Electronic Supplementory Information

$AlCl_3$-mediated hydroarylation / heteroarylation in a single pot: A direct access to densely functionalized olefins of pharmacological interest

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Experimental Section

Chemistry

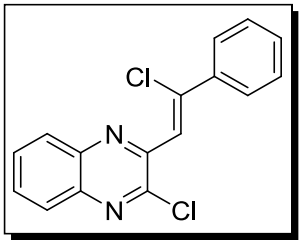
General methods: Unless stated otherwise, reactions were performed under nitrogen atmosphere using oven dried glassware. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254), visualizing with ultraviolet light or iodine spray. Flash chromatography was performed on silica gel (230-400 mesh) using distilled hexane, ethyl acetate. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$/DMSO-d_6 solutions by using 400 or 100 MHz spectrometers, respectively. Proton chemical shifts (δ) are relative to tetramethylsilane (TMS, δ = 0.00) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), dd (doublet of doublet), td (triplet of doublet), t (triplet) and m (multiplet) as well as b (broad). Coupling constants (J) are given in hertz. Infrared spectra were recorded on a FT- IR spectrometer. Melting points were determined by using melting point apparatus. MS spectra were obtained by using Agilent 6430 series Triple Quard LC-MS / MS spectrometer. Melting points (mp) were by using Buchi B-540 melting point apparatus.

General experimental procedure for the preparation of staring materials: All starting materials **2a-2f** were prepared according to the procedure developed by our group earlier.[1]

General procedure for the synthesis of 2-(2,2-diarylvinyl)-3-arylquinoxaline (4):

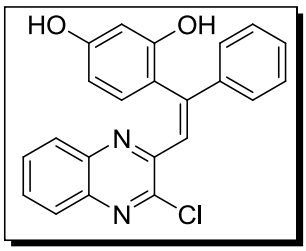
A mixture of alkyne (**2**) (0.37 mmol), and arene (**3**) (1.51 mmol) and anhydrous $AlCl_3$ (1.51mmol) in dichloroethane (4 mL) was stirred at 50 °C for 15-30 min under nitrogen atmosphere. The colour of the reaction gradually changed from yellow to dark yellow. After completion of the reaction as indicated by TLC, the reaction mixture was diluted with water (15 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were collected, dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Merck, 100–200 mesh) using *n*-hexane/ethyl acetate to afford the desired product.

(*Z*)-2-Chloro-3-(2-chloro-2-phenylvinyl)quinoxalines (5)



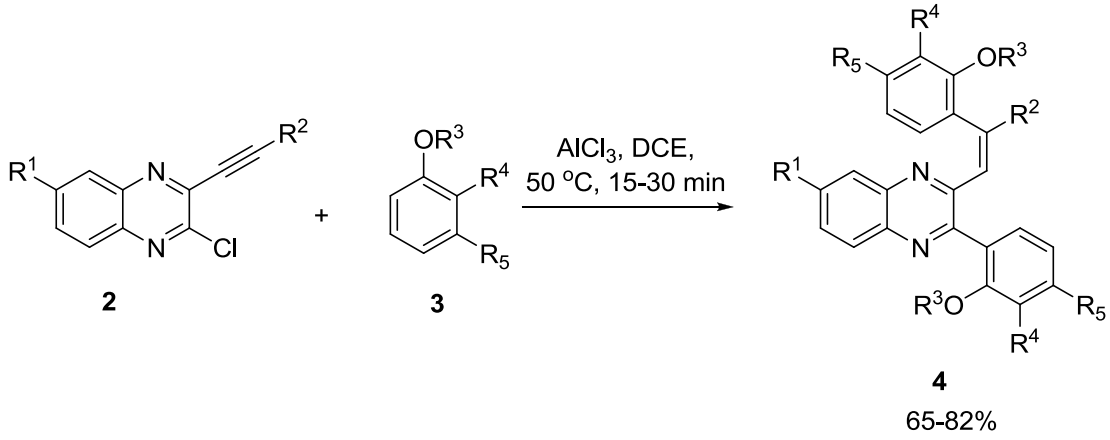
Light brown semi solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.17 (dd, *J* = 6.2, 3.5 Hz, 1H), 8.03 (dd, *J* = 6.9, 2.7 Hz, 1H), 7.87-7.78 (m, 4H), 7.54 (s, 1H), 7.49-7.44 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 148.1, 147.0, 140.8, 140.7 (2C), 138.0, 131.0, 130.4, 130.0, 129.2, 128.6 (2C), 128.1, 127.2 (2C), 120.2; IR (KBr, cm^{-1}): 1604, 1563, 1451, 943; MS (ES mass): m/z 301.6 (M^+).

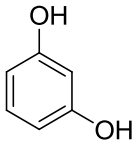
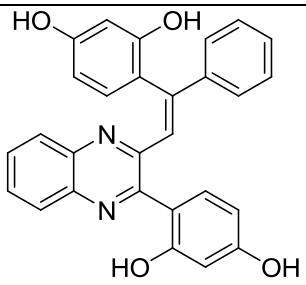
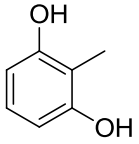
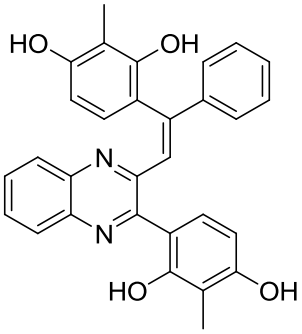
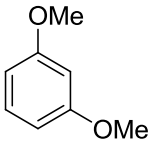
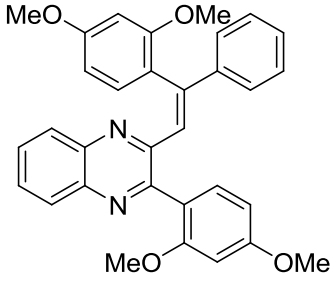
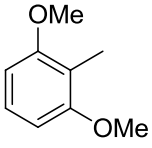
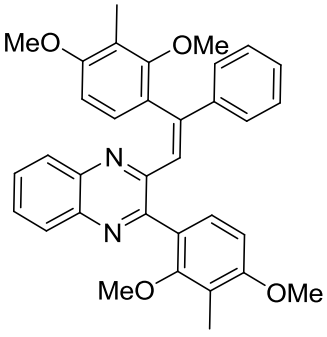
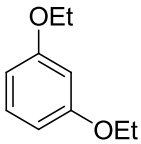
(*Z*)-4-(2-(3-Chloroquinoxalin-2-yl)-1-phenylvinyl)benzene-1,3-diol (6)

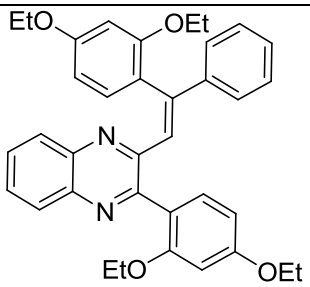
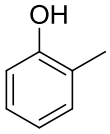
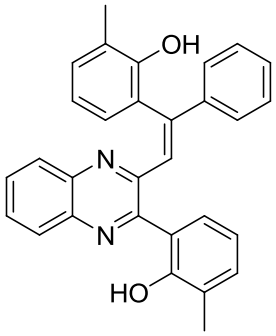
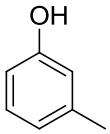
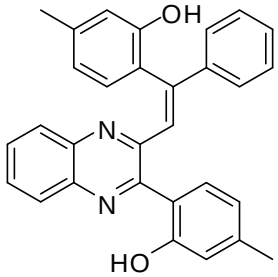
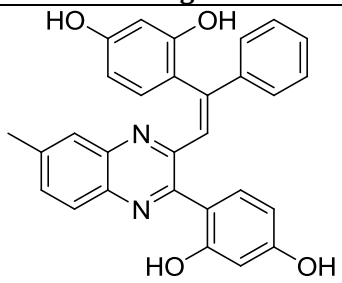
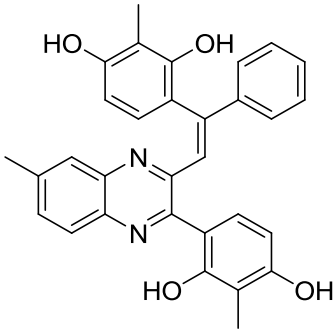


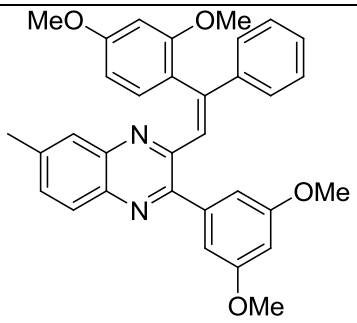
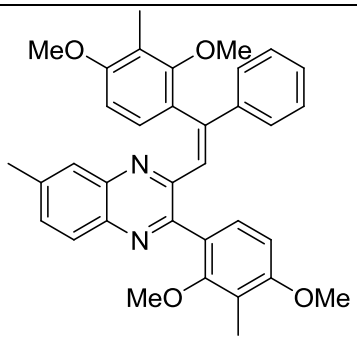
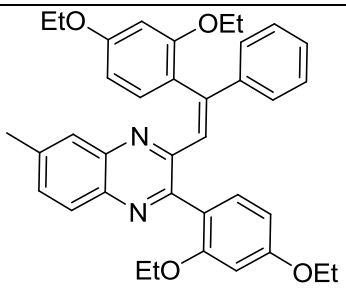
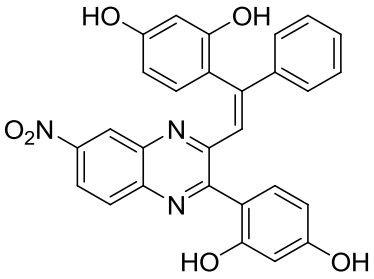
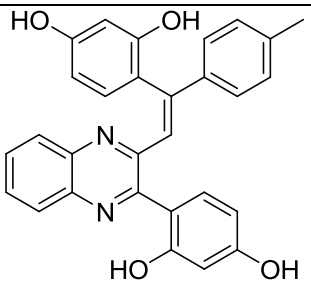
Brown semi solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 9.14 (s, 1H), 8.92 (s, 1H), 7.87-7.86 (m, 2H), 7.62-7.58 (m, 2H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.28 (m, 5H), 7.13 (s, 1H), 6.21 (s, 1H), 6.13 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 161.2 (2C), 161.0, 158.8, 149.8, 149.4, 140.3, 132.6, 132.5, 131.1, 129.9 (2C), 128.6, 127.3, 126.0 (2C), 125.9, 121.0, 114.1, 111.5, 108.1, 106.6; IR (KBr, cm^{-1}): 3341, 1610, 1533, 1427, 912; MS (ES mass): m/z 375.2 (M+1).

