Supplementary Information for:

Expanded Combinatorial Formation of Porphyrin Macrocycles in Aqueous Solution Containing Vesicles. A Prebiotic Model

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Table of Contents

I. ESI-MS data for porphyrins derived from pairwise reactions.

Table S1. ESI-MS data of each pairwise reaction following chemical oxidation with I_2.

Entry	Dione	Aminoketone	Porphyrin	*m/z* obsd	Formula (M + H)	*m/z* calcd $(M + H)^+$	ΔM (ppm)
1	**1-AcOH**	**2-PrOH**	$(AcOH/PrOH)_4Por$	831.2350[a]	$C_{40}H_{39}N_4O_{16}$	831.2356	0.72
2	**1-AcOH**	**2-BuOH**	$(AcOH/BuOH)_4Por$	887.2976	$C_{44}H_{47}N_4O_{16}$	887.2982	0.55
3	**1-PentOH**	**2-PrOH**	$(PentOH/PrOH)_4Por$	999.4230	$C_{52}H_{63}N_4O_{16}$	999.4234	0.32
4	**1-PentOH**	**2-BuOH**	$(PentOH/BuOH)_4Por$	1055.4856	$C_{56}H_{71}N_4O_{16}$	1055.4860	0.10
5	**1-AcOH**	**2-Et**	$(AcOH/Et)_4Por$	655.2758[b]	$C_{36}H_{39}N_4O_8$	655.2762	0.61
6	**1-AcOH**	**2-Pr**	$(AcOH/Pr)_4Por$	711.3389	$C_{40}H_{47}N_4O_8$	711.3388	0.05
7	**1-PentOH**	**2-Et**	$(PentOH/Et)_4Por$	823.4639	$C_{48}H_{63}N_4O_8$	823.4640	0.29
8	**1-PentOH**	**2-Pr**	$(PentOH/Pr)_4Por$	879.5266	$C_{52}H_{71}N_4O_8$	879.5266	-0.19
9	**1-Me**	**2-PrOH**	$(Me/PrOH)_4Por$	655.2756[a]	$C_{36}H_{39}N_4O_8$	655.2762	0.92
10	**1-Me**	**2-BuOH**	$(Me/BuOH)_4Por$	711.3376	$C_{40}H_{47}N_4O_8$	711.3388	1.75
11	**1-Hex**	**2-PrOH**	$(Hex/PrOH)_4Por$	935.5891	$C_{56}H_{79}N_4O_8$	935.5892	0.18
12	**1-Hex**	**2-BuOH**	$(Hex/BuOH)_4Por$	991.6547	$C_{60}H_{87}N_4O_8$	991.6518	-1.85
13	**1-Me**	**2-Et**	$(Me/Et)_4Por$	479.3192[b]	$C_{32}H_{39}N_4$	479.3169	-4.80
14	**1-Me**	**2-Pr**	$(Me/Pr)_4Por$	535.3787	$C_{36}H_{47}N_4$	535.3795	1.59
15	**1-Hex**	**2-Et**	$(Hex/Et)_4Por$	759.6299	$C_{52}H_{79}N_4$	759.6299	-0.21
16	**1-Hex**	**2-Pr**	$(Hex/Pr)_4Por$	815.6944	$C_{56}H_{87}N_4$	815.6925	-2.31

[a] Ref. 38. [b] Ref. 40.

II. Chemical oxidation vs aerobic photooxidation of the [4 x 4] reaction.

The absorption and fluorescence spectra of the crude mixture of the [4 x 4] reaction either upon chemical oxidation or aerobic photooxidation are shown in Figure S1 for comparison.

