5′-*O*-Alkylpyridoxamines: Lipophilic Analogs of Pyridoxamine are Potent Scavengers of 1,2-Dicarbonyls

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Supporting Information:

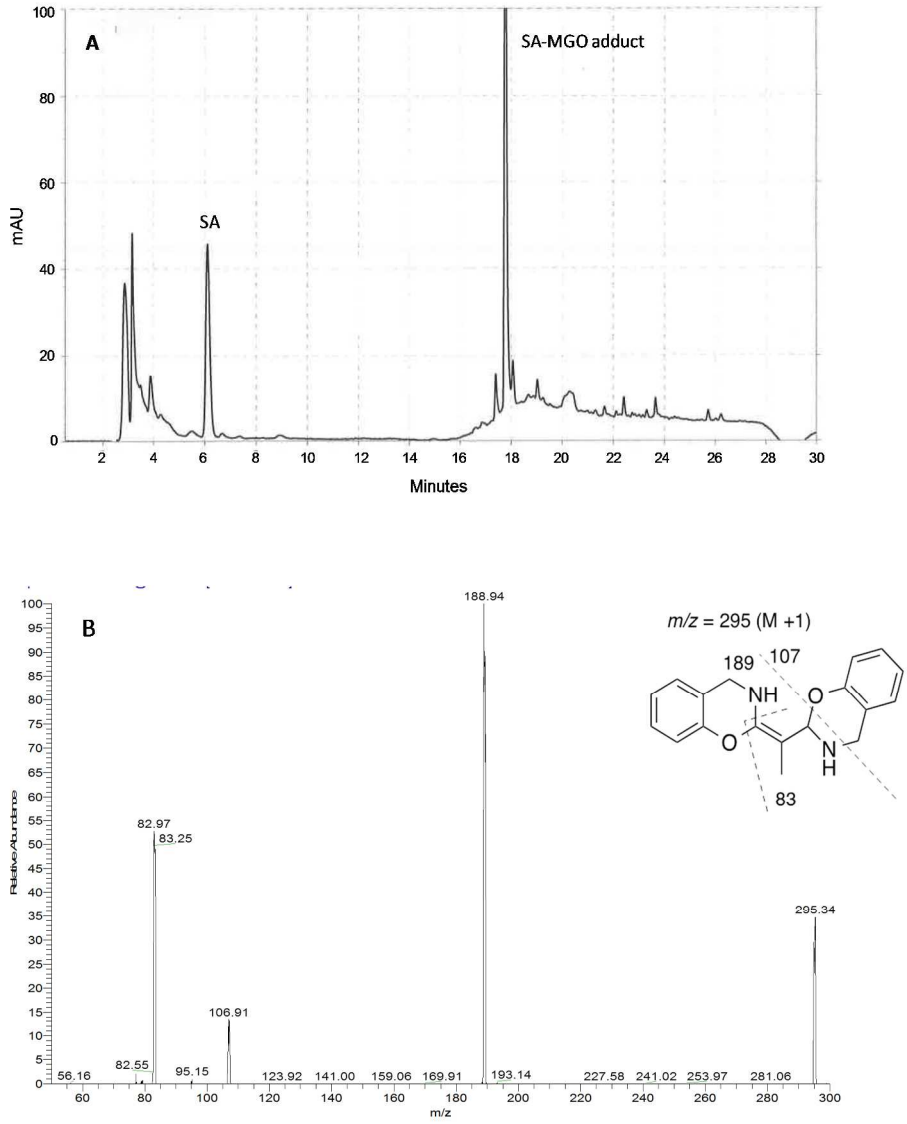

Figure S1. Purification and identification of the major reaction product of salicylamine (SA) and methylglyoxal (MGO). Reaction mixture containing SA and MGO was prepared and incubated as described under Experimental procedures. The mixture was analyzed using HPLC (A) and the major SA-MGO adduct identified using tandem mass-spectrometry (B).