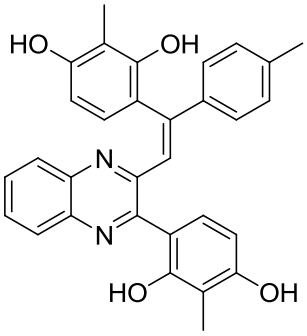
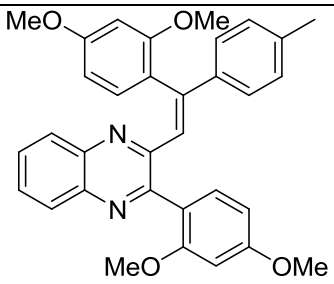
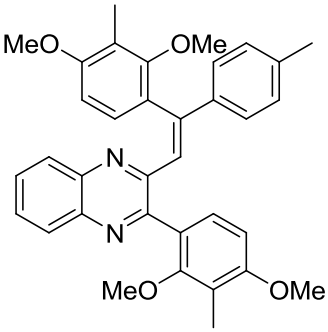
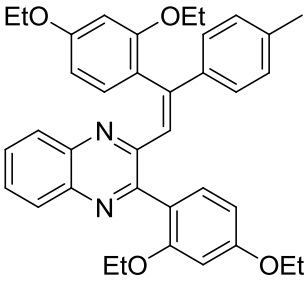
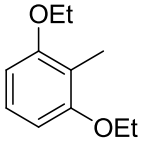
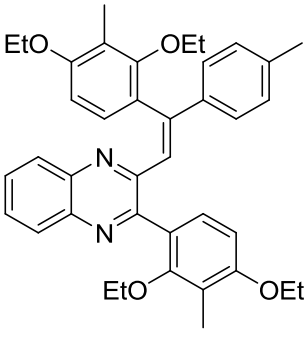
Table S1. synthesis of 2-(2,2-diarylvinyl)-3-arylquinoxaline (**4aa-4fe**).[a]

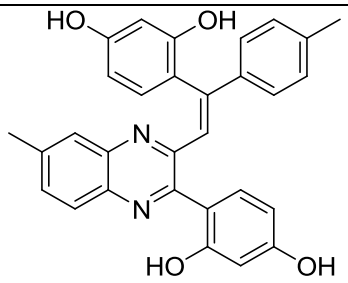
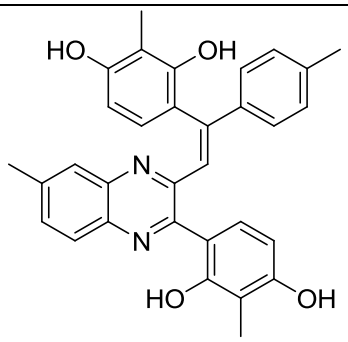
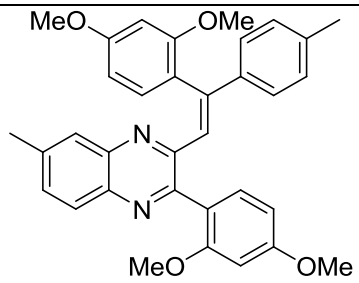
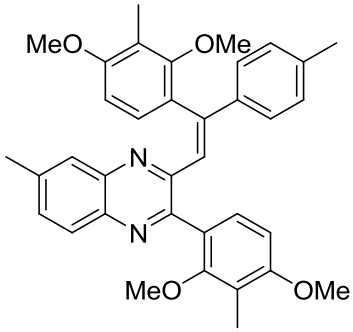
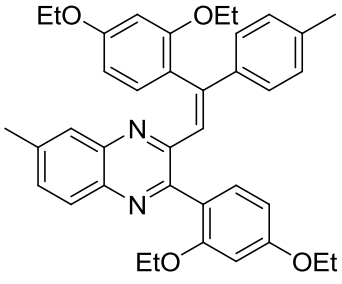


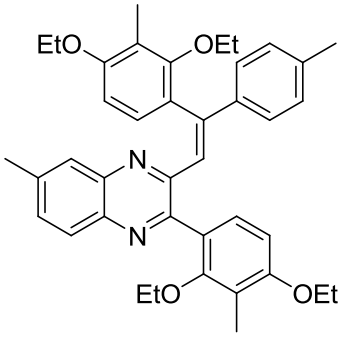
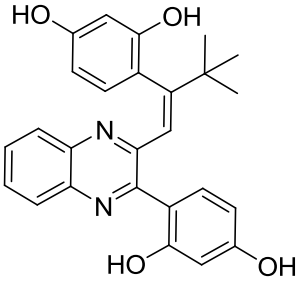
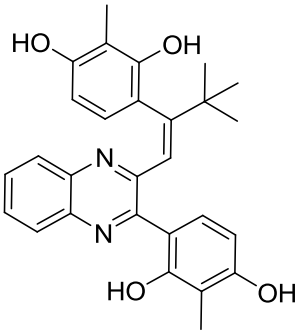
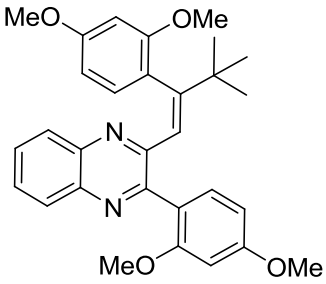
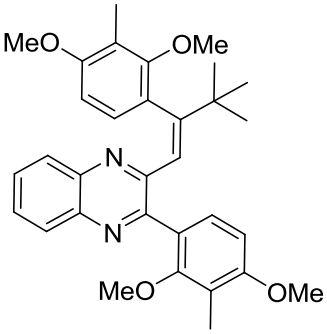
Entry	Alkyne (**2**) R^1, R^2	Arene (**3**)	Product (**4**)	Time (min)	Yield (%)[b]
1	H, Ph; **2a**	 **3a**	 **4aa**	15	82
2	**2a**	 **3b**	 **4ab**	15	79
3	**2a**	 **3c**	 **4ac**	15	64
4	**2a**	 **3d**	 **4ad**	15	68
5	**2a**			30	65

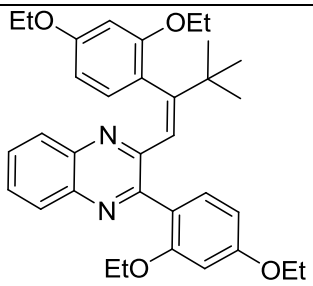
		3e	 **4ae**		
6	**2a**	 **3f**	 **4af**	30	62[c]
7	**2a**	 **3g**	 **4ag**	30	55[c]
8	CH_3, Ph; **2b**	**3a**	 **4ba**	15	80
9	**2b**	**3b**	 **4bb**	15	78

10	**2b**	**3c**	 **4bc**	15	73
11	**2b**	**3d**	 **4bd**	30	71
12	**2b**	**3e**	 **4be**	30	66
13	NO_2, Ph; **2c**	**3a**	 **4ca**	30	60
14	H,C_6H_4Me-*p*; **2d**	**3a**	 **4da**	15	71

15	**2d**	**3b**	 **4db**	15	69
16	**2d**	**3c**	 **4dc**	15	63
17	**2d**	**3d**	 **4dd**	30	67
18	**2d**	**3e**	 **4de**	30	58
19	**2d**	 **3h**	 **4dh**	30	55

20	CH_3, C_6H_4Me-*p*; **2e**	**3a**	 **4ea**	15	74
21	**2e**	**3b**	 **4eb**	15	71
22	**2e**	**3c**	 **4ec**	15	64
23	**2e**	**3d**	 **4ed**	15	60
24	**2e**	**3e**	 **4ee**	30	56

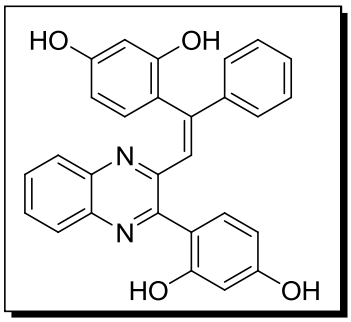
25	**2e**	**3h**	 **4eh**	30	58
26	H, CMe_3; **2f**	**3a**	 **4fa**	30	55
27	**2f**	**3b**	 **4fb**	30	62
28	**2f**	**3c**	 **4fc**	30	60
29	**2f**	**3d**	 **4fd**	30	63

30	**2f**	**3e**	 **4fe**	30	61

[a]All reactions were carried out using **2** (0.3787 mmol), **3** (1.5151 mmol) $AlCl_3$ (1.5151 mmol) in DCE (4 mL) at 50 °C.
[b]Isolated yield.
[c]A 1:1 mixture of two regioisomers was isolated (vide infra).

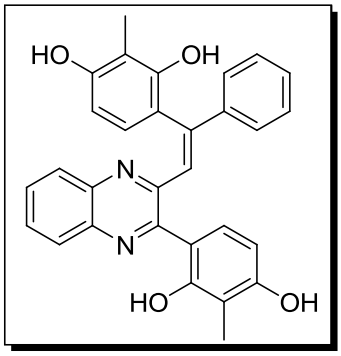
Spectral data of compound 4

(*Z*)-4-(3-(2-(2,4-Dihydroxyphenyl)-2-phenylvinyl)quinoxalin-2-yl)benzene-1,3-diol (4aa)



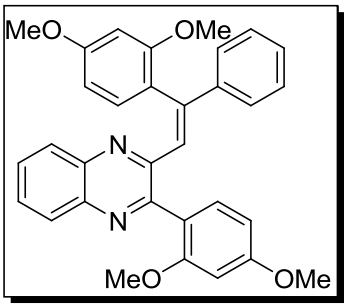
Yellow solid; mp: 206-208°C; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 10.31 (s, 1H), 9.61 (s, 1H), 9.13 (s, 1H), 8.78 (s, 1H), 7.97-7.85 (m, 1H), 7.65 (dd, *J* = 8.3, 3.5 Hz, 2H), 7.55-7.49 (m, 1H), 7.32-7.24 (m, 6H), 6.99 (s, 1H), 6.60 (d, *J* = 8.2 Hz, 1H), 6.38 (d, *J* = 2.1 Hz, 1H), 6.32 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.14 (d, *J* = 2.1 Hz, 1H), 6.08 (dd, *J* = 8.2, 2.1 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 170.7, 159.9, 158.0, 157.2, 156.2, 154.0, 152.3, 144.7, 143.4, 140.2, 139.6, 132.3, 129.6, 129.5, 128.8, 128.6, 128.4, 128.2 (2C), 127.5 (2C), 125.5, 118.0, 116.6, 107.3, 106.5, 102.9, 102.8; HPLC: 99.6%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 8.58 min; IR (KBr, cm^{-1}): 3357, 1613, 1508, 970; MS (ES mass): m/z 449.2 (M+1).

(*Z*)-4-(3-(2-(2,4-Dihydroxy-3-methylphenyl)-2-phenylvinyl)quinoxalin-2-yl)-2-methylbenzene-1,3-diol (4ab)



Brown semisolid; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 11.15 (s, 1H), 9.78 (s, 1H), 9.12 (s, 1H), 8.25 (s, 1H), 8.00-7.93 (m, 1H), 7.70 (dd, J = 13.3, 5.8 Hz, 2H), 7.63-7.57 (m, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.36-7.22 (m, 5H), 7.13 (s, 1H), 6.24 (d, J = 8.4 Hz, 1H), 6.48 (d, J = 8.4 Hz, 2H), 2.08 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 156.8, 156.0 (2C), 154.4, 151.4, 147.0, 144.4, 143.2, 139.4, 138.2, 129.0 (2C), 128.6, 128.5 (2C), 128.4, 128.3, 128.0 (2C), 127.9 (2C), 127.3, 119.0, 113.8, 112.4, 111.7, 111.6, 106.7, 9.5, 9.1; HPLC: 98.1%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B%: 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 7.39 min; IR (KBr, cm^{-1}): 3373, 2853, 1605, 1489, 598; MS (ES mass): m/z 476.8 (M+1).