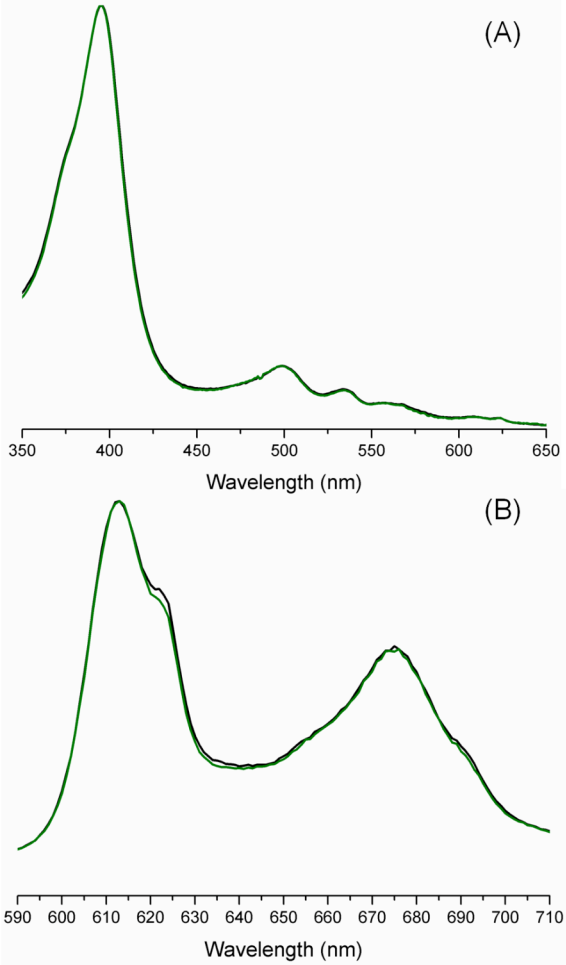

Figure S1. Absorption (panel A) and fluorescence emission (panel B) spectra of the crude mixture of the [4 x 4] reaction following aerobic photooxidation (black) or I_2 oxidation (green). Spectra were acquired in 0.1 M potassium phosphate buffer (pH 7).

III. Molecular formulas of products of [4 x 4] reaction.

The [4 x 4] reaction affords only 205 distinct molecular formulas, which are displayed in Table S2.

Table S2. Distinct molecular formulas from the [4 x 4] combinatorial reaction of four diones (**1-Me**, **1-Hex**, **1-AcOH**, **1-PentOH**) and four aminoketones (**2-Et, 2-Pr**, **2-PrOH**, **2-BuOH**).

