**Dual behaviour of ammonium acetate for the synthesis of diverse symmetrical /
unsymmetrical bis [1, 3] oxazines possessing anti-cancer activity.**

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SUPPORTING INFORMATION

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Experimental Procedure:

Chemicals were purchased from Aldrich and they were used without further purification. TLC -Thin layer chromatography (Merck, Silica gel 60 F254) was performed on pre-coated silica gel on alumina plates for monitoring the reaction. IR spectra were recorded in the range of 4000-400 cm^{-1} on Thermo Nicolet Avatar 330 FTIR spectrometer in KBr pellets. ^1H NMR and ^{13}C NMR spectra were recorded using a BRUKER AMX 400 FT; JOEL 400 MHz. HPLC was performed on a water's liquid chromatography equipped with a dual wavelength UV detector (Deuterium lamp, 192–600 nm), using a symmetry C18 column (10 cm X 4.6mm) 5 μ HPLC grade. Acetonitrile and water (80: 20) were used as the eluting solvents, flow rate is 1.00 ml/min and the injection volume is 5-20 μl at 25 $^{\circ}\text{C}$ column temperature. UV-Vis Spectrophotometer - Jasco V-670, scan speed – 400 nm/min was used to analysis UV-Vis. Mass Spectroscopy – ESI, Triple quad (Waters Quattro premier XE) was used to analysis the ESI mass. HRMS analysis was obtained from JEOL GC Mate.

General Procedure:

In dry 100ml Erlenmeyer flask ammonium acetate (1 mol %) in ethanol (10 ml) was taken and heated the solution. To this solution, naphthalene-2, 3-diol (1.0 mmol) and aromatic benzaldehydes (4.0 mmol) were added. The reaction mixture was gently warmed on a water bath for a minute and kept aside. The completion of the reaction was monitored by TLC (hexane/ ethylacetate – 40%). The solid obtained was separated and the crude product was purified by column chromatography on silica gel using ethylacetate/hexane as the eluents.

Cell Line Maintenance:

A panel of five cancer cells representing multiple cancers of clinical relevance were selected namely; ACHN (human renal cell, ATCC, CRL-1611), Panc-1 (human pancreatic, ATCC, CRL-1469) cultured on MEM with 2mM Lglutamine and 10% FBS, H460 (human non small cell lung carcinoma, ATCC, HTB- 177), Calu-1 (human lung carcinoma, ATCC, HTB-54) and MCF7 (human breast adenocarcinoma, ATCC HTB-22) cultured on RPMI, 2mM Lglutamine and 10% FBS, HCT-116 (human colon cancer, ATCC, CCL- 247) cultured on McCoy's 5a medium and 10% FBS and MCF10A (normal breast epithelium cells) cultured on MEM with 2mM L-glutamine and 10% FBS.

Table S1. Preliminary screening of 4{1,1,3}-4{1,14,1} for anticancer activity at 1 and 10 μ M concentration.

S.No	code	Screening conc. (μ M)	ACH N	Panc1	Calu1	H460	HCT1 16	HTS Remarks
1	4a	1	76	77	64	82	80	Active
		10	90	92	85	96	93	
2	4b	1	48	31	21	55	52	Not Active
		10	88	66	60	95	92	
3	4c	1	12	20	15	19	16	Not Active
		10	53	40	18	59	57	
4	4d	1	78	84	61	84	81	Active
		10	92	97	92	99	96	
5	4e	1	57	34	51	63	61	Active
		10	87	82	87	93	90	
6	4f	1	91	77	71	97	94	Active
		10	93	87	88	99	97	
7	4g	1	24	36	29	30	27	Not Active
		10	48	53	44	54	52	
8	4h	1	49	1	15	55	53	Not Active
		10	85	43	56	91	89	
9	4i	1	38	20	29	45	41	Not Active
		10	42	22	34	48	46	
10	4j	1	61	66	54	68	64	Active
		10	86	91	85	92	89	
11	4k	1	49	30	49	55	52	Active
		10	90	86	89	97	93	
12	4l	1	47	60	36	53	50	Active
		10	91	91	81	97	94	
13	4m	1	67	51	45	74	71	Active
		10	90	91	86	96	95	
14	4n	1	38	28	30	44	41	Active
		10	85	81	83	92	89	

Positive Control 1-->Flavopiridol	1000nM	88	81	89	80	87	Active
Positive Control 2 -->Gemcitabine	1000nM	79	88	82	80	75	Active

X-ray Crystallography:

