Supporting Information

Antitumor Agents 5. Synthesis, Structure-Activity Relationships and Biological Evaluation of Dimethyl-5*H*-pyridophenoxazin-5-ones, Tetrahydro-5*H*-benzopyridophenoxazin-5-ones and 5*H*-Benzopyridophenoxazin-5-ones with Potent Antiproliferative Activity

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Analytical data (UV, 1H-NMR, 13C, MS, mp) of compounds **1-9**

9,11-Dimethyl-5*H*-pyrido[3,2-*a*]phenoxazin-5-one (1). Mp 131-2 °C; UV ($CHCl_3$) λ_{max} (log ε) nm: 394.4 (3.7), 443.2 (3.7); ^{1}H NMR ($CDCl_3$) 9.07 (1H, d; J = 4.3 Hz), 9.03 (1H, d; J = 8.1 Hz), 7.68 (1H, dd; J = 4.3, 8.1 Hz), 7.05 (1H, d; J = 1.6 Hz), 6.97 (1H, d; J = 1.6 Hz), 6.59 (1H, s), 2.47 (3H, s), 2.44 (3H, s); ^{13}C NMR ($CDCl_3$) 182.57 (s), 169.32 (s), 153.49 (s),153.22 (d), 147.41 (s), 143.78 (s), 140.31 (s), 135.35 (s), 132.75 (d), 128.71 (s), 128.20 (d), 126.09 (d), 125.70 (s), 114.80 (d), 108.16 (d), 21.08 (q), 16.85 (q). MS-EI m/z 276 (M+). Yield 30%. Anal. ($C_{17}H_{12}N_2O_2$) C, H, N.

9,10-Dimethyl-5*H*-pyrido[3,2-*a*]phenoxazin-5-one (2). Mp > 300 °C; UV ($CHCl_3$) λ_{max} (log ε) nm: 458.6 (4.50); ^{1}H NMR ($CDCl_3$) 9.09 (1H, d; J = 4.3 Hz), 9.04 (1H, d; J = 8.1 Hz), 7.71 (1H, dd; J = 4.3, 8.1 Hz), 7.62 (1H, s), 7.16 (1H, s), 6.62 (1H, s), 2.40 (3H, s), 2.37 (3H, s); ^{13}C NMR ($CDCl_3$) 182.60 (s), 169.31 (s), 154.51 (s), 152.01 (d), 147.40 (s), 142.89 (d), 139.20 (s), 134.10 (s), 132.76 (d), 127.18 (s), 127.21 (s), 126.09 (d), 124.80 (s), 124.34 (d), 114.91 (d), 30.45 (q), 22.21 (q). MS-EI m/z 276 (M+). Yield 32%. Anal. ($C_{17}H_{12}N_2O_2$) C, H, N.

8,9-Dimethyl-5*H*-pyrido[3,2-*a*]phenoxazin-5-one (3). Mp 154-5 °C; UV ($CHCl_3$) λ_{max} (log ε) nm: 384.8 (4.11), 448.2 (4.11); ^{1}H NMR ($CDCl_3$) 9.13 (1H, d; J = 4.3 Hz), 9.05 (1H, d; J = 8.1 Hz), 7.72 (1H, dd; J = 4.3, 8.1 Hz), 7.61 (1H, d; J = 8.0 Hz), 7.22 (1H, d; J = 8.0 Hz), 6.66 (1H, s), 2.44 (3H, s), 2.40 (3H, s); ^{13}C NMR ($CDCl_3$) 182.53 (s), 169.29 (s), 154.49 (s),152.05 (d), 147.35 (s), 142.90 (d), 137.19 (s), 134.01 (s), 133.03 (d), 129.05 (d), 127.28 (d), 127.10 (d), 126.08 (d), 124.77, 114.89 (d), 22.05 (q), 16.05 (q); MS-EI m/z 276 (M+). Yield 31%. Anal. ($C_{17}H_{12}N_2O_2$) C, H, N.