Molecular formula	*m/z* (calcd)	Molecular formula	*m/z* (calcd)	Molecular formula	*m/z* (calcd)
$C_{32}H_{38}N_4$	478.3096	$C_{38}H_{38}N_4O_{12}$	742.2486	$C_{47}H_{56}N_4O_{12}$	868.3895
$C_{33}H_{40}N_4$	492.3253	$C_{51}H_{76}N_4$	744.6070	$C_{45}H_{50}N_4O_{14}$	870.3324
$C_{34}H_{42}N_4$	506.3409	$C_{49}H_{70}N_4O_2$	746.5499	$C_{43}H_{44}N_4O_{16}$	872.2752
$C_{35}H_{44}N_4$	520.3566	$C_{47}H_{64}N_4O_4$	748.4928	$C_{56}H_{82}N_4O_4$	874.6336
$C_{33}H_{38}N_4O_2$	522.2995	$C_{45}H_{58}N_4O_6$	750.4356	$C_{54}H_{76}N_4O_6$	876.5765
$C_{36}H_{46}N_4$	534.3722	$C_{43}H_{52}N_4O_8$	752.3785	$C_{52}H_{70}N_4O_8$	878.5194
$C_{34}H_{40}N_4O_2$	536.3151	$C_{41}H_{46}N_4O_{10}$	754.3214	$C_{50}H_{64}N_4O_{10}$	880.4622
$C_{37}H_{48}N_4$	548.3879	$C_{39}H_{40}N_4O_{12}$	756.2643	$C_{48}H_{58}N_4O_{12}$	882.4051
$C_{35}H_{42}N_4O_2$	550.3308	$C_{52}H_{78}N_4$	758.6226	$C_{46}H_{52}N_4O_{14}$	884.3480
$C_{38}H_{50}N_4$	562.4035	$C_{50}H_{72}N_4O_2$	760.5655	$C_{44}H_{46}N_4O_{16}$	886.2909
$C_{36}H_{44}N_4O_2$	564.3464	$C_{48}H_{66}N_4O_4$	762.5084	$C_{57}H_{84}N_4O_4$	888.6493
$C_{34}H_{38}N_4O_4$	566.2893	$C_{46}H_{60}N_4O_6$	764.4513	$C_{55}H_{78}N_4O_6$	890.5921
$C_{39}H_{52}N_4$	576.4192	$C_{44}H_{54}N_4O_8$	766.3942	$C_{53}H_{72}N_4O_8$	892.5350
$C_{37}H_{46}N_4O_2$	578.3621	$C_{42}H_{48}N_4O_{10}$	768.3370	$C_{51}H_{66}N_4O_{10}$	894.4779
$C_{35}H_{40}N_4O_4$	580.3050	$C_{40}H_{42}N_4O_{12}$	770.2799	$C_{49}H_{60}N_4O_{12}$	896.4208
$C_{40}H_{54}N_4$	590.4348	$C_{53}H_{80}N_4$	772.6383	$C_{47}H_{54}N_4O_{14}$	898.3637
$C_{38}H_{48}N_4O_2$	592.3777	$C_{51}H_{74}N_4O_2$	774.5812	$C_{45}H_{48}N_4O_{16}$	900.3065
$C_{36}H_{42}N_4O_4$	594.3206	$C_{49}H_{68}N_4O_4$	776.5241	$C_{58}H_{86}N_4O_4$	902.6649
$C_{41}H_{56}N_4$	604.4505	$C_{47}H_{62}N_4O_6$	778.4669	$C_{56}H_{80}N_4O_6$	904.6078