Crystallization trials for all compounds were made and quality crystals could be grown for 4b only. Suitable single crystals of 4b were grown from equimolar amounts (1:1) of dichloromethane and acetonitrile in 1ml of n-propanol. Slow evaporation of the solution yielded colourless crystals (m.p. 366.8 – 368.6 °F). Data were collected on a single-crystal Bruker SMART APEX2 diffractometer and processed using Saint-Plus.¹ The structure was solved by applying the direct phase-determination technique using SHELXS-97, and anisotropically refined by full-matrix least-square on F2 using SHELXL-97.² All structured calculations were performed with WinGX suit of programs (Version 1.80.05).³ Solvent possesses large thermal disorder and could not be reliably modelled. Non-polar hydrogens were placed in the geometrically expected positions and refined with the riding options. The torsion angles for the methyl group hydrogens were set with reference to a local difference Fourier calculation. Polar hydrogens (NH atoms) were isotropically refined. The distances with hydrogen atoms are: aromatic C—H = 0.93 Å, methyl C—H = 0.96 Å, methylene C—H = 0.97 Å, methane C—H = 0.98 Å, N—H = 0.71(5) — 0.72(5) Å, O—H = 0.82 Å and Uiso = 1.2 Ueq(parent), or 1.5Ueq(Cmethyl). Essential crystal data are listed in Table 5. Crystallographic data have been deposited at Cambridge Crystallographic Data Centre² with entry number, CCDC 912856.

Spectral Data:

6-((benzylideneamino) (phenyl) methyl)-2,3-dihydro-1,3-diphenyl-1H-naphtho[1,2-e][1,3]oxazin-5-ol 4a:

Creamy white solid; mp 179-180°C; R_f 0.83 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3315, 3061, 2922, 1598, 1494, 1307 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 2.17 (s, NH, 1H), 5.70-5.82 (s, CH, 3H), 6.48-6.52 (s, OH, 1H), 7.14-7.88 (ArH, 24H), 8.61-8.65 (Vinylic H, 1H) ppm; ^{13}C NMR (100MHz, CDCl_3): 29.69, 30.90, 54.14, 82.47, 115.17, 123.44, 124.01, 126.33, 127.51, 128.86, 129.41, 132.08, 134.33, 139.17, 142.67, 144.26, 162.00, 162.26 ppm; HRMS: Calculated 546.2307 ($[\text{M}]^+$), Found 546.2307.

6-((2-chlorobenzylideneamino)(2-chlorophenyl)methyl)-1,3-bis(2-chlorophenyl)-2,3-dihydro-1H-naphtho

[1,2-e][1,3]oxazin-5-ol 4b: Light yellow solid; mp 186-187°C; R_f 0.75 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3323, 3066, 2920, 1697, 1596, 742 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 1.30 (s, NH, 1H), 6.09-6.15 (s, CH, 3H), 7.01-7.07 (s, OH, 1H), 7.11-7.91 (ArH, 20H), 9.34 (Vinylic H, 1H) ppm; ^{13}C NMR (100MHz, CDCl_3): 29.73, 52.44, 71.30, 81.60, 109.59, 114.49, 121.95, 123.46, 124.53, 126.39, 127.36, 128.82, 130.37, 132.82, 134.25, 136.28, 139.14, 144.50, 145.40, 160.89 ppm; HRMS: Calculated 682.0748 ($[\text{M}]^+$), Found 682.0749.

6-((4-chlorobenzylideneamino)(4-chlorophenyl)methyl)-1,3-bis(4-chlorophenyl)-2,3-dihydro-1H-naphtho

[1,2-e][1,3]oxazin-5-ol 4c: Light yellow solid; mp 205-206°C; R_f 0.50 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3307, 3061, 2900, 1697, 1597, 1489, 748 cm^{-1} ; ^1H NMR (400 MHz, DMSO): 4.58-4.62 (NH, 1H), 5.48-5.71 (CH, 3H), 7.10-7.91 (ArH, 20H), 7.50 (Vinylic H, 1H), 8.72 (s, OH, 1H) ppm; ^{13}C NMR (100MHz, DMSO): 21.16, 78.58, 78.92, 79.25, 109.44, 122.76, 125.45, 128.70, 146.87, 172.09 ppm; HRMS: Calculated 682.0749 ($[\text{M}]^+$), Found 682.0749.

1,4-bis(((E)-(4-nitrobenzylidene)amino)(4-nitrophenyl)methyl)naphthalene-2,3-diol 4d:

Yellow solid; mp 187-188°C; R_f 0.40 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3454, 3307, 3061, 2885, 1602, 1510, 1346 cm^{-1} ; ^1H NMR (400 MHz, DMSO): 4.50-4.62 (CH, 2H), 7.07- 8.4 (ArH, 20H), 7.33 (vinylic H, 1H), 7.09 (vinylic H, 1H), 7.85-7.87 (OH, 2H), ppm; ^{13}C NMR (100MHz, DMSO): 56.45, 110.34, 114.98, 122.33, 122.74, 123.34, 123.61, 123.77, 124.179, 125.21, 126.54, 128.72, 144.28, 146.27, 148.41, 164.99 ppm; HRMS: Calculated 726.1710 ($[\text{M}]^+$), Found 726.1711.