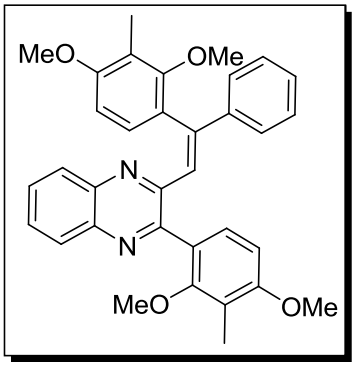
(*Z*)-2-(2,4-Dimethoxyphenyl)-3-(2-(2,4-dimethoxyphenyl)-2-phenylvinyl)quinoxalines (4ac)



Light brown semisolid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.04-7.94 (m, 1H), 7.73-7.68 (m, 1H), 7.65-7.53 (m, 3H), 7.06 (dd, J = 8.3, 9.0 Hz, 3H), 6.90-6.82 (m, 1H), 6.76 (d, J = 8.3 Hz, 1H), 6.31 (dd, J = 12.9, 4.9 Hz, 2H), 6.50 (d, J =13.3 Hz, 4H), 3.85-3.79 (m, 12H); ^{13}C NMR (100 MHz,

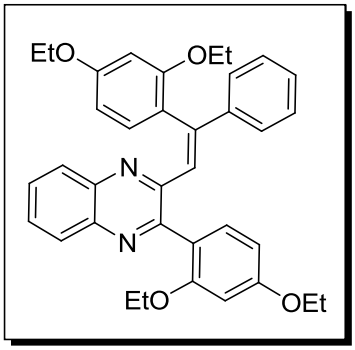
DMSO-d_6) ppm: 161.8, 160.5, 158.8, 158.0, 153.1, 152.3, 144.1, 142.7, 140.5, 140.3, 131.8, 131.6, 129.9, 129.7, 129.1, 128.8, 128.7, 128.2 (2C), 127.7, 126.9, 125.5, 121.1, 120.6, 105.9, 104.8, 98.8, 98.6, 56.0, 55.7, 55.6, 55.4; HPLC: 96.7%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 7.12 min; IR (KBr, cm^{-1}): 2926, 1616, 1398, 816; MS (ES mass): m/z 504.8 (M^+).

(*Z*)-2-(2,4-Dimethoxy-3-methylphenyl)-3-(2-(2,4-dimethoxy-3-methylphenyl)-2 phenylvinyl)quinoxalines (4ad)



Light yellow liquid; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 7.98 (dd, J = 7.7, 1.6 Hz, 1H), 7.75-7.68 (m, 2H), 7.51-7.45 (m, 1H), 7.32-7.26 (m, 4H), 6.95 (s, 1H), 7.22-7.17 (m, 2H), 6.90 (d, J = 8.5 Hz, 1H), 6.73 (s, 1H), 6.63 (s, 1H), 3.85 (d, J = 7.9 Hz, 3H), 3.75 (s, 3H), 3.52 (s, 3H), 3.38 (s, 3H), 2.15 (d, J = 10.2 Hz, 3H), 1.99 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 182.9, 168.4, 158.1 (2C), 157.3, 156.9, 153.7, 151.5, 142.8, 140.6, 130.2, 130.0, 128.9, 128.8 (2C), 128.7(2C), 128.6 (2C), 128.5, 127.5, 127.2, 126.0, 125.1, 119.1, 118.6, 109.9, 106.9, 61.5, 60.0, 56.1, 55.9, 9.4 (2C); HPLC: 91.8 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.31 min; IR (KBr, cm^{-1}): 2913, 1604, 1381, 907; MS (ES mass): m/z 532.8 (M^+).

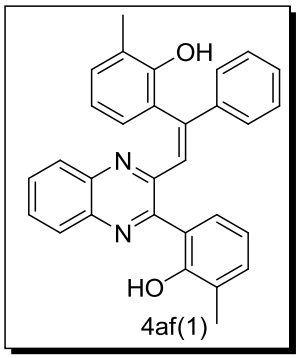
(*Z*)-2-(2,4-Diethoxyphenyl)-3-(2-(2,4-diethoxyphenyl)-2-phenylvinyl)quinoxalines (4ae)



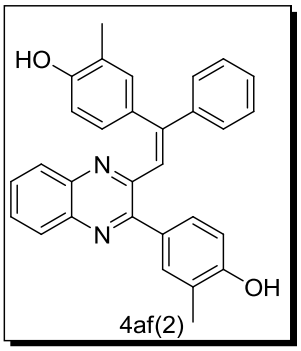
Light yellow liquid; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 7.91 (t, J = 8.9 Hz, 1H), 7.58 (d, J = 9.2 Hz, 1H), 7.46-7.45 (m, 1H), 7.26 (s, 1H), 7.14 (dd, J = 8.3, 2.5 Hz, 1H), 7.06 (s, 1H), 6.98 (q, J = 7.2 Hz, 2H), 6.85 (s, 1H), 6.77 (dd, J = 7.7, 2.3 Hz, 1H), 6.49-6.41 (m, 3H), 6.39-6.29 (m, 1H), 6.25 (d, J = 1.8 Hz, 1H), 6.20 (dd, J = 8.3, 2.0 Hz, 1H), 4.03-4.01 (m, 8H), 1.46-1.31 (m, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 160.7, 159.6, 158.0, 157.1, 152.2, 144.1, 143.8, 139.0, 132.2, 131.6, 131.5, 131.0, 129.0 (2C), 128.3, 127.7, 127.1 (2C), 127.0 (2C), 126.2 (2C), 126.1, 121.4, 105.4 (2C), 100.4, 99.5, 63.7, 63.5, 63.4, 63.3, 14.8 (2C), 14.7 (2C); HPLC: 92.6 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.28 min; IR (KBr, cm^{-1}): 2938, 1603, 1460, 823; MS (ES mass): m/z 561.2 (M+1).

(*Z*)-2-(3-(2-(2-Hydroxy-3-methylphenyl)-2-phenylvinyl)quinoxalin-2-yl)-6-methylphenol (4af (1)) and ***(Z)*-4-(3-(2-(4-hydroxy-3-methylphenyl)-2-phenylvinyl)quinoxalin-2-yl)-2-methylphenol (4af(2)):** A ~ 1:1 mixture of regioisomers i.e. **4af(1)** and **4af(2)** was isolated in this case which could not be separated by using standard column chromatography. The mixture was confirmed by HPLC analysis (see the data and the copy of the HPLC). While an attempt to separate the individual isomer by using preparative HPLC was failed, the LC-MS analysis indicated that both the component present in the mixture possess same mass.

All the spectral data presented here was recorded on 1:1 mixture of compounds.



4af(1)

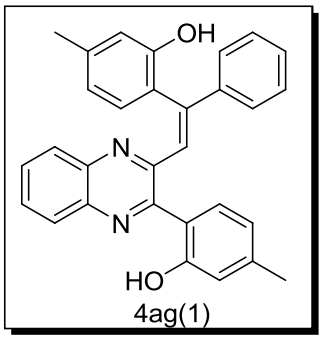


4af(2)

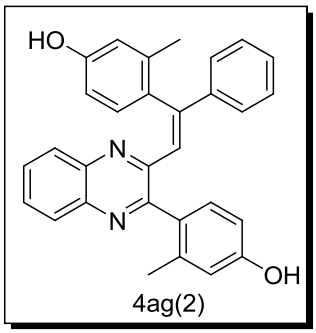
Yellow semi solid; 9.64 (s, 1H), 9.58 (s, 1H), 9.52 (s, 1H), 9.28 (s, 1H), 7.97-7.85 (m, 3H), 7.74-7.68 (m, 3H), 7.66 (s, 2H), 7.30 (dd, *J* = 13.2, 7.7 Hz, 7H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.14 (d, *J* = 6.5 Hz, 2H), 7.06 (dd, *J* = 12.8, 6.9 Hz, 5H), 6.92 (d, *J* = 8.3 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 2H), 6.69 (t, *J* = 7.9 Hz, 3H), 6.36 (d, *J* = 8.1 Hz, 1H), 6.18 (d, *J* = 8.0 Hz, 1H), 6.04 (s, 1H), 2.12 (s, 3H), 2.08 (s, 6H), 1.81 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 156.8, 156.5, 156.4, 155.4, 154.1, 152.6, 151.7, 147.4, 147.1, 142.8, 140.3, 140.2, 140.1, 140.0, 139.9, 132.9, 132.3, 132.2, 132.0, 130.6, 130.1, 129.5, 129.1, 128.8 (2C), 128.7 (2C), 128.6 (2C), 128.5, 128.4 (2C), 128.0, 127.9, 127.3, 127.0, 124.9, 124.2, 123.9, 123.7, 123.6, 114.8, 114.2, 113.8, 16.5, 16.4, 16.3, 16.2; HPLC (mixture): 48.1 and 45.9 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 220 nm, retention time 13.5 and 13.9 min; IR (KBr, cm^{-1}): 3055, 2952, 1606, 1444, 820; MS (ES mass): m/z 444.5 (M^+).

(*Z*)-2-(3-(2-(4-Hydroxy-2-methylphenyl)-2-phenylvinyl)quinoxalin-2-yl)-5-methylphenol (4ag(1)) and ***(Z)*-4-(3-(2-(4-hydroxy-2-methylphenyl)-2-phenylvinyl)quinoxalin-2-yl)-3-methylphenol (4ag(2)):** A ~ 1:1 mixture of regioisomers i.e. **4ag(1)** and **4ag(2)** was isolated in this case which could not be separated by using standard column chromatography. The mixture was confirmed by HPLC analysis (see the data and the copy of the HPLC). While an attempt to separate the individual isomer by using preparative HPLC was failed, the LC-MS analysis indicated that both the component present in the mixture possess same mass.

All the spectral data presented here was recorded on 1:1 mixture of compounds.



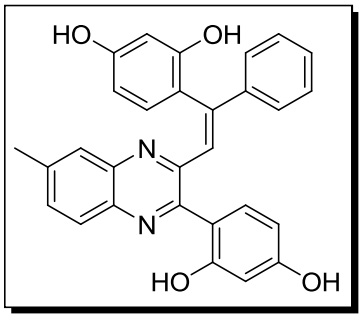
4ag(1)



4ag(2)

Yellow semi solid; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 9.67 (s, 1H), 9.61 (s, 1H), 9.55 (s, 1H), 9.31 (s, 1H), 7.93 (s, 2H), 7.91-7.85 (m, 2H), 7.71 (d, J = 4.2 Hz, 1H), 7.65 (s, 2H), 7.33 (s, 3H), 7.25 (d, J = 12.6 Hz, 3H), 7.13 (d, J = 6.4 Hz, 2H), 7.05 (dd, J = 11.4, 6.9 Hz, 5H), 6.92 (d, J = 8.0 Hz, 1H), 6.78-6.73 (m, 2H), 6.69 (d, J = 6.6 Hz, 2H), 6.36 (d, J = 8.1 Hz, 1H), 6.17 (d, J = 8.0 Hz, 1H), 6.02 (s, 1H), 2.11 (s, 3H), 2.09 (s, 6H), 1.80 (s, 3H); HPLC (mixture): 46.7 and 43.1%; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/20, 3/20, 12/95, 23/95, 25/20, 30/20; flow rate: 1.0 mL/min; UV 220 nm, retention time 12.6 and 12.9 min; IR (KBr, cm^{-1}): 3362, 2941, 1608, 1421, 866; MS (ES mass): m/z 444.5 (M^+).

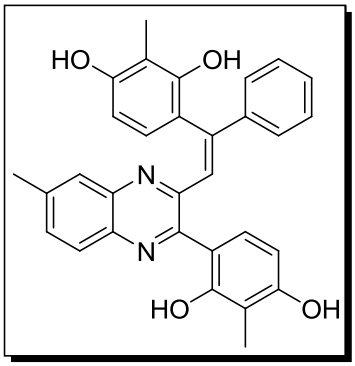
(*Z*)-4-(3-(2-(2,4-Dihydroxyphenyl)-2-phenylvinyl)-6-methylquinoxalin-2-yl)benzene-1,3-diol (4ba)



Light brown solid; mp: 158-160°C; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 10.32 (s, 1H), 9.62 (s, 1H), 9.13 (s, 1H), 8.78 (s, 1H), 7.95-7.90 (m, 1H), 7.69-7.63 (m, 2H), 7.53 (d, J = 7.74 Hz, 2H), 7.28-7.26 (m, 5H), 7.00 (s, 1H), 6.61 (d, J = 8.2 Hz, 2H), 6.32 (d, J = 8.4 Hz, 1H), 6.09 (d, J = 8.2 Hz, 1H) 2.69 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 159.6, 157.7, 156.8, 156.0, 153.9, 152.4, 144.7, 143.1, 140.1, 139.6, 132.3, 132.2, 129.8 (2C), 129.7, 128.7 (2C), 128.6, 128.4, 127.4 (2C), 125.5, 118.0, 116.7, 107.3, 106.4, 102.7, 102.6, 21.1; HPLC: 93.2 %; column: Symmetry C-18

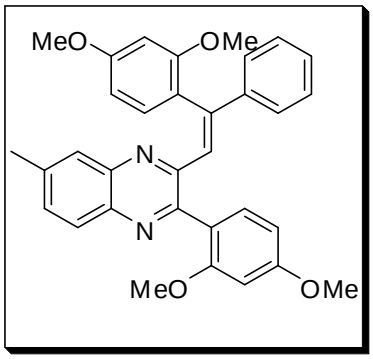
75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 7.02 min; IR (KBr, cm^{-1}): 3410, 2929, 1611, 1416, 829; MS (ES mass): m/z 462.8 (M^+).