$C_{39}H_{50}N_4O_2$	606.3934	$C_{45}H_{56}N_4O_8$	780.4098	$C_{54}H_{74}N_4O_8$	906.5507
$C_{37}H_{44}N_4O_4$	608.3363	$C_{43}H_{50}N_4O_{10}$	782.3527	$C_{52}H_{68}N_4O_{10}$	908.4935
$C_{35}H_{38}N_4O_6$	610.2791	$C_{41}H_{44}N_4O_{12}$	784.2956	$C_{50}H_{62}N_4O_{12}$	910.4364
$C_{42}H_{58}N_4$	618.4661	$C_{39}H_{38}N_4O_{14}$	786.2385	$C_{48}H_{56}N_4O_{14}$	912.3793
$C_{40}H_{52}N_4O_2$	620.4090	$C_{54}H_{82}N_4$	786.6539	$C_{46}H_{50}N_4O_{16}$	914.3222
$C_{38}H_{46}N_4O_4$	622.3519	$C_{52}H_{76}N_4O_2$	788.5968	$C_{57}H_{82}N_4O_6$	918.6234
$C_{36}H_{40}N_4O_6$	624.2948	$C_{50}H_{70}N_4O_4$	790.5397	$C_{55}H_{76}N_4O_8$	920.5663
$C_{43}H_{60}N_4$	632.4818	$C_{48}H_{64}N_4O_6$	792.4826	$C_{53}H_{70}N_4O_{10}$	922.5092
$C_{41}H_{54}N_4O_2$	634.4247	$C_{46}H_{58}N_4O_8$	794.4255	$C_{51}H_{64}N_4O_{12}$	924.4521
$C_{39}H_{48}N_4O_4$	636.3676	$C_{44}H_{52}N_4O_{10}$	796.3683	$C_{49}H_{58}N_4O_{14}$	926.3950
$C_{37}H_{42}N_4O_6$	638.3104	$C_{42}H_{46}N_4O_{12}$	798.3112	$C_{47}H_{52}N_4O_{16}$	928.3378
$C_{44}H_{62}N_4$	646.4974	$C_{40}H_{40}N_4O_{14}$	800.2541	$C_{58}H_{84}N_4O_6$	932.6391
$C_{42}H_{56}N_4O_2$	648.4403	$C_{55}H_{84}N_4$	800.6696	$C_{56}H_{78}N_4O_8$	934.5820
$C_{40}H_{50}N_4O_4$	650.3832	$C_{53}H_{78}N_4O_2$	802.6125	$C_{54}H_{72}N_4O_{10}$	936.5248
$C_{38}H_{44}N_4O_6$	652.3261	$C_{51}H_{72}N_4O_4$	804.5554	$C_{52}H_{66}N_4O_{12}$	938.4677
$C_{36}H_{38}N_4O_8$	654.2690	$C_{49}H_{66}N_4O_6$	806.4982	$C_{50}H_{60}N_4O_{14}$	940.4106
$C_{45}H_{64}N_4$	660.5131	$C_{47}H_{60}N_4O_8$	808.4411	$C_{48}H_{54}N_4O_{16}$	942.3535
$C_{43}H_{58}N_4O_2$	662.4560	$C_{45}H_{54}N_4O_{10}$	810.3840	$C_{59}H_{86}N_4O_6$	946.6547
$C_{41}H_{52}N_4O_4$	664.3989	$C_{43}H_{48}N_4O_{12}$	812.3269	$C_{57}H_{80}N_4O_8$	948.5976