6-((2-fluorobenzylideneamino)(2-fluorophenyl)methyl)-1,3-bis(2-fluorophenyl)-2,3-dihydro-1H-naphtho

[1,2-e][1,3]oxazin-5-ol 4e: Light yellow solid; mp 163-165°C; R_f 0.38 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3315, 3068, 2897, 1697, 756 cm^{-1} ; ^1H NMR (400 MHz, DMSO): 4.72-4.78 (NH, 2H), 5.90-5.99 (CH, 4H), 6.94-7.71 (ArH, 20H) ppm; ^{13}C NMR (100MHz, DMSO): 21.12, 47.56, 77.67, 79.14, 113.35, 115.57, 122.64, 123.88, 124.31, 125.38, 128.38, 129.56, 130.17, 144.65, 158.76, 160.54, 161.22, 172.114 ppm; HRMS: Calculated 618.1930 ($[\text{M}]^+$), Found 618.1930.

6-((4-fluorobenzylideneamino)(4-fluorophenyl)methyl)-1,3-bis(4-fluorophenyl)-2,3-dihydro-1H-naphtho

[1,2-e][1,3]oxazin-5-ol 4f: Light yellow solid; mp 202-203°C; R_f 0.55 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3311, 3066, 2868, 1600, 744 cm^{-1} ; ^1H NMR (400 MHz, DMSO): 4.57 (NH, 1H), 5.20-5.67 (CH, 2H), 6.81 (CH, 1H), 7.15-8.76 (ArH, 20H), 9.87 (OH, 1H) ppm; ^{13}C NMR (100MHz, DMSO): 21.74, 79.13, 129.65, 130.04, 130.09, 130.89, 131.19, 172.81 ppm; HRMS: Calculated 618.1930 ($[\text{M}]^+$), Found 618.1931.

1,4-bis((E)-((naphthalen-1-yl)methyleneamino)(naphthalen-1-yl)methyl)naphthalene-2,3-diol 4g: Light yellow solid; mp 186-187°C; R_f 0.75 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3541, 3309, 3045, 2870, 1687 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 2.95 (OH, 2H), 6.35-6.44 (CH, 2H), 6.49-8.17 (ArH, 32H), 8.04-8.10 (vinyl H, 2H) ppm; ^{13}C NMR (100MHz, CDCl_3): 51.66, 52.11, 76.69, 77.33, 81.35, 109.24, 115.56, 122.92, 123.43, 124.27, 125.45, 126.46, 127.30, 128.79, 129.30, 130.60, 131.51, 133.62, 134.07, 134.41, 136.83, 144.96 ppm; HRMS: Calculated 746.2933 ($[\text{M}]^+$), Found 746.2933.

6-(((2-methylbenzylidene)amino)(o-tolyl)methyl)-1,3-di-o-tolyl-2,3-dihydro-1H-naphtho[1,2-e][1,3]oxazin-5-ol 4h: White solid; mp 172-173°C; R_f 0.66 (30% ethyl acetate: hexane); FTIR (KBr) ν : 3518, 3313, 3064, 2910, 1693 cm^{-1} ; ^1H NMR (400 MHz, DMSO): 1.81-1.88 (CH_3 , 6H), 2.61-2.68 (CH_3 , 6H), 4.12-4.29 (NH, 1H), 5.74-5.81 (CH, 3H), 6.79-7.82 (ArH, 20H), 7.18 (Vinyl H, 1H), 7.74 (OH, 1H) ppm; ^{13}C NMR (100MHz, DMSO): 17.48, 18.78, 50.85, 78.93, 80.46, 114.66, 115.58, 122.95, 123.22, 124.97, 125.44, 126.36, 127.13, 128.00, 129.92, 130.64, 135.62, 136.79, 137.00, 140.54, 144.63, 146.50 ppm; HRMS: Calculated 602.2933 ($[\text{M}]^+$), Found 602.2936.

6-(((4-methylbenzylidene)amino)(p-tolyl)methyl)-1,3-di-p-tolyl-2,3-dihydro-1H-naphtho[1,2-e][1,3]oxazin-5-ol 4i: Light orange solid; mp 199-200°C; R_f 0.67 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3421, 3313, 3014, 2862, 1602 cm^{-1} ; ^1H NMR (400 MHz, DMSO): 2.17-2.40 (CH_3 , 12H), 5.35-5.62 (NH, 1H), 6.6-6.75 (CH, 3H), 7.09-7.99 (ArH, 20H), 7.81 (OH, 1H), 9.87 (Vinyl H, 1H) ppm; ^{13}C NMR (100MHz, DMSO): 17.90, 19.27, 52.11, 80.76, 81.68, 108.85, 114.92, 115.33, 123.21, 124.01, 125.77, 127.47, 128.11, 130.31, 130.70, 137.08, 137.11, 144.88 ppm; HRMS: Calculated 602.2933 ($[\text{M}]^+$), Found 602.2934.