(*Z*)-4-(3-(2-(2,4-Dihydroxy-3-methylphenyl)-2-phenylvinyl)-6-methylquinoxalin-2-yl)-2-methylbenzene-1,3-diol (4bb)



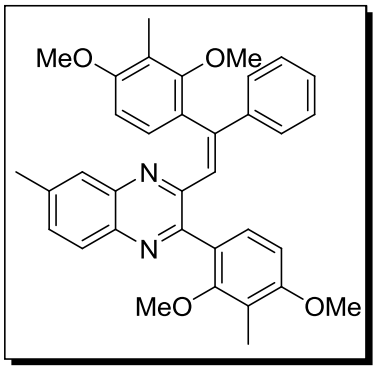
Yellow solid; mp: 168-170°C; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 11.15 (s, 1H), 9.71 (s, 1H), 9.13 (s, 1H), 8.29 (s, 1H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.76 (s, 1H), 7.56-7.55 (m, 2H), 7.35-7.23 (m, 4H), 7.13 (s, 1H), 6.50 (d, *J* = 3.2 Hz, 1H), 6.46 (d, *J* = 8.4 Hz, 1H), 6.25 (dd, *J* = 8.2, 2.4 Hz, 1H), 2.50 (d, *J* = 5.1 Hz, 3H), 2.06 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 158.4, 156.9, 156.0, 151.1, 148.9, 145.2, 144.1 (2C), 140.4, 139.3, 137.4, 132.1, 129.0, 128.7 (2C), 128.6, 128.2 (2C), 127.6 (2C), 127.5, 126.5 (2C), 125.1, 118.4 (2C), 111.6, 106.8, 20.2, 11.6 (2C); HPLC: 99.8 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 7.32 min; IR (KBr, cm^{-1}): 3390, 2913, 1601, 1413, 832; MS (ES mass): m/z 490.8 (M^+).

(*Z*)-2-(3,5-Dimethoxyphenyl)-3-(2-(2,4-dimethoxyphenyl)-2-phenylvinyl)-6-methylquinoxaline (4bc)



Yellow liquid; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 7.83 (d, J = 8.5 Hz, 1H), 7.54 (dd, J = 8.8, 1.4 Hz, 1H), 7.40 (s, 1H), 7.31-7.25 (m, 2H), 7.17 (d, J = 7.7 Hz, 2H), 7.11 (dd, J = 8.2, 4.8 Hz, 1H), 6.93 (d, J = 4.7 Hz, 1H), 6.74 (d, J = 7.0 Hz, 1H), 6.68-6.59 (m, 2H), 6.51 (s, 1H), 6.47-6.42 (m, 1H), 6.34 (dd, J = 8.3, 1.9 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 3.73 (s, 3H), 3.31 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 159.8, 159.7, 158.8, 157.7, 157.4, 156.7, 156.4, 155.9, 143.1 (2C), 142.9, 140.2, 137.7, 128.8 (2C), 128.7 (2C), 128.0, 127.5 (2C), 120.2, 119.8, 114.0, 107.2, 106.3, 104.5, 100.3, 99.4, 55.8 (4C), 21.2; HPLC: 92.7 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.22 min; IR (KBr, cm^{-1}): 2936, 1604, 1411, 795; MS (ES mass): m/z 518.9 (M^+).

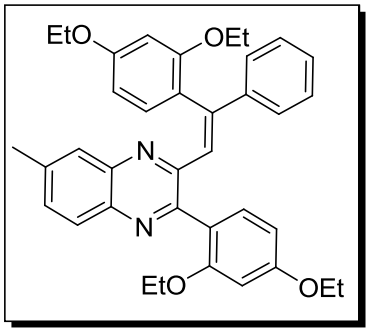
(*Z*)-2-(2,4-Dimethoxy-3-methylphenyl)-3-(2-(2,4-dimethoxy-3-methylphenyl)-2-phenylvinyl)-6-methylquinoxaline (4bd)



Yellow liquid; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 7.98 (dd, J = 7.7, 1.6 Hz, 1H), 7.76-7.66 (m, 2H), 7.49 (s, 1H), 7.34-7.26 (m, 5H), 7.22-7.16 (m, 2H), 6.95 (s, 1H), 6.90 (d, J = 8.5 Hz, 1H), 6.73 (s, 1H), 6.62 (d, J = 8.5 Hz, 2H), 3.85 (s, 3H), 3.75 (s, 3H), 3.52 (s, 3H), 3.38 (s, 3H), 2.15 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 168.4, 158.1, 157.3, 156.9, 153.7, 151.5, 142.7 (2C), 140.6 (2C), 130.2, 130.0, 129.3, 128.8 (2C), 128.7, 127.9, 127.5, 127.2 (2C), 126.0, 125.1(2C),

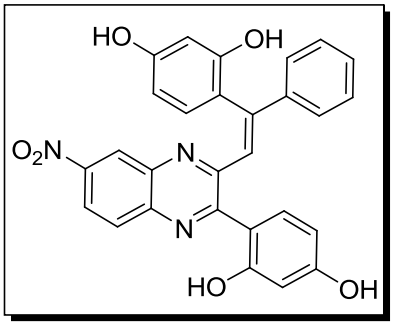
119.1, 118.6, 113.6, 109.9, 98.0, 61.5, 60.0, 56.1, 55.9, 21.4, 9.4 (2C); HPLC: 94.1 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 7.54 min; IR (KBr, cm^{-1}): 2941, 1599, 1411, 795; MS (ES mass): m/z 547.1 (M+1).

(*Z*)-2-(2,4-Diethoxyphenyl)-3-(2-(2,4-diethoxyphenyl)-2-phenylvinyl)-6-methylquinoxaline (4be)



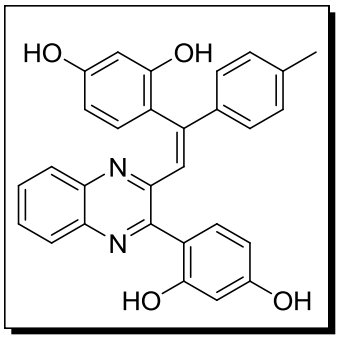
Brown semi solid; ^1H NMR (400 MHz, $CDCl_3$) ppm: 8.08-7.98 (m, 1H), 7.80 (d, *J* = 9.7 Hz, 1H), 7.66-7.59 (m, 2H), 7.22-7.21 (m, 3H), 7.14 (d, *J* = 8.3 Hz, 1H), 7.07 (s, 1H), 6.98 (d, *J* = 5.4 Hz, 1H), 6.79 (d, *J* = 7.9 Hz, 2H), 6.69 (d, *J* = 8.3 Hz, 1H), 6.37 (d, *J* = 8.3 Hz, 1H), 6.26 (d, *J* = 6.2 Hz, 1H), 4.06-4.00 (m, 8H), 2.38 (s, 3H), 1.45-1.36 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 161.2, 157.9, 150.1, 149.7, 149.6, 144.7, 144.3, 140.5, 139.6, 138.9, 132.1(2C), 131.0, 130.7, 130.4 (2C), 130.3, 129.6, 129.4, 128.9 (2C), 128.5, 127.9, 127.1 (2C), 115.2, 111.0, 105.5, 63.8, 63.5 (2C), 63.3, 21.1, 14.8 (2C), 14.7 (2C); HPLC: 95.9 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 5.42 min; IR (KBr, cm^{-1}): 2937, 1589, 1424, 817; MS (ES mass): m/z 575.1 (M^+).

(*Z*)-4-(3-(2-(2,4-Dihydroxyphenyl)-2-phenylvinyl)-6-nitroquinoxalin-2-yl)benzene-1,3-diol (4ca)



Light yellow solid; mp: 234-236°C; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 10.45 (s, 1H), 9.20 (s, 1H), 8.66 (s, 1H), 8.38 (s, 1H), 8.07 (s, 1H), 7.46-7.42 (m, 5H), 7.22-7.12 (m, 2H), 7.09-7.02 (m, 1H), 6.88 (d, J = 8.3 Hz, 1H), 6.87-6.80 (m, 1H), 6.79-6.69 (m, 1H), 6.55 (s, 1H), 6.48-6.29 (m, 1H), 6.23-6.04 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 160.3, 159.3, 158.9, 156.2, 147.5, 144.9, 144.3, 141.3, 139.9, 134.1, 129.7 (2C), 129.6, 129.0 (2C), 128.7, 128.6 (2C), 128.3, 127.9 (2C), 127.6 (2C), 112.3, 109.7, 107.6, 106.7, 104.7; HPLC: 80.3 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 5.42 min; IR (KBr, cm^{-1}): 3386, 2937, 1589, 1424, 817; MS (ES mass): m/z 493.8 (M^+).

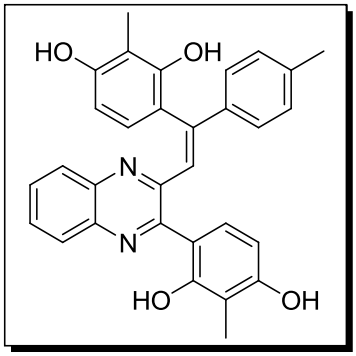
(*Z*)-4-(3-(2-(2,4-Dihydroxyphenyl)-2-*p*-tolylvinyl)quinoxalin-2-yl)benzene-1,3-diol (4da)



Dark brown solid; mp: 154-156°C; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 10.36 (s, 1H), 9.64 (s, 1H), 9.14 (s, 1H), 8.77 (s, 1H), 7.94 (d, J = 6.2 Hz, 1H), 7.66 (d, J = 9.9 Hz, 2H), 7.53 (d, J = 5.7 Hz, 1H), 7.34 (d, J = 8.3 Hz, 1H), 7.14 (d, J = 8.2 Hz, 4H), 6.97 (s, 1H), 6.62 (d, J = 8.2 Hz, 1H), 6.41 (d, J = 2.1 Hz, 1H), 6.38-6.30 (m, 1H), 6.16 (d, J = 2.1 Hz, 1H), 6.11 (d, J = 8.2 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 159.9, 157.9, 157.2, 156.2, 154.0, 152.3, 144.6, 140.6, 140.2, 139.5, 137.6, 132.3 (2C), 129.5, 129.4, 129.3 (2C), 129.2, 128.7, 128.3, 127.5, 124.7,

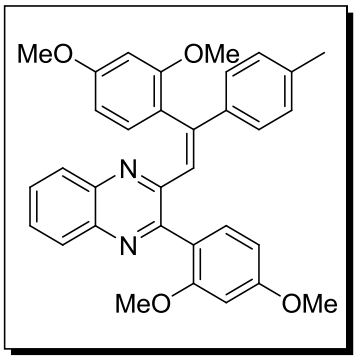
118.1, 116.5, 107.2, 106.4, 102.9, 102.8, 21.1; HPLC: 94.0 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.1 min; IR (KBr, cm^{-1}): 3256, 2871, 1566, 1398, 802; MS (ES mass): m/z 462.9 (M^+).