10,11-Dimethyl-5*H*-pyrido[3,2-*a*]phenoxazin-5-one (4). Mp 295-6 °C; UV ($CHCl_3$) λ_{max} (log ε) nm: 439 (3.51); ^{1}H NMR ($CDCl_3$) 9.18 (1H, d; J = 4.3 Hz), 9.08 (1H, d; J = 8.1 Hz), 7.72 (1H, dd; J = 4.3, 8.1 Hz), 7.33 (1H, d; J = 8.3 Hz), 7.11 (1H, d; J = 8.3 Hz), 6.62 (1H, s), 2.69 (3H, s), 2.39 (3H, s); ^{13}C NMR ($CDCl_3$) 182.58 (s), 169.27 (s), 154.39 (s),152.15 (d), 147.35 (s), 142.91 (d), 137.19 (s), 134.01 (s), 133.03 (d), 127.85 (d), 127.28 (d), 127.10 (d), 126.08 (d), 124.77, 114.89 (d), 22.01 (q), 17.05; MS-EI m/z 276 (M+). Yield 33%. Anal. ($C_{17}H_{12}N_2O_2$) C, H, N.

8,11-Dimethyl-5*H*-pyrido[3,2-*a*]phenoxazin-5-one (5). Mp 242-3 °C; UV ($CHCl_3$) λ_{max} (log ε) nm: 334.8 (3.31), 400.8 (3.63); ^{1}H NMR ($CDCl_3$) 9.08 (1H, d; J = 4.3 Hz), 9.04 (1H, d; J = 8.1 Hz), 7.72 (1H, dd; J = 4.3, 8.1 Hz), 7.28 (1H, d; J = 7.6 Hz), 7.14 (1H, d; J = 7.6 Hz), 6.64 (1H, s), 2.71 (3H, s), 2.44 (3H, s); ^{13}C NMR ($CDCl_3$) 182.21 (s), 169.33 (s), 154.51 (s), 153.39 (d), 147.42 (s), 142.79 (d), 133.59 (d), 133.28 (d), 130.20 (s), 128.35 (s), 126.30 (s), 126.16 (s), 126.13 (d), 124.80 (s), 108.28 (d), 15.74 (q), 15.46 (q); MS-EI m/z 276 (M+). Yield 30%. Anal. ($C_{17}H_{12}N_2O_2$) C, H, N.

8,10-Dimethyl-5*H*-pyrido[3,2-*a*]phenoxazin-5-one (6). Mp 211-2 °C; UV ($CHCl_3$) λ_{max} (log ε) nm: 368.4 (3.87), 466.4 (3.71); ^{1}H NMR ($CDCl_3$) 9.07 (1H, d; J = 4.3 Hz), 9.04 (1H, d; J = 8.1 Hz), 7.72 (1H, dd; J = 4.3, 8.1 Hz), 7.08(1H, d; J = 1.6 Hz), 6.99 (1H, d; J = 1.6 Hz), 6.59 (1H, s), 2.44 (3H, s), 2.42 (3H, s); ^{13}C NMR ($CDCl_3$) 180.57 (s)169.23 (s), 153.49 (s)153.22 (d), 151. 33 (s), 147.42 (s), 144.44 (s), 143.78 (d), 139.15 (s), 133.73 (s), 133.15 (d), 128.732 (s), 128.40 (s), 128.20 (d), 126.19 (s), 126.09 (d), 115.03 (s), 114.17 (d), 108.41 (s), 108.16 (d), 22.21 (q), 16.84 (q); MS-EI m/z 276 (M+). Yield 33%. Anal. ($C_{17}H_{12}N_2O_2$) C, H, N.