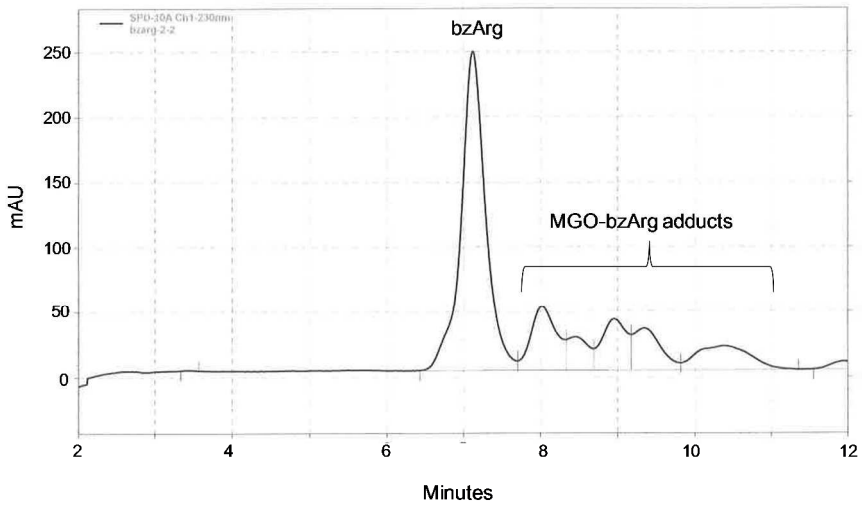

Figure S2. Detection of products of reaction between MGO and bzArg. Reaction mixture containing 5 mM MGO and 5 mM bzArg was incubated at 37°C for 2 h and analyzed using HPLC as described under Experimental procedures.

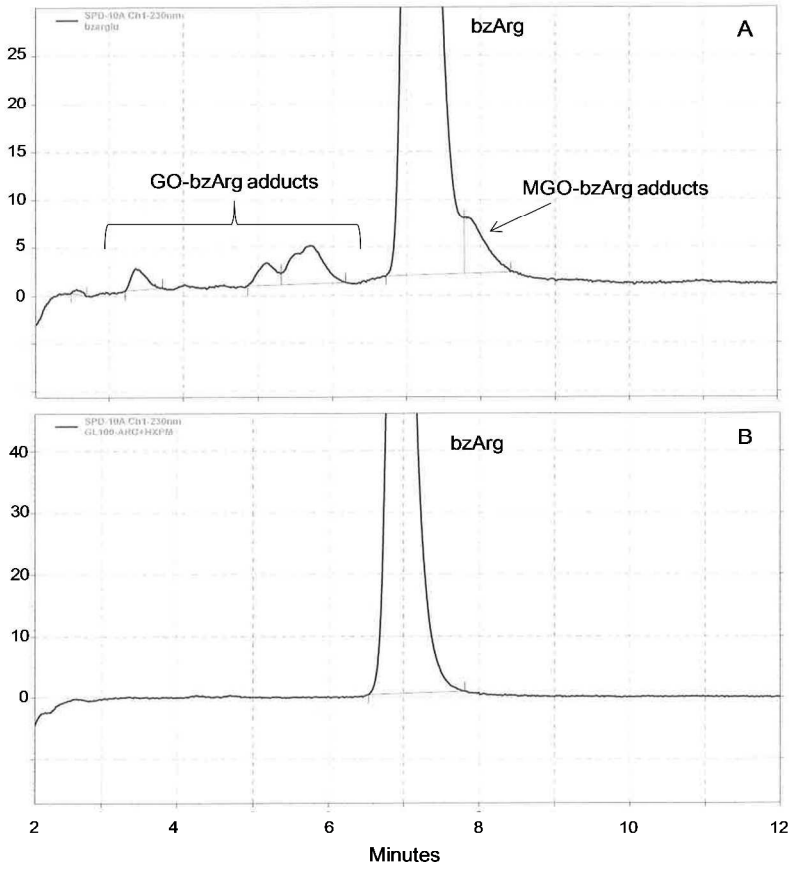

Figure S3. Detection of products of reaction between glucose and bzArg. Reaction mixture containing 100 mM D-glucose and 2 mM bzArg either without (A) or with (B) 2 mM hexyl-PM was incubated at 37°C for 40 d and analyzed using HPLC as described under Experimental procedures.