6-((2-methoxybenzylideneamino)(2-methoxyphenyl)methyl)-2,3-dihydro-1,3-bis(2-methoxyphenyl)-1H-naphtho[1,2-e][1,3]oxazin-5-ol 4j: Yellow solid; mp 174-175°C; R_f 0.42 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3325, 3068, 2937, 1637, 1020 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 3.60-3.78 (OCH_3 , 12H), 5.32 (NH, 1H), 5.54 (CH, 1H), 5.65 (CH, 2H), 6.28 (OH, 1H), 6.67-8.39 (ArH, 20H), 9.78 (OH, 1H) ppm; ^{13}C NMR (100MHz, CDCl_3): 55.45, 58.23, 109.05, 113.77, 114.25, 114.34, 123.25, 123.96, 126.41, 127.38, 128.76, 130.77, 132.05, 159.11 ppm; HRMS: Calculated 666.2730 ($[\text{M}]^+$), Found 666.2732.

6-((4-methoxybenzylideneamino)(4-methoxyphenyl)methyl)-2,3-dihydro-1,3-bis(4-methoxyphenyl)-1H-naphtho[1,2-e][1,3]oxazin-5-ol 4k: White solid; mp 159-164°C; R_f 0.53 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3313, 2999, 2858, 1610, 1030 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 2.19 (NH, 1H), 3.72-3.87 (OCH_3 , 12H), 5.65-5.75 (CH, 1H), 6.39-6.42 (CH, 1H), 6.78 (CH, 1H), 6.81-7.88 (ArH, 20H), 7.82-7.85 (OH, 1H), 8.51-8.55 (vinyl H, 1H) ppm; ^{13}C NMR (100MHz, CDCl_3): 55.46, 55.61, 68.12, 110.57, 111.08, 111.61, 120.67, 120.84, 121.17, 122.05, 122.96, 123.32, 126.50, 128.58, 128.86, 132.88, 135.97, 156.68, 158.85, 189.90 ppm; HRMS: Calculated 666.2730 ($[\text{M}]^+$), Found 666.2731.

6-((4-ethoxybenzylideneamino)(4-ethoxyphenyl)methyl)-2,3-dihydro-1,3-bis(4-ethoxyphenyl)-1H-naphtho[1,2-e][1,3]oxazin-5-ol 4l: White solid; mp 159-164°C; R_f 0.53 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3313, 3068, 2895, 1608, 1047 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 1.35-1.47 (CH_3 , 12H), 3.90-4.13 (OCH_2 , 8H), 5.64-5.76 (CH, 3H), 6.38 (NH, 1H), 6.80-7.86 (ArH, 20H), 7.00 (OH, 1H), 8.50-8.52 (vinyl H, 1H) ppm; ^{13}C NMR

(100MHz, CDCl₃): 14.62, 17.78, 19.01, 51.99, 63.90, 80.26, 114.16, 119.24, 122.84, 124.83, 126.06, 128.21, 130.38, 131.44, 136.17, 137.09, 140.00, 153.10, 164.04, 190.85 ppm; HRMS: Calculated 722.3356 ([M]⁺), Found 722.3355.

6-((3,4-dimethoxybenzylideneamino)(3,4-dimethoxyphenyl)methyl)-2,3-dihydro-1,3-bis(3,4-dimethoxyphenyl)-1H-naphtho[1,2-e][1,3]oxazin-5-ol 4m: Yellow solid; mp 124-126°C; R_f 0.14 (40% ethyl acetate: hexane); FTIR (KBr) v: 3448, 3315, 2937, 2835, 1678, 1022 cm⁻¹; ¹H NMR (400 MHz, DMSO): 3.65-3.80 (OCH₃, 24H), 3.83-3.86 (CH, 3H), 5.54-5.71 (NH, 1H), 6.79-7.57 (ArH, 16H), 7.89 (OH, 1H), 9.82 (Vinyl H, 1H) ppm; ¹³C NMR (100MHz, DMSO): 21.15, 55.45, 55.84, 77.26, 109.35, 111.22, 122.87, 126.87, 126.10, 129.60, 148.65, 149.14, 154.15, 172.08, 191.34 ppm; HRMS: Calculated 786.3152 ([M]⁺), Found 786.3153.