(*Z*)-4-(3-(2-(2,4-Dihydroxy-3-methylphenyl)-2-*p*-tolylvinyl)quinoxalin-2-yl)-2-methylbenzene-1,3-diol (4db)



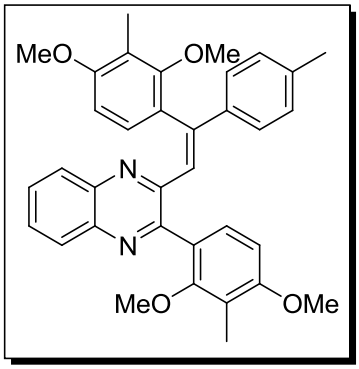
Yellow solid; mp: 160-162 °C. ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 10.39 (s, 1H), 9.62 (s, 1H), 9.14 (s, 1H), 8.78 (s, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.57-7.47 (m, 1H), 7.33 (d, *J* = 4.0 Hz, 1H), 7.18-7.08 (m, 4H), 6.95 (d, *J* = 4.1 Hz, 1H), 6.62 (d, *J* = 8.2 Hz, 1H), 6.39 (d, *J* = 2.1 Hz, 1H), 6.32 (d, *J* = 8.3 Hz, 1H), 6.16 (d, *J* = 6.3 Hz, 1H), 6.12-6.07 (m, 1H), 2.50 (s, 6H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 159.9, 157.9, 157.2, 156.2, 154.0, 152.3, 144.6, 140.6, 140.2, 139.5, 137.6, 132.3, 129.5 (2C), 129.4, 129.3, 129.2 (2C), 128.7, 128.3, 127.5, 124.6, 118.1, 116.5, 107.2, 106.5, 102.9, 102.8, 21.2, 9.6 (2C); HPLC: 92.3 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 8.21 min; IR (KBr, cm^{-1}): 3345, 2931, 1610, 1421, 826; MS (ES mass): m/z 490.8 (M^+).

(*Z*)-2-(2,4-Dimethoxyphenyl)-3-(2-(2,4-dimethoxyphenyl)-2-*p*-tolylvinyl)quinoxalines (4dc)



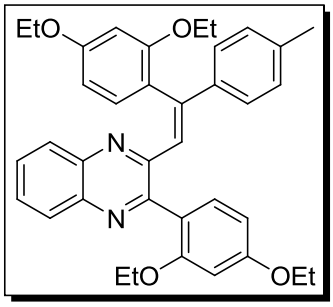
Brown solid; mp: 56-58 °C; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 7.99 (d, *J* = 7.0 Hz, 1H), 7.69-7.65 (m, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 5.5 Hz, 1H), 7.15 (s, 1H), 7.06 (d, *J* = 8.1 Hz, 2H), 7.03 (d, *J* = 7.8 Hz, 2H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.54 (d, *J* = 8.3 Hz, 2H), 6.51-6.48 (m, 1H), 6.34 (d, *J* = 2.4 Hz, 1H), 6.30 (d, *J* = 8.2 Hz, 1H), 3.85 (d, *J* = 6.8 Hz, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.34 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 160.0, 158.5 (2C), 158.0, 157.9, 144.1, 142.1, 141.0, 138.6 (2C), 137.5, 137.3, 129.1, 128.9 (2C), 128.7 (2C), 128.6, 128.3, 127.8, 127.5, 127.1, 126.2, 114.0, 105.2, 103.9, 99.2, 99.6, 66.4, 55.3, 55.2 (2C), 21.1; HPLC: 90.2 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 7.34 min; IR (KBr, cm^{-1}): 2953, 1604, 1433, 921; MS (ES mass): m/z 519.2 (M+1).

(*Z*)-2-(2,4-Dimethoxy-3-methylphenyl)-3-(2-(2,4-dimethoxy-3-methylphenyl)-2-*p*-tolylvinyl)quinoxalines (4dd)



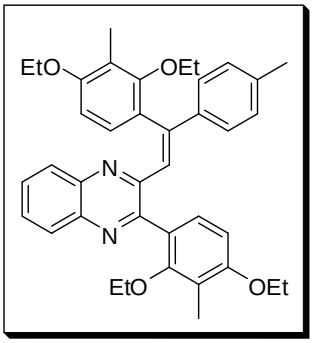
Brown solid; mp: 68-70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.00 (d, *J* = 7.7 Hz, 1H), 7.69-7.64 (m, 1H), 7.61-7.54 (m, 2H), 7.20 (d, *J* = 8.3 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 2H), 7.06 (s, 1H), 7.04 (s, 2H), 6.77 (d, *J* = 8.3 Hz, 1H), 6.57-6.52 (m, 1H), 6.50 (s, 1H), 6.43 (d, *J* = 8.5 Hz, 1H), 6.34 (s, 1H), 6.31 (d, *J* = 8.3 Hz, 1H), 3.93-3.75 (m, 12H), 3.34 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 160.4, 158.8, 158.4, 140.9, 140.5, 140.3, 138.8, 132.6, 132.5, 131.1 (2C), 129.9 (2C), 128.6 (2C), 127.8, 127.3 (2C), 126.0, 125.9 (2C), 114.1, 111.5, 108.1, 106.6, 105.1, 102.8, 98.8, 56.2 (2C), 55.0 (2C), 21.1 (2C), 9.9; HPLC: 93.9 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 7.21 min; IR (KBr, cm^{-1}): 2964, 2857 1611, 1454, 870; MS (ES mass): m/z 547.1 (M+1).

(*Z*)-2-(2,4-Diethoxyphenyl)-3-(2-(2,4-diethoxyphenyl)-2-*p*-tolylvinyl)quinoxalines (4de)



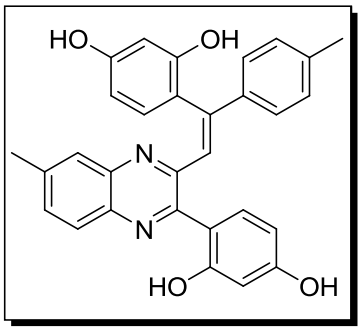
Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 7.63-7.58 (m, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 7.04 (t, *J* = 8.2 Hz, 4H), 6.77 (d, *J* = 8.1 Hz, 1H), 6.73-6.67 (m, 1H), 6.64 (s, 1H), 6.50-6.39 (m, 2H), 6.26 (s, 1H), 6.24 (s, 1H), 4.08-3.98 (m, 8H), 2.32 (s, 3H), 1.46-1.37 (m, 9H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 160.1, 159.4, 158.9 (2C), 156.2, 153.8, 143.2, 142.3, 141.8, 138.4, 137.9, 131.2 (2C), 129.6 (2C), 128.0 (2C), 127.3 (2C), 125.8 (2C), 114.2, 109.9, 107.1, 105.5, 104.1, 100.9, 99.1, 63.3 (4C), 21.2, 14.1 (4C); HPLC: 93.6 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 7.38 min; IR (KBr, cm^{-1}): 2937, 2841, 1609, 1427, 843; MS (ES mass): m/z 575.3 (M+1).

(*Z*)-2-(2,4-Diethoxy-3-methylphenyl)-3-(2-(2,4-diethoxy-3-methylphenyl)-2-*p*-tolylvinyl)quinoxalines (4dh)



Light yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.02 (d, *J* = 7.7 Hz, 2H), 7.59 (s, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 10.8 Hz, 2H), 7.12 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 3H), 6.69 (t, *J* = 9.6 Hz, 2H), 6.47 (d, *J* = 8.3 Hz, 2H), 4.01 (d, *J* = 6.8 Hz, 3H), 4.09-4.03 (m, 3H), 2.32 (s, 3H), 2.22 (s, 3H), 2.05 (s, 3H), 1.44-1.42 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 159.7, 158.9, 157.0, 155.1, 152.7, 143.9, 143.1, 140.4, 138.9 (2C), 136.8, 134.4, 129.4 (2C), 129.2, 125.9 (2C), 124.1, 123.5 (2C), 120.2, 113.2, 112.1, 110.7, 106.4 (2C), 105.4, 104.0, 65.5, 65.1, 64.8, 64.2, 21.4, 13.9 (4C), 9.7 (2C); HPLC: 94.8 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.58 min; IR (KBr, cm^{-1}): 2953, 2866, 1597, 1461, 912; MS (ES mass): m/z 603.1 (M+1).

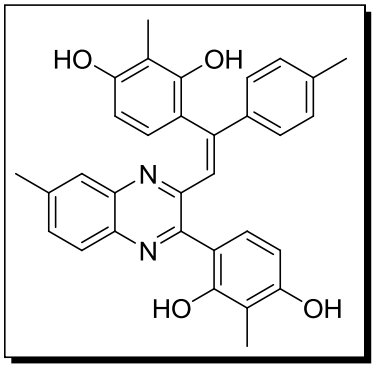
(*Z*)-4-(3-(2-(2,4-Dihydroxyphenyl)-2-p-tolylvinyl)-6-methylquinoxalin-2-yl)benzene-1,3-diol (4ea)



Yellow solid; mp: 230-232 °C; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 11.19 (s, 1H), 9.79 (s, 1H), 9.13 (s, 1H), 8.24 (s, 1H), 7.98 (d, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 7.1 Hz, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 4H), 7.11 (s, 1H), 6.49 (d, *J* = 8.3 Hz, 2H), 6.26 (d, *J* = 8.2 Hz, 1H), 2.30 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 158.4, 156.9, 155.9, 154.4, 153.5, 151.4, 146.3, 144.3, 140.3, 139.3, 138.2, 137.8, 130.3, 129.9 (2C), 129.3, 128.8,

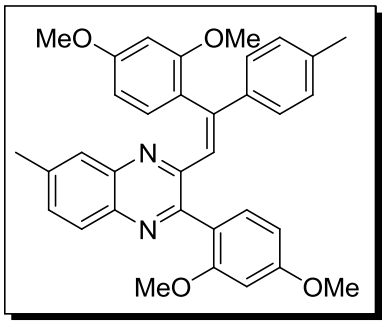
128.2, 128.1, 127.8, 127.6, 125.4, 119.2, 113.8, 111.6, 111.5, 109.9, 106.8, 21.1 (2C); HPLC: 94.2 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 8.21 min; IR (KBr, cm^{-1}): 3538, 2926, 2851, 1607, 1458, 845; MS (ES mass): m/z 476.9 (M+1).

(*Z*)-4-(3-(2-(2,4-Dihydroxy-3-methylphenyl)-2-p-tolylvinyl)-6-methylquinoxalin-2-yl)-2 methylbenzene-1,3-diol (4eb)



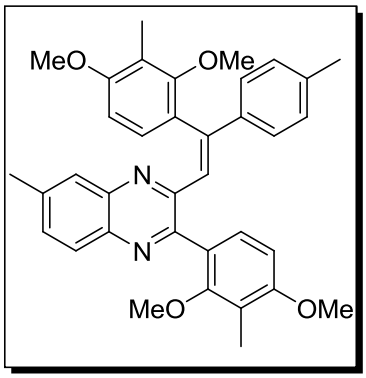
Brown solid; mp: 140-142 °C; ^{1}H NMR (400 MHz, DMSO-d_6) ppm: 11.22 (s, 1H), 9.75 (s, 1H), 9.11 (s, 1H), 8.29 (s, 1H), 7.90-7.84 (m, 2H), 7.55 (d, *J* = 8.2 Hz, 4H), 7.42-7.39 (m, 1H), 7.29 (d, *J* = 4.0 Hz, 1H), 7.12 (s, 1H), 6.52-6.47 (m, 1H), 6.46-6.41 (m, 1H), 6.27-6.21 (m, 1H), 2.48 (s, 6H), 2.28 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) ppm: 157.1, 156.9, 156.2, 153.8, 142.3, 141.8, 140.4, 139.1, 138.4, 135.6, 134.3 (2C), 131.2, 128.0, 127.3 (2C), 125.8, 125.7, 125.0, 123.1, 121.7 (2C), 115.6, 114.2, 113.6, 112.7, 109.9, 106.3, 22.3 (2C), 9.2 (2C); HPLC: 93.7 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 8.10 min; IR (KBr, cm^{-1}): 3431, 2946, 2842, 1604, 1440, 871; MS (ES mass): m/z 504.8 (M^+).

