-3.14 (m, 2H), 3.05-3.01 (m, 3H), 2.91-2.83 (m, 2H), 1.38 (d, 3H, J = 6.7). ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.3, 136.1, 129.3, 129.1, 128.4, 128.3, 126.2, 118.65, 118.56, 115.6, 115.4, 61.3, 60.4, 58.6, 43.8, 37.3, 14.5. MS (ESI): *m*/*z* 204 $[M+H]^+$, Anal. Calcd. (%) for $C_{12}H_{17}N_3$; C, 70.90; H, 8.43; N, 20.67; Found: C, 70.96; H, 8.51; N, 20.61.

(2*S*,4a*R*)-2-Benzyl-2,3,4,4a,5,6-hexahydro-1*H*-pyrazino[1,2-*a*]-quinoxaline (20a). Light brown oil. Yield, 62%; R_f, 0.51 (9.0 : 1.0, chloroform–methanol); IR (neat, cm^{-1}): 3022, 2364, 1216, 766. ^1H NMR (300 MHz, $CDCl_3$) δ 7.34-7.22 (m, 5H), 6.68 (s, 3H), 6.55-6.53 (m, 1H), 3.51-3.39 (m, 3H), 3.29-3.18 (m, 2H), 3.04-2.94 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 135.5, 129.3, 128.7, 126.5, 120.0, 118.7, 114.6, 114.2, 54.5, 53.6, 43.8, 36.8. MS (ESI): *m*/*z* 280 $[M+H]^+$, Anal. Calcd. (%) for $C_{18}H_{21}N_3$; C, 77.38; H, 7.58; N, 15.04; Found: C, 77.34; H, 7.51; N, 15.11.

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Notes and references

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