$C_{39}H_{46}N_4O_6$	666.3417	$C_{41}H_{42}N_4O_{14}$	814.2698	$C_{55}H_{74}N_4O_{10}$	950.5405
$C_{37}H_{40}N_4O_8$	668.2846	$C_{56}H_{86}N_4$	814.6852	$C_{53}H_{68}N_4O_{12}$	952.4834
$C_{46}H_{66}N_4$	674.5287	$C_{54}H_{80}N_4O_2$	816.6281	$C_{51}H_{62}N_4O_{14}$	954.4263
$C_{44}H_{60}N_4O_2$	676.4716	$C_{52}H_{74}N_4O_4$	818.5710	$C_{49}H_{56}N_4O_{16}$	956.3691
$C_{42}H_{54}N_4O_4$	678.4145	$C_{50}H_{68}N_4O_6$	820.5139	$C_{58}H_{82}N_4O_8$	962.6133
$C_{40}H_{48}N_4O_6$	680.3574	$C_{48}H_{62}N_4O_8$	822.4568	$C_{56}H_{76}N_4O_{10}$	964.5561
$C_{38}H_{42}N_4O_8$	682.3003	$C_{46}H_{56}N_4O_{10}$	824.3996	$C_{54}H_{70}N_4O_{12}$	966.4990
$C_{47}H_{68}N_4$	688.5444	$C_{44}H_{50}N_4O_{12}$	826.3425	$C_{52}H_{64}N_4O_{14}$	968.4419
$C_{45}H_{62}N_4O_2$	690.4873	$C_{42}H_{44}N_4O_{14}$	828.2854	$C_{50}H_{58}N_4O_{16}$	970.3848
$C_{43}H_{56}N_4O_4$	692.4302	$C_{40}H_{38}N_4O_{16}$	830.2283	$C_{59}H_{84}N_4O_8$	976.6289
$C_{41}H_{50}N_4O_6$	694.3730	$C_{55}H_{82}N_4O_2$	830.6438	$C_{57}H_{78}N_4O_{10}$	978.5718
$C_{39}H_{44}N_4O_8$	696.3159	$C_{53}H_{76}N_4O_4$	832.5867	$C_{55}H_{72}N_4O_{12}$	980.5147
$C_{37}H_{38}N_4O_{10}$	698.2588	$C_{51}H_{70}N_4O_6$	834.5295	$C_{53}H_{66}N_4O_{14}$	982.4576
$C_{48}H_{70}N_4$	702.5600	$C_{49}H_{64}N_4O_8$	836.4724	$C_{51}H_{60}N_4O_{16}$	984.4004
$C_{46}H_{64}N_4O_2$	704.5029	$C_{47}H_{58}N_4O_{10}$	838.4153	$C_{60}H_{86}N_4O_8$	990.6446
$C_{44}H_{58}N_4O_4$	706.4458	$C_{45}H_{52}N_4O_{12}$	840.3582	$C_{58}H_{80}N_4O_{10}$	992.5874
$C_{42}H_{52}N_4O_6$	708.3887	$C_{43}H_{46}N_4O_{14}$	842.3011	$C_{56}H_{74}N_4O_{12}$	994.5303
$C_{40}H_{46}N_4O_8$	710.3316	$C_{41}H_{40}N_4O_{16}$	844.2439	$C_{54}H_{68}N_4O_{14}$	996.4732
$C_{38}H_{40}N_4O_{10}$	712.2744	$C_{56}H_{84}N_4O_2$	844.6594	$C_{52}H_{62}N_4O_{16}$	998.4161
$C_{49}H_{72}N_4$	716.5757	$C_{54}H_{78}N_4O_4$	846.6023	$C_{59}H_{82}N_4O_{10}$	1006.6031
$C_{47}H_{66}N_4O_2$	718.5186	$C_{52}H_{72}N_4O_6$	848.5452	$C_{57}H_{76}N_4O_{12}$	1008.5460
$C_{45}H_{60}N_4O_4$	720.4615	$C_{50}H_{66}N_4O_8$	850.4881	$C_{55}H_{70}N_4O_{14}$	1010.4889
$C_{43}H_{54}N_4O_6$	722.4043	$C_{48}H_{60}N_4O_{10}$	852.4309	$C_{53}H_{64}N_4O_{16}$	1012.4317
$C_{41}H_{48}N_4O_8$	724.3472	$C_{46}H_{54}N_4O_{12}$	854.3738	$C_{58}H_{78}N_4O_{12}$	1022.5616
$C_{39}H_{42}N_4O_{10}$	726.2901	$C_{44}H_{48}N_4O_{14}$	856.3167	$C_{56}H_{72}N_4O_{14}$	1024.5045
$C_{50}H_{74}N_4$	730.5913	$C_{42}H_{42}N_4O_{16}$	858.2596	$C_{54}H_{66}N_4O_{16}$	1026.4474
$C_{48}H_{68}N_4O_2$	732.5342	$C_{57}H_{86}N_4O_2$	858.6751	$C_{57}H_{74}N_4O_{14}$	1038.5202
$C_{46}H_{62}N_4O_4$	734.4771	$C_{55}H_{80}N_4O_4$	860.6180	$C_{55}H_{68}N_4O_{16}$	1040.4630
$C_{44}H_{56}N_4O_6$	736.4200	$C_{53}H_{74}N_4O_6$	862.5608	$C_{56}H_{70}N_4O_{16}$	1054.4787
$C_{42}H_{50}N_4O_8$	738.3629	$C_{51}H_{68}N_4O_8$	864.5037		
$C_{40}H_{44}N_4O_{10}$	740.3057	$C_{49}H_{62}N_4O_{10}$	866.4466		