(*Z*)-2-(2,4-Dimethoxyphenyl)-3-(2-(2,4-dimethoxyphenyl)-2-*p*-tolylvinyl)-6-methylquinoxaline (4ec)



Light brown solid; mp: 84-86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 7.87 (d, *J* = 8.3 Hz, 1H), 7.48-7.37 (m, 2H), 7.20-7.12 (m, 3H), 7.08-6.99 (m, 3H), 6.77 (t, *J* = 10.1 Hz, 1H), 6.56-6.50 (m, 1H), 6.48 (t, *J* = 2.2 Hz, 1H), 6.33 (t, *J* = 2.7 Hz, 1H), 6.30 (d, *J* = 8.3 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.76 (s, 3H), 3.33 (s, 3H), 2.51 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 161.5, 160.2, 158.6, 158.0, 157.9, 152.5, 143.6, 140.9, 140.2, 139.2, 137.3, 131.9 (2C), 131.6, 129.1, 128.6, 128.4, 128.2, 128.0, 127.7, 127.6, 127.1, 125.1, 121.3, 105.1, 103.8, 98.5, 98.4, 55.4 (4C), 21.1 (2C); HPLC: 90.3 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.46 min; IR (KBr, cm^{-1}): 2937, 2830, 1615, 1416, 902; MS (ES mass): m/z 533.2 (M+1).

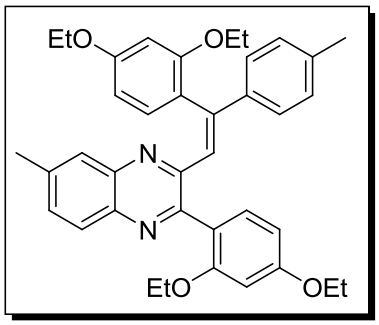
(*Z*)-2-(2,4-Dimethoxy-3-methylphenyl)-3-(2-(2,4-dimethoxy-3-methylphenyl)-2-*p*-tolylvinyl)-6-methylquinoxaline (4ed)



Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 7.98-7.87 (m, 2H), 7.47 (s, 2H), 7.16 (d, *J* = 5.7 Hz, 4H), 7.05 (s, 1H), 6.85-6.76 (m, 2H), 6.75-6.68 (m, 2H), 6.53 (s, 1H), 6.49-6.45 (m, 2H), 6.34 - 6.32 (m, 2H), 3.80 (m, 12H), 2.32 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 159.2, 158.8, 157.7, 154.4, 144.1, 141.7, 139.4, 138.4, 134.3, 132.5, 129.9, 129.2, 128.6, 128.4 (2C), 127.3, 126.0, 125.7, 125.6 (2C), 123.0, 119.0, 117.7, 116.4, 110.8, 105.7, 104.5, 103.3, 68.7 (2C), 65.7 (2C), 21.2 (2C),

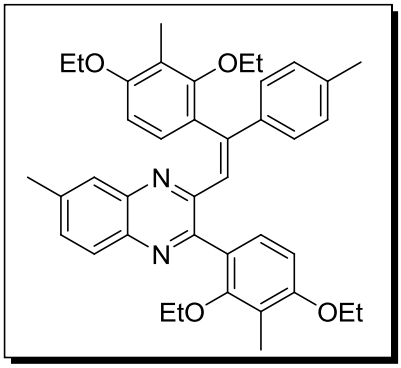
9.5 (2C); HPLC: 95.4 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.31 min; IR (KBr, cm^{-1}): 2948, 2834, 1591, 1422, 907; MS (ES mass): m/z 561.2 (M+1).

(*Z*)-2-(2,4-Diethoxyphenyl)-3-(2-(2,4-diethoxyphenyl)-2-*p*-tolylvinyl)-6-methylquinoxaline (4ee)



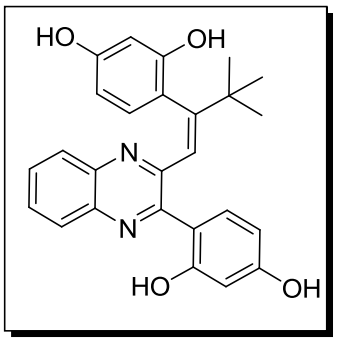
Light yellow; ^1H NMR (400 MHz, $CDCl_3$) ppm: 7.47-7.41 (m, 1H), 7.11 (d, *J* = 7.9 Hz, 2H), 7.03-7.02 (m, 3H), 7.01 (s, 1H), 6.73-6.66 (m, 1H), 6.65-6.58 (m, 1H), 6.45 (s, 3H), 6.26 (s, 1H), 6.24-6.17 (m, 1H), 4.01 (m, 8H), 2.54 (s, 3H), 2.31 (s, 3H), 1.35-1.20 (m, 9H), 0.74 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 159.4, 156.2, 154.8, 151.9, 142.3, 140.4, 139.1, 137.9, 136.0, 135.9, 134.6, 134.3, 131.2, 128.0, 127.3, 125.8, 124.4, 123.5, 123.1, 121.7, 120.1, 114.2, 112.7, 111.8, 109.9, 106.4, 105.5, 104.1, 65.0 (2C), 64.5 (2C), 21.2 (2C), 14.3 (4C); HPLC: 92.7 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.28 min; IR (KBr, cm^{-1}): 2953, 2844, 1586, 1439, 802; MS (ES mass): m/z 589.1 (M+1).

(*Z*)-2-(2,4-Diethoxy-3-methylphenyl)-3-(2-(2,4-diethoxy-3-methylphenyl)-2-*p*-tolylvinyl)-6-methylquinoxaline (4eh)



Yellow semi solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 7.90 (s, 1H), 7.80 (s, 1H), 7.48 (s, 2H), 7.41 (d, *J* = 8.6 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 3H), 7.11 (s, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 6.73 (s, 1H), 6.67 (d, *J* = 8.5 Hz, 2H), 6.44 (d, *J* = 8.3 Hz, 2H), 4.03-4.02 (m, 8H), 2.32 (s, 3H), 2.23 (s, 3H), 1.02 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 159.4, 156.2, 154.8, 151.9, 142.3, 140.4, 139.1, 137.9, 136.0, 135.9, 134.6, 134.3, 131.2, 128.0, 127.3, 125.8, 124.4, 123.5, 123.1, 121.7, 120.1, 114.2, 112.7, 111.8, 109.9, 106.4, 105.5, 104.1, 65.0 (2C), 64.5 (2C), 21.2 (2C), 14.3 (4C), 9.7 (2C); HPLC: 94.8 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 7.12 min; IR (KBr, cm^{-1}): 2939, 2867, 1577, 1442, 817; MS (ES mass): m/z 617.2 (M+1).

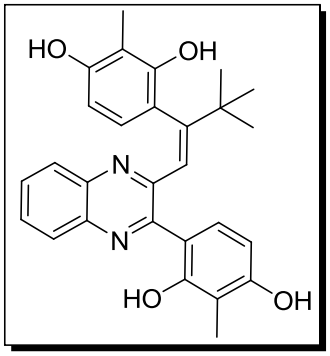
(*Z*)-4-(3-(2-(2,4-Dihydroxyphenyl)-3,3-dimethylbut-1-enyl)quinoxalin-2-yl)benzene-1,3-diol (4fa)



Yellow solid; mp: 208-210°C; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 10.56 (s, 1H), 9.72 (s, 1H), 8.91 (s, 1H), 8.46 (s, 1H), 7.94-7.80 (m, 1H), 7.63 (t, *J* = 7.0 Hz, 2H), 7.54-7.49 (m, 1H), 7.46 (d, *J* = 8.3 Hz, 1H), 6.72 (s, 1H), 6.58 (d, *J* = 8.8 Hz, 1H), 6.49-6.29 (m, 2H), 6.06 (d, *J* = 6.3 Hz, 2H), 1.09-1.01 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 160.1, 157.7, 156.9, 155.7, 153.6, 153.5, 152.4, 140.0, 139.0, 132.7, 131.4, 129.5, 129.3, 128.7 (2C), 123.9, 117.6, 115.8, 106.9, 105.4, 102.9, 102.4,

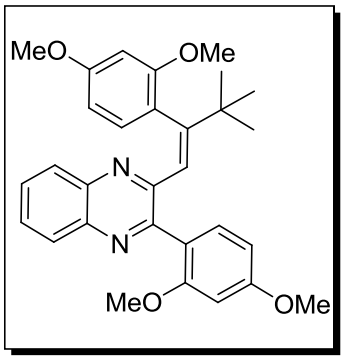
60.1, 29.7 (3C); HPLC: 95.1 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 8.31 min; IR (KBr, cm^{-1}): 3341, 2915, 2842, 1563, 1452, 826; MS (ES mass): m/z 428.9 (M^+).

(*Z*)-4-(3-(2-(2,4-Dihydroxy-3-methylphenyl)-3,3-dimethylbut-1-enyl)quinoxalin-2-yl)-2-methylbenzene-1,3-diol (4fb)



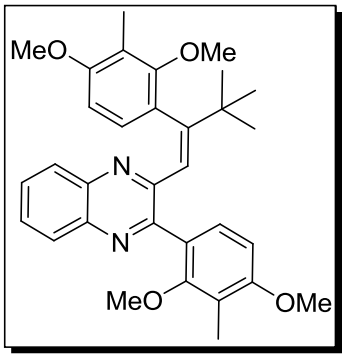
Light yellow solid; mp: 240-242 °C; ^1H NMR (400 MHz, $CDCl_3$) ppm: 11.73 (s, 1H), 11.05 (s, 1H), 9.93 (s, 1H), 8.97 (s, 1H), 7.95 (d, *J* = 6.1 Hz, 1H), 7.82 (s, 1H), 7.71 (d, *J* = 9.1 Hz, 1H), 7.64 (d, *J* = 9.1 Hz, 1H), 6.84 (s, 1H), 6.51 (d, *J* = 8.3 Hz, 2H), 6.21 (d, *J* = 8.4 Hz, 2H), 2.08 (s, 3H), 1.95 (s, 3H), 1.11 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 159.6, 156.9, 154.1, 145.1, 138.1, 137.7, 129.7, 129.4 (2C), 128.5, 128.2 (2C), 127.5, 127.4, 120.5, 120.4, 115.3, 112.2, 110.2, 108.1, 104.4, 101.1, 60.2, 29.6 (3C), 9.2 (2C); HPLC: 98.3 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 8.47 min; IR (KBr, cm^{-1}): 3347, 2927, 2834, 1542, 1419, 918; MS (ES mass): m/z 457.1 (M+1).

(*Z*)-2-(2,4-Dimethoxyphenyl)-3-(2-(2,4-dimethoxyphenyl)-3,3-dimethylbut-1-enyl)quinoxalines (4fc)



Yellow semi solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 8.08-7.92 (m, 1H), 7.56 (d, *J* = 5.4 Hz, 3H), 7.28 (s, 1H), 6.72 (s, 1H), 6.65 (d, *J* = 8.2 Hz, 2H), 6.57 (d, *J* = 2.1 Hz, 1H), 6.39 (s, 1H), 6.34-6.23 (m, 1H), 3.91 (s, 3H), 3.80 (s, 3H), 3.75 (s, 3H), 3.72 (s, 3H), 1.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 159.7, 158.9, 158.2, 157.9, 156.5, 141.4, 140.5, 138.9, 132.1, 131.0, 130.7, 128.9, 128.5 (2C), 127.9, 127.1, 111.0, 108.7, 105.5, 105.1, 101.3, 99.5, 57.5, 56.1 (2C), 54.2 (2C), 29.6 (3C); HPLC: 91.4 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.46 min; IR (KBr, cm^{-1}): 2932, 2841, 1563, 1422, 913; MS (ES mass): m/z 484.8 (M^{+}).