6-((3,4,5- trimethoxy benzylidene amino)(3,4,5- trimethoxy phenyl) methyl) -2,3- dihydro- 1,3 -bis(3,4,5-trimethoxyphenyl)-1H-naphtho[1,2-e][1,3]oxazin-5-ol 4n: White solid; mp 153-155°C; R_f 0.70 (40% ethyl acetate: hexane); FTIR (KBr) v: 3159, 2935, 1689, 1126 cm⁻¹; ¹H NMR (400 MHz, DMSO): 3.63-3.78 (OCH₃, 36H), 3.83-3.86 (CH, 3H), 4.54 (NH, 1H), 5.62 (OH, 1H), 6.62-7.41 (ArH, 12H), 9.92 (Vinyl H, 1H) ppm; ¹³C NMR (100MHz, DMSO): 21.22, 55.90, 59.89, 104.17, 104.98, 105.36, 106.70, 131.62, 135.85, 142.79, 152.65, 153.30, 172.36, 191.84 ppm; HRMS: Calculated 906.3575 ([M]⁺), Found 906.3574.

4,9-bis(2- chlorophenyl)-2,11 -bis(4- methoxyphenyl)-2, 3, 4, 9, 10, 11- hexahydronaphtho [1, 2:4, 3] bis([1,3]oxazine) 4o: Yellow solid; mp 192-194°C; R_f 0.38 (40% ethyl acetate: hexane); FTIR (KBr) v: 3422, 3308, 3034, 2872, 1612 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): 1.25 (NH, 1H), 3.75 (CH, 1H), 3.95 (OCH₃, 3H), 4.05 (OCH₃, 3H), 6.17 – 6.22 (CH, 2H), 6.91- 8.06 (ArH, 20H), 9.29 (vinyl H, 1H), 10.51 (OH, 1H) ppm; ¹³C NMR (100MHz, CDCl₃): 20.62, 52.5, 80.87, 111.26, 115.27, 121.32, 123.81, 126.38, 127.40, 128.99, 130.72, 132.66, 134.17, 135.94, 136.24, 147.80, 156.96, 159.90, 190.00 ppm; HRMS: Calculated 674.1739 ([M]⁺), Found 674.1738.

4,9-bis(4- chlorophenyl)-2, 11 -bis(2- methoxyphenyl)-2, 3, 4, 9, 10, 11- hexahydronaphtho [1, 2:4, 3]bis([1,3]oxazine) 4p: White solid; mp 162-164°C; R_f 0.42 (40% ethyl acetate: hexane); FTIR (KBr) v: 3414, 3298, 3021, 2867, 1601 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): 2.08 (NH, 1H), 3.88 (OCH₃, 3H), 4.00 (OCH₃, 3H), 5.64 – 5.68 (CH, 1H), 5.70 – 5.89 (CH, 1H), 6.13 (CH, 1H), 6.84- 7.85 (ArH, 20H), 8.68 (vinyl H, 1H), 10.48 (OH, 1H) ppm; ¹³C NMR (100MHz, CDCl₃): 49.00, 53.53, 55.76, 110.85, 11.46, 120.99, 121.45, 122.24, 123.89, 126.41, 127.78, 128.63, 129.45, 130.91, 131.04, 156.60, 190.02 ppm; HRMS: Calculated 674.1739 ([M]⁺), Found 674.1739.

2,11-bis(2-methoxyphenyl)-4,9-di-p-tolyl-2,3,4,9,10,11-hexahydronaphtho[1,2:4,3]bis([1,3]oxazine) 4q: Yellow solid; mp 190-192°C; R_f 0.60 (40% ethyl acetate: hexane); FTIR (KBr) v: 3452, 3327, 3051, 2905, 1634 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): 2.25 (NH, 1H), 2.31-2.44 (CH₃, 6H), 3.74-3.89 (OCH₃, 6H), 2.37 – 2.44 (OCH₃, 6H), 5.47 – 5.78 (CH, 2H), 6.41 (CH, 1H), 6.80 – 7.85 (ArH, 20H), 8.54-8.57 (vinyl H, 1H), 9.89 (OH, 1H) ppm; ¹³C NMR (100MHz, CDCl₃): 21.20, 21.77, 55.35, 55.73, 114.35, 114.46, 123.49, 126.38, 127.66, 129.13, 129.45, 129.68, 129.86, 130.00, 132.15 ppm; HRMS: Calculated 634.2832 ([M]⁺), Found 634.2833.

4,9-bis(2-chlorophenyl)-2,11-di-p-tolyl-2,3,4,9,10,11-hexahydronaphtho[1,2:4,3]-bis([1,3]oxazine) 4r: Light Yellow solid; mp 152-153°C; R_f 0.25 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3444, 3322, 3034, 2823, 1667 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 2.25-2.44 (CH_3 , 3H), 2.30 – 2.34 (OCH_3 , 3H), 2.37 – 2.44 (OCH_3 , 6H), 5.67 – 6.06 (CH, 1H), 6.11 – 6.15 (CH, 1H), 6.45 (CH, 1H), 6.95 – 7.93 (ArH, 20H), 8.55 (vinylic H, 1H), 9.96 (OH, 1H) ppm; ^{13}C NMR (100MHz, CDCl_3): 21.23, 31.06, 126.42, 127.62, 128.02, 129.21, 129.85, 130.00 ppm; HRMS: Calculated 642.1841 ($[\text{M}]^+$), Found 642.1844.