10,11,12,13-Tetrahydro-5*H*-benzo[*a*]pyrido[2,3-*j*]phenoxazin-5-one (7). Mp 174-5 °C; UV ($CHCl_3$) λ_{max} (log ε) nm: 376.2 (3.84), 443.9 (4.03); ^{1}H NMR ($CDCl_3$) 9.08 (1H, d; J = 4.3 Hz), 9.04 (1H, d; J = 8.1 Hz), 7.65 (1H, dd; J = 4.3, 8.1 Hz), 7.53 (1H, d; J = 7.8 Hz), 6.83 (1H, d; J = 7.8 Hz), 6.47 (1H, s), 2.90 (4H, m), 1.76 (4H, m); ^{13}C NMR ($CDCl_3$) 182.60 (s), 169.31 (s), 154.51 (s), 153.21 (d), 147.5 (s), 138.5 (d), 137.4 (s), 134,5 (s), 133.4 (s), 128.2 (d), 127.4 (d), 124.0 (s), 112.3 (d), 108 (d), 34.6 (t), 34.3 (t), 32.5(t), 30.1(t); MS-EI m/z 302 (M+). Yield 35%.Anal. ($C_{19}H_{14}N_2O_2$) C, H, N.

9,10,11,12-tetrahydro-5*H*-benzo[*i*]pyrido[3,2-*a*]phenoxazin-5-one (8). Mp 174-5 °C; UV ($CHCl_3$) λ_{max} (log ε) nm: 374.0 (3.81), 443.6 (4.02); ^{1}H NMR ($CDCl_3$) 9.07 (1H, d; J = 4.3 Hz), 9.07 (1H, d; J = 8.1 Hz), 7.68 (1H, dd; J = 4.3, 8.1 Hz), 7.53 (1H, s), 7.04 (1H, s), 6.59 (1H, s), 2.90 (2H, m), 1.88 (2H, m), 1.59 (4H, m); ^{13}C NMR ($CDCl_3$) 185.1 (s), 164.5 (s), 156.0 (s), 154.1 (s), 153.2 (d), 147.5 (s), 138.5 (s), 138.0 (d), 134,5 (2C, s), 128.2 (d), 124.4 (s), 122.3 (d), 118 (d), 106 (s), 34.6 (2, t), 34.3 (t), 32.0(t), 31.1(t); MS-EI m/z 302 (M+). Yield 35%. Anal. ($C_{19}H_{14}N_2O_2$) C, H, N.

8,9,10,11-tetrahydro-5*H*-benzo[*h*]pyrido[3,2-*a*]phenoxazin-5-one (9). Mp 174-5 °C; UV ($CHCl_3$) λ_{max} (log ε) nm: 376.2 (3.84), 443.9 (4.03); ^{1}H NMR ($CDCl_3$) 9.09 (1H, d; J = 4.3 Hz), 9.05 (1H, d; J = 8.1 Hz), 8.03 (1H, d; J = 7.8 Hz), 7.68 (1H, dd; J = 4.3, 8.1 Hz), 6.83 (1H, d; J = 7.8 Hz), 6.45 (1H, s), 2.88 (2H, m), 2.79 (2H, m),1.75 (4H, m); ^{13}C NMR ($CDCl_3$) 185.2 (s), 164.7 (s), 156.1 (s), 154.5 (s), 153.2 (d), 149.5 (s), 138.5 (d), 137.4 (s), 134,5 (s), 130.4 (s), 128.2 (d), 124.1 (s), 123.4 (d), 122.3 (d), 108.1 (d), 34.9 (t), 34.6 (t), 31.5(t), 22.0(t); MS-EI m/z 302 (M+). Yield 33%. Anal. ($C_{19}H_{14}N_2O_2$) C, H, N.

Elemental analysis data of compounds **1-12**

Compd	**C**		**H**		**N**	
	Calcd	Found	Calcd	Found	Calcd	Found
1	73.90	73.93	4.38	4.39	10.14	10.16
2	73.90	73.92	4.38	4.36	10.14	10.15
3	73.90	73.90	4.38	4.36	10.14	10.13
4	73.90	73.89	4.38	4.35	10.14	10.15
6	73.90	73.88	4.38		10.14	10.16
7	75.48	75.50	4.67	4.65	9.27	9.30
8	75.48	75.50	4.67	4.65	9.27	9.30
9	75.48	75.46	4.67	4.68	9.27	9.28
10	76.50	76.51	3.38	3.36	9.39	9.37
11	76.50	76.48	3.38	3.39	9.39	9.40
12	76.50	76.49	3.38	3.37	9.39	9.38