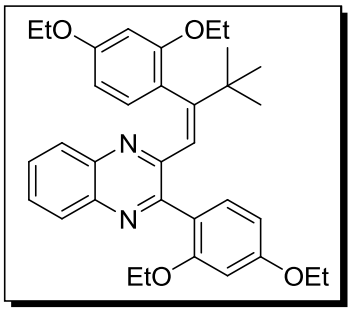
(*Z*)-2-(2,4-Dimethoxy-3-methylphenyl)-3-(2-(2,4-dimethoxy-3-methylphenyl)-3,3-dimethylbut-1-enyl)quinoxalines (4fd)



Yellow semi solid; ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 7.95 (d, *J* = 7.3 Hz, 1H), 7.58 (d, *J* = 4.2 Hz, 1H), 7.55-7.49 (m, 1H), 7.30-7.24 (m, 1H), 6.70 (s, 1H), 6.64 (d, *J* = 8.3 Hz, 1H), 6.56 (d, *J* = 2.1 Hz, 1H), 6.39 (s, 1H), 6.26 (d, *J* = 8.2 Hz, 1H), 3.90 (s, 3H), 3.79 (s, 3H), 3.74 (s, 3H), 3.72 (s, 3H), 1.25 (s, 6H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 161.7, 159.5, 158.1, 152.9, 140.9, 140.1, 131.8 (2C), 130.0, 128.9 (2C), 128.7 (2C), 128.5, 128.4, 128.0, 123.0 (2C), 121.1, 104.6,

102.7, 59.9, 55.4 (2C), 55.1 (2C), 37.4, 29.6 (3C), 9.6 (2C); HPLC: 90.6 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.37 min; IR (KBr, cm^{-1}): 2927, 2854, 1603, 1571, 1443, 804; MS (ES mass): m/z 512.9 (M^+).

(*Z*)-2-(2,4-Diethoxyphenyl)-3-(2-(2,4-diethoxyphenyl)-3,3-dimethylbut-1-enyl)quinoxalines (4fe)



Light yellow liquid; ^1H NMR (400 MHz, $CDCl_3$) ppm: 7.95 (d, *J* = 6.3 Hz, 1H), 7.68-7.59 (m, 1H), 7.58-7.48 (m, 2H), 7.27-7.19 (m, 1H), 6.78 (d, *J* = 6.2 Hz, 1H), 6.59 (d, *J* = 8.3 Hz, 1H), 6.55 (d, *J* = 4.3 Hz, 1H), 6.28 (s, 1H), 6.25 (d, *J* = 8.0 Hz, 1H), 5.28 (s, 1H), 4.16-4.08 (m, 2H), 4.03 (q, *J* = 6.9 Hz, 2H), 3.96 (q, *J* = 6.9 Hz, 2H), 3.92 (q, *J* = 6.9 Hz, 2H), 1.50 (t, *J* = 6.8 Hz, 3H), 1.37 (t, *J* = 7.0 Hz, 3H), 1.28 (m, 6H), 1.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) ppm: 160.9, 158.6 (2C), 157.7, 157.4, 153.1, 140.7, 132.2, 128.8 (2C), 128.5, 128.3(2C), 123.1 (2C), 121.2, 114.8, 112.8, 105.1 (2C), 103.3, 102.2, 63.6, 63.5, 63.2, 63.0, 37.4, 29.7 (3C), 14.8, 14.7 (2C), 14.6; HPLC: 96.4 %; column: Symmetry C-18 75*4.6 mm, 3.5µm, mobile phase A: 0.1 % Formic Acid in water mobile phase B: CH_3CN (gradient) T/B% : 0/50, 1/50, 3/98, 10/98, 10.5/50, 12/50; flow rate: 1.0 mL/min; UV 220 nm, retention time 6.53 min; IR (KBr, cm^{-1}): 2963, 2847, 1604, 1565, 1429, 811; MS (ES mass): m/z 540.9 (M^+).

Reference

1. A. Nakhi, M. S. Rahman, R. Kishore, C. L. T. Meda, G. S. Deora, K. V. L. Parsa, M. Pal, *Bioorg. Med. Chem. Lett.* 2012, 22, 6433–6441

Docking studies

The docking analysis of molecules was performed using FRED, version 3.0.1[1,2] implemented from OpenEye Scientific Software. All molecules were sketched in 3D format with VIDA program of OpenEye. Omega[3] module was used to produce maximum conformers of the molecules and charges were added from mmff94s force field. The crystal structure coordinates of NAD-dependent protein deacetylase were obtained from the protein data bank (PDB ID: 2HJH).[4] The protein is preprocessed by removal of water molecules and assigning bond orders. Hydrogens were added to the protein from the program Reduce version 3.1.[5] The final protein was obtained by optimizing the added hydrogens using conjugate gradient algorithm from SZYBKI version 1.7. The grid for molecular docking was generated with bound co-crystallized ligand. Finally FRED was used to dock the conformers of the molecules into the active site. Exhaustive conformation search was implemented during docking to generate 10 best scoring poses per each molecule.

Results and Discussion: Molecular docking study was carried out to find out the binding mode of compound **4bb** with the catalytic active site of yeast Sir2. The hydroxyl groups of resrcinol substituent on the vinylic double bond makes two hydrogen bond interactions with backbone -NH group of Asp 498 (2.82 Å) and side chain -NH_2 group of Asn 496 (2.88 Å) respectively (Fig. 1). The dock score and its contributing factors were listed in Table S2.

Table S2:

Molecule	Dock Score[a]	Shape	Protein Desolvation	Ligand Desolvation	Hydrogen bond
4bb	-8.0	-15.7	7.8	3.02	-3.09

[a]FRED Chemgauss4 score

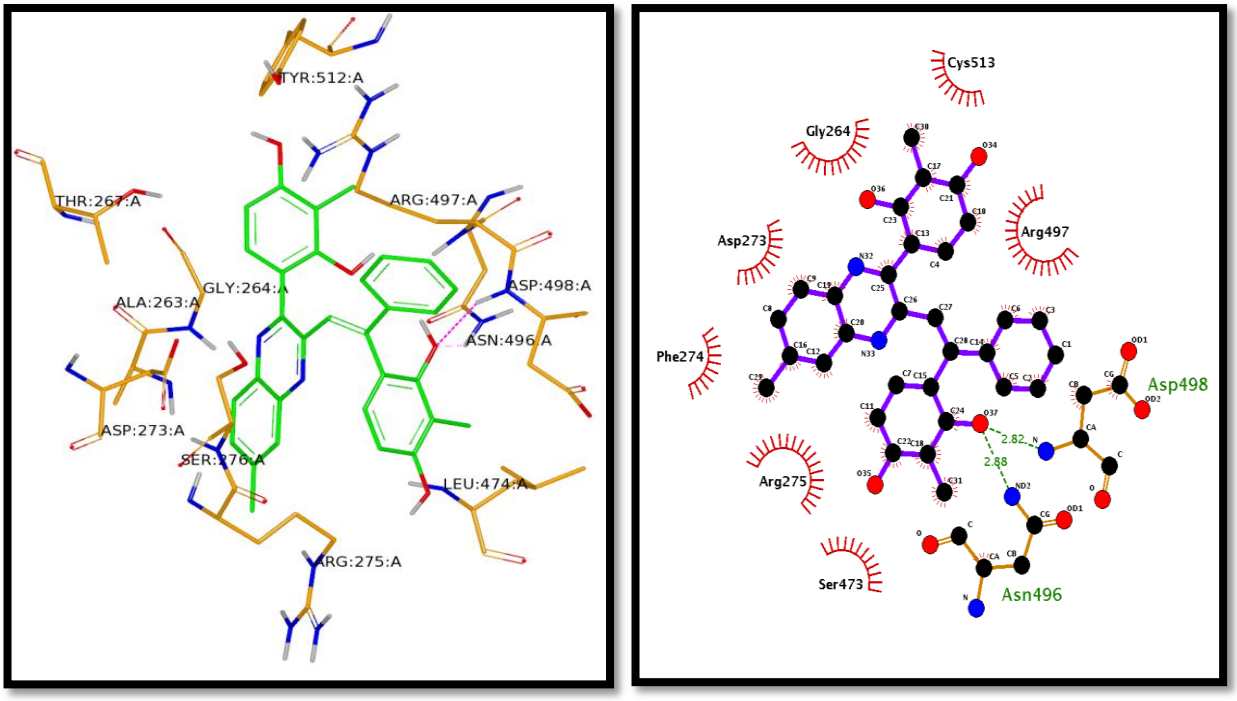
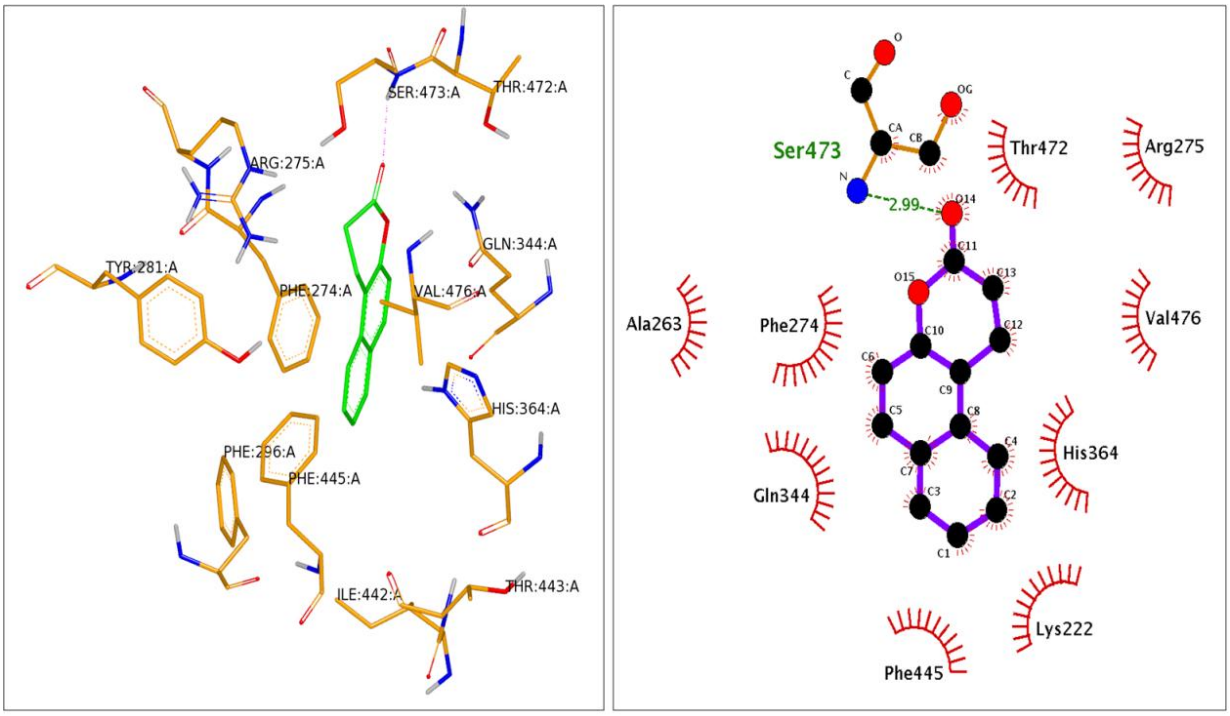


Fig. S1. The binding mode of compound **4bb** and 2d interaction plot.

Docking Studies of splitomicin:

Splitomicin binds at the active site by making a hydrogen bond interaction with the amino group of Ser 473 through the carbonyl group (Figure S2).



a b

Fig. S2: a) Splitomicin at the active site with hydrogen bonding to Ser 473 b) splitomicin bound at active site surface mapped with electrostatic property.