4,9-bis(2-fluorophenyl)-2,11-di-p-tolyl-2,3,4,9,10,11-hexahydronaphtho[1,2:4,3]bis([1,3]oxazine) 4s: White solid; mp 150-152°C; R_f 0.26 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3461, 3343, 3022, 2854, 1621 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 2.25 – 2.37 (CH_3 , 6H), 2.40 (CH, 1H), 3.85 (NH, 1H), 5.65 – 5.68 (CH, 1H), 5.77 – 5.86 (CH, 1H), 6.85 – 7.79 (ArH, 20H), 8.65 (vinylic H, 1H), 9.96 (OH, 1H) ppm; ^{13}C NMR (100MHz, CDCl_3): 76.72, 77.35, 81.72, 112.71, 115.69, 116.00, 119.19, 122.88, 123.56, 126.85, 128.79, 129.41, 130.17, 131.51 ppm; HRMS: Calculated 610.2432 ($[\text{M}]^+$), Found 610.2432.

4,9-bis(4-nitrophenyl)-2,11-di-p-tolyl-2,3,4,9,10,11-hexahydronaphtho[1,2:4,3]bis([1,3]oxazine) 4t: Yellow solid; mp 158-160°C; R_f 0.18 (40% ethyl acetate: hexane); FTIR (KBr) ν : 3452, 3317, 3064, 2881, 1629 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): 1.82 – 1.87 (Me, 6H), 1.96 (NH, 1H), 2.58 – 2.73 (CH, 1H), 2.77 (CH_3 , 3H), 5.62 – 5.67 (CH, 1H), 5.70 – 5.81 (CH, 1H), 5.94 (OH, 1H), 7.00 – 7.86 (ArH, 20H), 7.81 (vinylic H, 1H) ppm; ^{13}C NMR (100MHz, CDCl_3): 19.42, 19.73, 52.53, 80.92, 81.93, 123.35, 124.41, 125.54, 126.47, 127.77, 128.67, 129.22, 130.31, 130.90, 131.05, 132.20, 133.80 ppm; HRMS: Calculated 664.2322 ($[\text{M}]^+$), Found 664.2321.

1-(phenyl((-1-phenylethyl)amino)methyl)-4-(phenyl((-1-phenylethyl)amino)methyl)naphthalene-2,3-diol 4u: Yellow solid; mp 223-225°C; R_f 0.63 (40% ethyl acetate: hexane); $[\alpha]_D^{21} = -39.08$ ($c = 0.1$, CH_3CN) FTIR (KBr) ν : 2996, 3008, 1641, 934 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 1.49-1.50 (b, CH_3 , 3 H), 1.59-1.60 (b, CH_3 , 3 H), 1.96 (s, NH, 2 H), 3.9-4.03 (q, CH, 2 H), 5.20 (s, CH, 2 H), 5.58 (s, OH, 2 H), 7.17-8.78 (ArH, 24 H) ppm; ^{13}C NMR (100MHz, CDCl_3): δ 24.72, 54.11, 60.62, 69.69, 77.02, 108.98, 120.88, 123.10, 126.13, 127.34, 128.08, 128.38, 128.92, 129.00, 129.75, 130.60, 136.31, 140.92, 142.63, 145.07, 147.35, 159.610 ppm; HRMS : calc'd. 578.2933 ($[\text{M}]^+$), Found 578.2935.

Fig.S1: LC-MS spectra for the reaction mixture of compound 4a

Data File C:\CHEM32\1\DATA\SNAPSHOT.D

Sample Name: R2

Acq. Operator : sandeep

Location : Vial 2

Injection Date : 3/22/2012 5:22:00 PM

Inj : 1

Acq. Method : BASIC COMPOUND .M

Analysis Method : C:\CHEM32\1\METHODS\BASIC COMPOUND .M

Last changed : 3/22/2012 5:19:24 PM by narayan

(modified after loading)

Method Info : acidic

Sample-related custom fields:

Name | Value

Additional Info : Peak(s) manually integrated

MS Signal: MSD1 TIC, MS File, MM-ES+APCI, Pos, Scan

Spectra averaged over upper half of peaks.

Noise Cutoff: 500 counts.

Reportable Ion Abundance: > 10%.