IV. Contour plots for amphiphilic porphyrins.

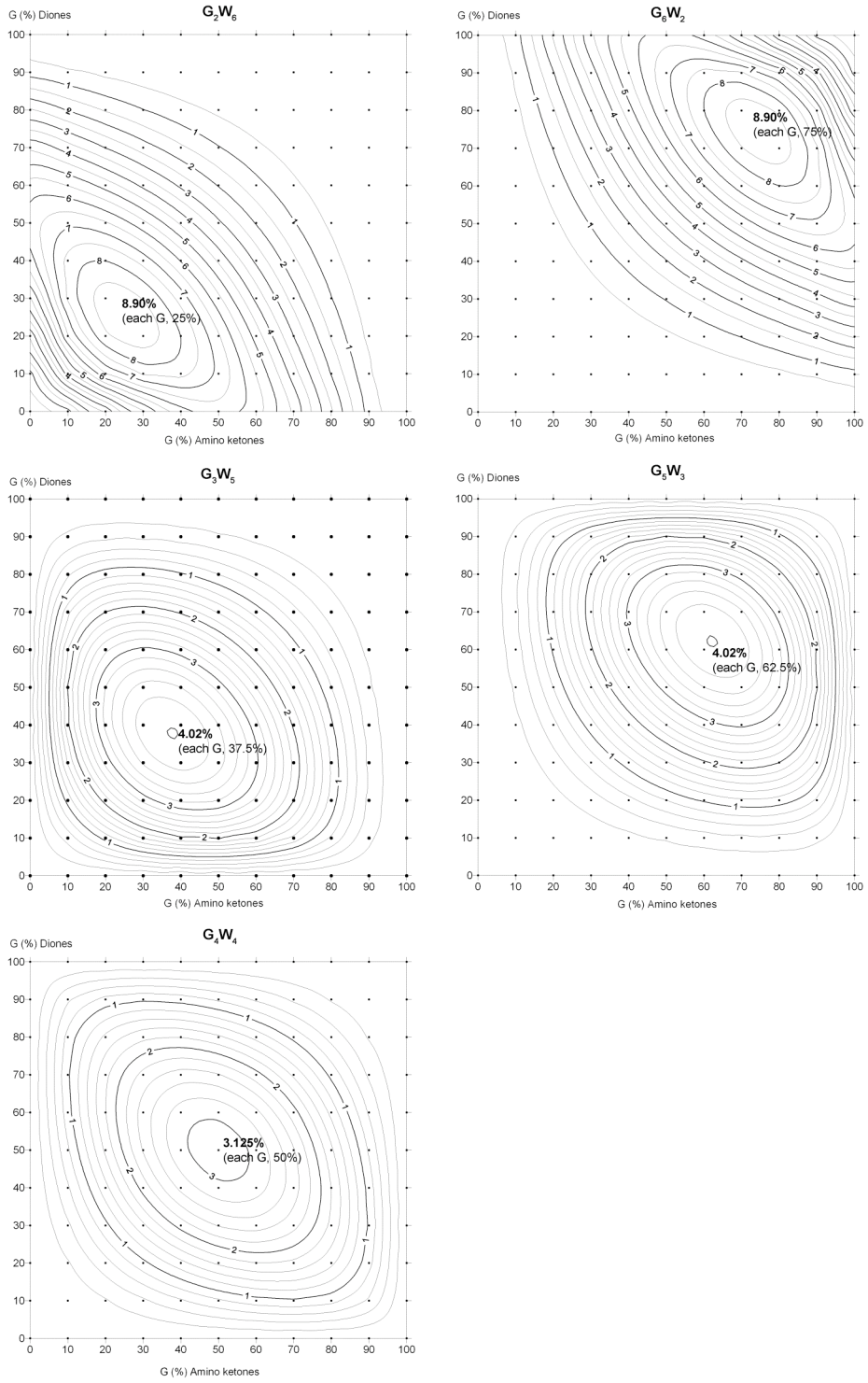

Figure S2. Relative amount of given types of amphiphilic porphyrins as a function of percentage of W or G substituents in the two pools of reactants (diones, aminoketones). The sum of the five individual contour plots gives the composite plot shown in the upper left corner of the figure in the text.

The individual contour plots for the five types of amphiphilic porphyrins are shown in Figure S2. The five types of amphiphilic porphyrins are as follows: G_6W_2 (GG-GG-GG-WW-, GG-GG-GW-WG-), G_5W_3 (GG-GG-GW-WW-), G_4W_4 (GG-GG-WW-WW-, GG-GW-WW-WG-), G_3W_5 (GG-GW-WW-WW-), and G_2W_6 (GG-WW-WW-WW-, GW-WW-WW-WG-).

V. [2 x 2] Combinatorial reaction at various W and G ratios.

To study the effect of substituent polarity in combinatorial reactions, a [2 x 2] reaction of two diones (**1-Me** and **1-AcOH**) and two aminoketones (**2-Et** and **2-PrOH**) was carried out employing various ratios of W and G substituents. The reaction was performed in aqueous solution at 60 mM (60 mM for each pool of reactants) in the presence of SDS. The volumes of each constituent of the reaction mixture are listed in Table S3.

Table S3. Volume of each constituent of the [2 x 2] reaction for various W and G ratios.[a]

Entry	Volume (μL)							χ_W
	1-Me (0.5 M)	**1-AcOH** (0.5 M)	**2-Et** (0.5 M)	**2-PrOH** (0.5 M)	SDS (0.5 M)	Buffer (0.5 M)	Water	
1	48	12	48	12	100	100	180	0.2
2	36	24	36	24	100	100	180	0.4
3	45	15	15	45	100	100	180	0.5
4	30	30	30	30	100	100	180	0.5
5	15	45	45	15	100	100	180	0.5
6	24	36	24	36	100	100	180	0.6
7	12	48	12	48	100	100	180	0.8

[a]60 mM for each pool of reactants.