Molecule	Dock Score[a]	Steric	Protein Desolvation	Ligand Desolvation	Hydrogen bond
Splitomicin	-8.5	-14.3	6.6	0.6	-1.35

[a] FRED Chemgauss4 score

References:

1. G.B. McGaughey, R.P. Sheridan, C.I. Bayly, J.C. Culberson, C. Kreatsolas, S. Lindsley, V. Maiorov, J.-F. Truchon and W.D. Cornell, "Comparison of Topological, Shape, and Docking Methods in Virtual Screening", *J. Chem. Inf. Model.*, **2007**, *47 (4)*, pp 1504-1519
2. M. McGann, "FRED Pose Prediction and Virtual Screening Accuracy", J. Chem. Inf. Model., **2011**, 51 (3), 578-596
3. Paul C.D. Hawkins, A. Geoffrey Skillman, Gregory L. Warren, Benjamin A. Ellingson, and Matthew T. Stahl. Conformer Generation with OMEGA: Algorithm and Validation Using High Quality Structures from the Protein Databank and Cambridge Structural Database. J. Chem. Inf. Model., **2010**, 50, 572-584
4. Hall, B.E., Buchberger, J.R., Gerber, S.A., Ambrosio, A.L.B., Gygi, S.P., Filman, D., Moazed, D., Ellenberger, T., Autoregulation of the yeast Sir2 deacetylase by reaction and trapping of a pseudosubstrate motif in the active site. To be Published (DOI: http://www.rcsb.org/pdb/explore/explore.do?structureId=2hjh)

5. Word, et. al. (1999) Asparagine and glutamine: using hydrogen atom contacts in the choice of side-chain amide orientation. J. Mol. Biol. 285, 1735-1747.

Pharmacology

A yeast cell based assay[1] for identification of potential inhibitors of HDAC Sir2 Reporter silencing assay: In this assay a yeast strain (TEL::URA3 strain (MATα ura3-52 lys2-801 ade2-101 trpΔ63 his3Δ200 leu3Δ200 leu2-Δ1 TEL adh4::URA) was used in which, a reporter gene URA3 was inserted in the silenced telomeric region where it is silenced by yeast Sir2 protein. A compound having the Sir2 protein inhibitory effect will inhibit the Sir2 protein, and thus the URA3 gene will be expressed and this will result in the death of the yeast cell in presence of 5-fluoro orotic acid (5-FOA) through formation of toxic 5-fluorouracil. This assay can also test the toxicity of compounds. The cells when grown in absence of 5-FOA should grow if the compound is not toxic. However in case of a toxic compound yeast cells would die. The yeast strain was inoculated in 5.0 mL of YPDA media. The cells growing at the exponential phase were dispensed in the round bottom 96-well plate using cell dispenser. A Stock concentration of 10% 5-FOA was used to make a final concentration of 0.3% 5-FOA in the wells of 96-well plate. The compounds at a concentration of 50 uM were added to each well and the plates were incubated at 30 °C. Absorbance at 590 was measured using 96 well plate reader after 24 and 48h. The inhibitory effect of compounds was analyzed after plotting the OD vs concentration of the compound in Excel data sheet. Splitomicin was used as a control.

Dose Response for Compound 4bb against Mammalian SIRT1:

A dose response study was carried out with the compound, **4bb** using Invitro cyclex SIRT1/Sir2 Deacetylase Fluorometric Assay Kit to determine its IC_{50} using Graph pad software. IC_{50} for the compound **4bb** is found to be 32.92 µM (Figure S-1).

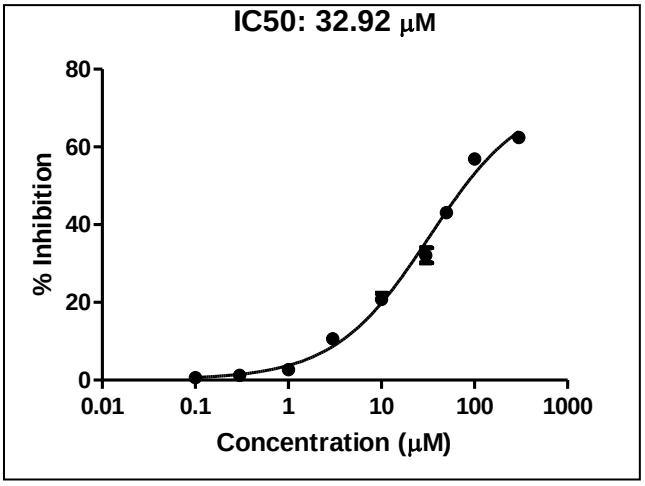


Figure S-1: IC_{50} of compound **4bb** by in vitro assay

Treatment of Cancerous cells with inhibitor 4bb:

The HEPG2 Hepatic cells are seeded into three different 70 mm plates, one million cells in each. The cells are treated with the compound **4bb** at 50 µM and 100 µM concentrations for 48 h time point as shown in the Figure S-2. The untreated cells show a triangular morphology and are well adhered. In the treated cells, the growth of the cells is inhibited and rounded morphology was observed and the cells are released into media.

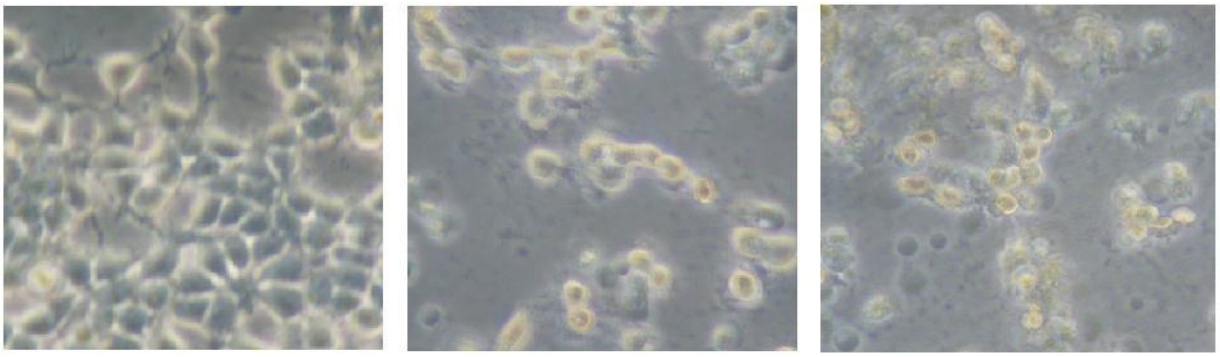


Figure S-2: 4bb treatment to the HEPG2 cells

Reference

1. C. M. Grozinger, E. D. Chao, H. E. Blackwell, D. Moazed, S. L. Schreiber, *J. Biol. Chem.* 2001, **276**, 38837.

Zebrafish embryo toxicity studies

Materials & Methods:

Husbandry:

Wild type zebrafish were procured from Vikrant Aquaculture, Mumbai, India and maintained in a re-circulation system containing purified water (Millipore- Elix Advantage 3/5/10/15) with 0.2% sea salt, with optimal growth conditions like pH 7.4, temperature 28˚C and 14-10 hrs light dark cycle. Males and females were maintained in separate tanks. They were allowed to breed in the breeding chamber with ratio of 2 females: 3 males (Westerfield, 2000). Embryos obtained were collected, sorted and allowed to grow in E3 medium at 28˚C.

Drug Exposure:

1 day post fertilization (dpf) embryos were collected and checked for general health and development. Embryos were dechorinated using 0.5mg/ml pronaseE treatment for 4 min followed by several washes with E3 medium. Working concentrations of the compound was prepared by serially diluting the compound in final concentration of 0.1% DMSO in E3 medium. Embryos (n=6) were distributed in 24 well plate followed by addition of drug and incubated at 28.5˚C until 5 dpf.

Morphological Scoring:

Embryos were removed from drug solution, washed and allowed to anesthetize using tricaine (0.008%) and observed for morphological toxicity for parameters like Body Shape, Somites, Notochord, Tail, Intestine, Fins, Brain, Upper jaw, Heart, Lower jaw, Liver and Swim Bladder. Morphological assessment and scoring was done according to the procedure described (Panzica-Kelly et al, 2010).

Results:

Morphological evaluation was carried out by trained personnel in a blinded fashion. All the embryos in control group were found normal. 3mM Phenobarbital was taken as positive control, where toxic effects were found. The compound was tested at concentrations starting from 10nM till 30µM (i.e. the highest soluble concentration). At all concentrations, the compound was found to be non toxic with no adverse effects. Mild liver, intestine and swim bladder toxicity were observed at high concentrations of 3µM and 10µM. No Observed Adverse Effect Level (NOAEL) was observed at 10 µM.

Statistical Analysis:

Each embryo was scored based on their level of toxicity from 5 being non toxic and 0.5 being highly toxic. The lesion scoring was analyzed statistically using graphpad prism software using Kruskal–Wallis one-way analysis of variance by ranks followed by Dunnet's post test.

Interpertation:

The compound was found to be non toxic until the concentrations tested.

Figures & Tables:

Figure 1: Mean (±S.D.) lesion score of all parameters different treatment groups. (*$p<0.05$, **$p<0.01$ and ***$p<0.001$). Statistical significance were analysed as control group vs all groups.

Table S2. Results of zebrafish embryo toxicity study with toxicological indices and major organs/systems affected in positive control and at MTC in test compounds. (- no effect, x- slightly toxic, xx-moderately toxic, xxx-severely toxic).

	Compound 4bb	**Phenobarbital**
Test Concentrations (µM)	0.01, 0.03, 0.1, 0.3, 1, 3, 10, 30.	3000
Statistically Significant Toxic Concentration (µM)	-	Positive Control
No Observed Adverse Effect Level (NOAEL) (µM)	10	
Minimal Toxic Concentration (MTC) (µM)	30	
Parameters of toxicity at MTC		
Body Shape	-	xxx
Somites	-	xxx
Notochord	-	xxx
Tail	-	xxx
Fins	-	xxx
Brain	-	xxx
Upper jaw	x	xxx
Heart	-	xx
Intestine	xx	xxx
Lower jaw	x	xx
Liver	x	xxx
Swim Bladder	xx	xxx

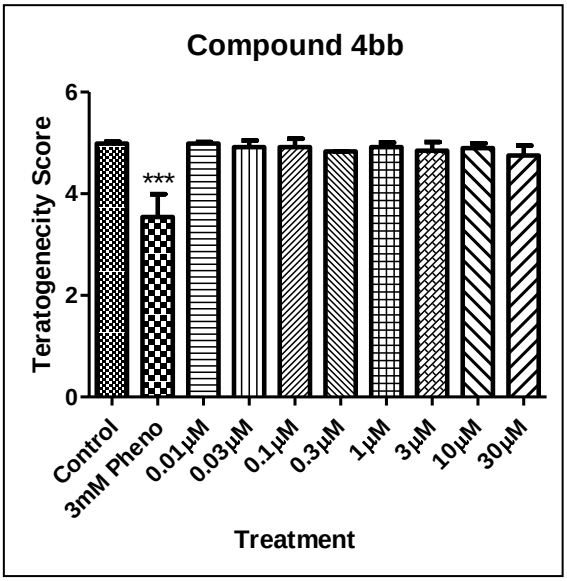


Fig. S3. Toxicioty studies on zebrafish embryos with compound **4bb** at different concentrations.

References:

1. Panzica-Kelly J. M., Zhang C. X., Danberry T. L., Flood , A., DeLan, J. W., K. C. Brannen and K. A. Augustine-Rauch (2010) Morphological Score Assignment Guidelines for the Dechorionated Zebrafish Teratogenicity Assay. *Birth Defects Research* (Part B) 89:382–395 (2010) PMID: 20836125.
2. Westerfield M: The Zebrafish Book. A Guide for the Laboratory Use of Zebrafish (Danio rerio). *4th edition. Eugene, OR: University of Oregon Press*, 2000.