Retention Time (MS)	MS Area	Mol. Weight or Ion
1.731	2673749	336.85 I
		336.50 I
		318.95 I
4.448	21250860	369.95 I
		248.65 I
		122.00 I
		105.00 I

[M] : 336.1150

(int6)

[M] : 105.0578

(int2)

[M] : 248.0837

(int4)

*** End of Report ***

¹H-NMR spectra of compound 4a

¹³C-NMR spectra of compound 4a

Mass spectra for compound 4a

¹H-NMR spectra of compound 4b

¹³C-NMR spectra of compound 4b

Mass spectra for compound 4b

ORTEP diagram of compound 4b

¹H-NMR spectra of compound 4c

¹³C-NMR spectra of compound 4c

Mass spectra for compound 4c

¹H-NMR spectra of compound 4d

¹³C-NMR spectra of compound 4d

Mass spectra for compound 4d

¹H-NMR spectra of compound 4e

¹³C-NMR spectra of compound 4e

Mass spectra for compound 4e

¹H-NMR spectra of compound 4f

¹³C-NMR spectra of compound 4f

Mass spectra for compound 4f

¹H-NMR spectra of compound 4g

¹³C-NMR spectra of compound 4g

Mass spectra for compound 4g

¹H-NMR spectra of compound 4h

¹³C-NMR spectra of compound 4h

Mass spectra for compound 4h

¹H-NMR spectra of compound 4i

¹³C-NMR spectra of compound 4i

Mass spectra for compound 4i

¹³C-NMR spectra of compound 4j

Mass spectra for compound 4j

¹H-NMR spectra of compound 4k

¹³C-NMR spectra of compound 4k

Mass spectra for compound 4k

¹H-NMR spectra of compound 4l

¹³C-NMR spectra of compound 4l

Mass spectra for compound 4l

¹H-NMR spectra of compound 4m

¹³C-NMR spectra of compound 4m

Mass spectra for compound 4m

¹H-NMR spectra of compound 4n

¹³C-NMR spectra of compound 4n

HPLC data of compound 4n in Acetonitrile

Default Individual Report

Reported by User: System

Project Name: Defaults

SAMPLE INFORMATION

Sample Name:	ditom	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	9/7/2012 9:53:09 AM
Vial:	1	Acq. Method Set:	vit
Injection #:	5	Date Processed:	9/7/2012 10:48:39 AM
Injection Volume:	5.00 ul	Processing Method:	VIT
Run Time:	10.0 Minutes	Channel Name:	2487Channel 2
Sample Set Name:		Proc. Chnl. Descr.:	254

	RT	Area	% Area	Height
1	1.637	36934931	68.22	3264728
2	1.799	17204472	31.78	2844117

HPLC data of compound 4n in Chloroform

Default Individual Report

Reported by User: System

Project Name: Defaults

SAMPLE INFORMATION

Sample Name:	diTOM CHCl3	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	9/24/2012 12:09:37 PM
Vial:	1	Acq. Method Set:	vit1
Injection #:	5	Date Processed:	9/24/2012 12:52:15 PM
Injection Volume:	5.00 ul	Processing Method:	VIT 1
Run Time:	8.0 Minutes	Channel Name:	2487Channel 2
Sample Set Name:		Proc. Chnl. Descr.:	254

	RT	Area	% Area	Height
1	1.714	1628141	4.84	231734
2	1.924	2403801	7.14	337863
3	2.102	29621556	88.02	3198430

HPLC data of compound 4n in Ethanol

Default Individual Report

Reported by User: System

Project Name: Defaults

SAMPLE INFORMATION

Sample Name:	diTOM EtOH	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	9/24/2012 11:51:24 AM
Vial:	1	Acq. Method Set:	vit1
Injection #:	3	Date Processed:	9/24/2012 12:35:36 PM
Injection Volume:	10.00 ul	Processing Method:	VIT 1
Run Time:	10.0 Minutes	Channel Name:	2487Channel 2
Sample Set Name:		Proc. Chnl. Descr.:	254

	RT	Area	% Area	Height
1	1.749	620380	3.16	108896
2	1.977	1344095	6.85	208099
3	2.195	17653476	89.99	2472241

HPLC data of compound 4n in Methanol

Default Individual Report

Reported by User: System

Project Name: Defaults

SAMPLE INFORMATION

Sample Name: diTOM MeOH
Sample Type: Unknown
Vial: 1
Injection #: 4
Injection Volume: 5.00 ul
Run Time: 10.0 Minutes
Sample Set Name:

Acquired By: System
Date Acquired: 9/24/2012 12:00:50 PM
Acq. Method Set: vit1
Date Processed: 9/24/2012 12:41:02 PM
Processing Method: VIT 1
Channel Name: 2487Channel 2
Proc. Chnl. Descr.: 254