NMR experiments

NMR runs were acquired using a 14.0 T Bruker magnet equipped with a Bruker AV-III console operating at 600.13 MHz. All spectra were acquired in 3mm NMR tubes using a Bruker 5 mm TCI cryogenically cooled NMR probe. Chemical shifts were referenced internally to DMSO-d_6 (2.49 ppm) which also served as the ^{2}H lock solvent. For 1D ^{1}H NMR, typical experimental conditions included 32K data points, 13 ppm sweep width, a recycle delay of 1.5 seconds and 32 scans. Parameters for 1D 13C NMR included 32K data points, 240 ppm sweep width, 1.5 second recycle delay and 15,000 scans. For 2D ^{1}H-^{1}H COSY, experimental conditions included 2048 x 1024 data matrix, 13 ppm sweep width, recycle delay of 1.5 seconds and 4 scans per increment. The data was processed using squared sinebell window function, symmetrized, and displayed in magnitude mode. Multiplicity-edited ^{1}H-^{13}C HSQC experiment was acquired using a 1024 x 256 data matrix, a J(C-H) value of 145 Hz which resulted in a multiplicity selection delay of 34 ms, a recycle delay of 1.5 seconds and 8 scans per increment along with GARP decoupling on ^{13}C during the acquisition time (150 ms). The data was processed using a □/2 shifted squared sine window function and displayed with CH/CH_3 signals phased positive and CH_2 signals phased negative. J_1(C-H) filtered ^{1}H-^{13}C HMBC experiment was acquired using a 2048 x 256 data matrix, a J(C-H) value of 9 Hz for detection of long range couplings resulting in an evolution delay of 55ms, J_1(C-H) filter delay of 145 Hz (34 ms) for the suppression of one-bond couplings, a recycle delay of 1.5 seconds and 16 scans per increment. The HMBC data was processed using a □/2 shifted squared sine window function and displayed in magnitude mode.

^{1}H NMR (DMSO, 600MHz) δ 1.18 (d, J = 6.63 Hz, 3H), 3.79 (m, 1H), 5.22 (s, 4H), 6.76 (t, J = 3.98 Hz, 1H), 6.82 (d, J = 8.20 Hz, 1H), 6.95 (t, J = 8.56 Hz, 2H), 7.13 (t, J = 7.98 Hz, 1H), 7.17 (d, J = 7.23 Hz, 2H), 7.27 (d, J = 7.59 Hz, 1H)

^{13}C NMR (DMSO, 150 MHz) δ 21.06, 46.13, 48.19, 67.20, 77.92, 115.61, 115.68, 118.52, 119.70, 120.60, 129.39, 130.11, 130.22, 156.45, 156.48, 177.84

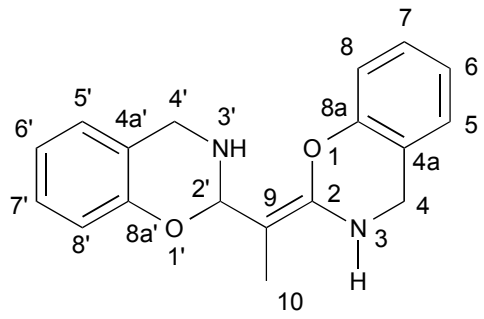

Table S1 NMR Assignments

Position #	1H NMR (PPM)	13C NMR (PPM)	COSY	HMBC
1	N/A	N/A	N/A	N/A
2	N/A	177.84	N/A	1.18, 3.79
3	N/A	N/A	N/A	N/A
4	5.22	48.19	N/A	120.6,130.22,156.48
4a	N/A	120.6	N/A	5.22,6.74,6.95, 7.17
5	7.27	130.22	6.74	48.19,115.68,156.48
6	6.76	118.52	6.95,7.27	115.68,120.6, 130.11
7	6.95	115.68	6.74,7.17	118.52,120.6,156.45
8	7.17	130.11	6.95	115.68, 118.52, 120.6,156.48
8a	N/A	156.48	N/A	5.22, 6.95,7.17, 7.27
9	N/A	77.92	N/A	3.79
10	1.18	21.06	N/A	67.20,177.84

Position #	1H NMR (PPM)	13C NMR (PPM)	COSY	HMBC
1’	N/A	N/A	N/A	N/A
2’	3.79	67.20	N/A	77.92, 177.84
3’	N/A	N/A	N/A	N/A
4’	5.22	46.13	N/A	119.7,130.11,156.45
4a’	N/A	119.7	N/A	5.22
5’	7.17	130.11	6.76	46.13,129.39,156.45
6’	6.95	115.68	7.13,7.17	119.7
7’	7.13	129.39	6.76,6.82	130.11,156.45
8’	6.82	115.61	7.13	119.7, 156.45
8a’	N/A	156.45	N/A	5.22, 7.13,7.17

Scheme S1. Possible Pathways for the Reaction Between Pyridoxamine and Methylglyoxal