	RT	Area	% Area	Height
1	1.798	516062	4.91	91620
2	2.044	657870	6.26	108792
3	2.280	9337323	88.83	1480280

HPLC data of compound 4n in Trifluoroacetic acid

Default Individual Report

Reported by User: System

Project Name: Defaults

SAMPLE INFORMATION

Sample Name:	diTOM TFA	Acquired By:	System
Sample Type:	Unknown	Date Acquired:	9/24/2012 11:40:24 AM
Vial:	1	Acq. Method Set:	vit1
Injection #:	2	Date Processed:	9/24/2012 12:32:14 PM
Injection Volume:	20.00 ul	Processing Method:	VIT 1
Run Time:	20.0 Minutes	Channel Name:	2487Channel 2
Sample Set Name:		Proc. Chnl. Descr.:	254

	RT	Area	% Area	Height
1	1.322	31475001	51.22	3437477
2	1.383	22340276	36.36	3154754
3	1.754	7631710	12.42	1057997

UV spectra of compound 4n in HCl

UV spectra of compound 4n in Acetic acid

UV spectra of compound 4n in Chloroform

UV spectra of compound 4n in DMSO

UV spectra of compound 4n in Acetonitrile

UV spectra of compound 4n in Ethanol

Mass spectra for compound 4n

¹H-NMR spectra of compound 4o

¹³C-NMR spectra of compound 4o

Mass spectra for compound 4o

¹H-NMR spectra of compound 4p

^{13}C -NMR spectra of compound 4p

Mass spectra for compound 4p

¹H-NMR spectra of compound 4q

¹³C-NMR spectra of compound 4q

Mass spectra for compound 4q

¹H-NMR spectra of compound 4r

¹³C-NMR spectra of compound 4r

Mass spectra for compound 4r

¹H-NMR spectra of compound 4s

¹³C-NMR spectra of compound 4s

Mass spectra for compound 4s

¹H-NMR spectra of compound 4t

¹³C-NMR spectra of compound 4t

Mass spectra for compound 4t

ms

18B_031112 171 (0.705)

Scan ES+
1.21e7

Fig.S2: Possible ring-chain tautomerism for compound 4a-4t in solvents.

Few more Isomers are possible in solution form

Fig.S3: Intermolecular N-H...N interactions generate a closed dimers in the plane

Table S2. Crystal data for (4b)

Entry	Crystal Data	Parameter
1	Chemical formula	C ₃₈ H ₂₆ Cl ₄ N ₂ O ₂ , C ₃ H ₈ O
2	Molecular Weight	744.5
3	Crystal size (mm)	0.35×0.30×0.30
4	Morphology	plate, colourless
5	Crystal system	Monoclinic
6	Space group	P21/n
7	Unit cell parameters, a(Å), b(Å), c(Å), α(°), β(°), γ(°)	14.8007(10), 12.1500(9), 21.3520(15), 105.977(3)
8	Volume (Å ³)	3691.4(5)
9	Z/Z'	4/1
10	Cell measuring reflections	5121
11	θ-range (°)	2.2–25.3
12	absorption correction, μ (mm ⁻¹)	multi-scan, 0.362
13	F(000)	1544
14	D _x (calculated) (g cm ⁻³)	1.340
<i>Data Collection</i>		
15	Radiation (Å)	0.71073 (MoKα)
16	Temperature (°K)	295
17	θ Range (°)	1.95– 25.6
18	Indices	h = -17 → 12 k = -14 → 14 l = -19 → 25
19	Scan type	φ and ω scans
20	Independent reflections	6922
21	Observed Reflections [I > 2σ(I)]	4884
<i>Refinement</i>		
22	Final Indices	R=0.0603, wR = 0.1618
23	Goodness of fit (S)	1.045
24	(Δ/σ) _{max}	0.04
25	Δρ _{max} and Δρ _{min} (e Å ⁻³)	0.649, -0.703
26	Data/restraints/ parameter	6922/1/450

$$w = 1 / [\sigma^2 (F_o^2) + (aP)^2 + bP] \text{ where } P = (F_o^2 + 2F_c^2)/3, \text{ parameters a and b are: 0.0791, 4.2307 respectively.}$$

Table S3: Interactions observed in (4b).

Interactions	D-H...A	D-H (Å)	H...A (Å)	D...A (Å)	D-H...A (°)
Intra-molecular	C2—H2A...Cl1	0.98	2.65	3.021(3)	103
	C3—H3...Cl2	0.98	2.62	3.019(3)	105
	C12-H12...Cl3	0.98	2.59	3.046(3)	109
	C13-H13...Cl4	0.98	2.68	3.023(3)	101
	C20-H20...O1	0.93	2.40	2.725(4)	100
	C38-H38...O2	0.93	2.39	2.722(5)	101

Symmetry codes: (i) 2-x, 2-y, -z,