Nucleophilic reactivity of terminal amino groups of PAMAM dendrimers

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I. Potentiometric titrations of AcEn

All AcEn potentiometric titrations 6-30 mM with the addition of 2 equivalents of standardized HCl in an initial volume of 10 mL of solution, were carried out in a thermostated cell at 25.0±0.1°C, under a continuous flow of nitrogen. Freshly standardized 0.1-0.2 mM NaOH solutions were used as titrants and the ionic strength was maintained constant 100 mM using NaCl.

Table S1. Potentiometric titrations AcEn. (A) 10 mM, (B) 11.9 mM, (C) 9.78 mM, (D) 10.89 mM, (E) 27.9 mM, (F) 6.36 mM, (G) 10.0 mM. (H) 10.0 mM

Titration A		Titration B		Titration C		Titration D	
mL NaOH 0.093 M	pH	mL NaOH 0.189 M	pH	mL NaOH 0.189 M		mL NaOH 0.173 M	pH
0	2.19	0	2.07	0	2.15	0	2.01
0.01	2.20	0.02	2.09	0.02	2.18	0.02	2.02
0.025	2.21	0.04	2.11	0.04	2.20	0.04	2.04
0.045	2.22	0.06	2.13	0.06	2.23	0.06	2.05
0.075	2.23	0.08	2.15	0.08	2.26	0.08	2.07
0.115	2.26	0.10	2.17	0.10	2.29	0.10	2.09
0.155	2.29	0.12	2.20	0.12	2.32	0.12	2.11
0.205	2.33	0.14	2.22	0.14	2.35	0.14	2.13
0.255	2.37	0.16	2.25	0.16	2.39	0.16	2.15
0.305	2.42	0.18	2.28	0.18	2.42	0.19	2.18
0.355	2.47	0.20	2.31	0.20	2.47	0.22	2.21
0.405	2.53	0.22	2.34	0.22	2.51	0.25	2.24
0.455	2.59	0.24	2.37	0.24	2.56	0.28	2.29
0.505	2.67	0.26	2.41	0.26	2.62	0.31	2.33
0.545	2.74	0.28	2.45	0.28	2.69	0.34	2.37
0.585	2.82	0.30	2.49	0.30	2.77	0.37	2.43
0.625	2.93	0.32	2.54	0.32	2.86	0.40	2.48
0.655	3.03	0.34	2.59	0.335	2.95	0.43	2.55
0.685	3.16	0.36	2.65	0.350	3.05	0.46	2.63
0.705	3.28	0.38	2.73	0.36	3.14	0.49	2.73
0.715	3.35	0.40	2.81	0.37	3.25	0.52	2.85
0.725	3.45	0.42	2.92	0.38	3.39	0.55	3.01
0.735	3.57	0.44	3.06	0.39	3.60	0.58	3.28
0.745	3.74	0.455	3.20	0.40	3.98	0.61	4.01
0.755	4.02	0.47	3.42	0.41	6.04	0.63	7.11
0.765	4.83	0.48	3.65	0.42	7.53	0.64	7.52
0.775	6.61	0.49	4.15	0.43	7.91	0.65	7.76
0.785	7.11	0.50	6.77	0.44	8.14	0.66	7.92
0.795	7.40	0.51	7.51	0.45	8.29	0.67	8.04
0.805	7.60	0.52	7.82	0.46	8.42	0.68	8.14

0.815	7.74	0.53	8.01	0.47	8.52	0.69	8.22
0.825	7.86	0.54	8.16	0.48	8.61	0.70	8.30
0.835	7.95	0.55	8.28	0.49	8.69	0.72	8.42
0.845	8.03	0.56	8.37	0.50	8.76	0.74	8.52
0.860	8.13	0.57	8.45	0.51	8.83	0.76	8.61
0.875	8.22	0.58	8.52	0.52	8.85	0.78	8.69
0.890	8.29	0.59	8.59	0.535	8.97	0.81	8.80
0.905	8.36	0.60	8.64	0.55	9.04	0.84	8.89
0.920	8.42	0.62	8.75	0.57	9.14	0.87	8.98
0.935	8.47	0.64	8.84	0.59	9.23	0.9	9.06
0.950	8.52	0.66	8.92	0.61	9.31	0.93	9.14
0.965	8.57	0.68	8.99	0.63	9.39	0.96	9.21
0.980	8.61	0.70	9.06	0.65	9.47	1.00	9.31
1.00	8.65	0.72	9.12	0.67	9.55	1.04	9.41
1.02	8.70	0.74	9.18	0.69	9.63	1.08	9.51
1.04	8.75	0.76	9.25	0.71	9.71	1.12	9.61
1.06	8.79	0.78	9.30	0.73	9.79	1.16	9.72
1.09	8.85	0.80	9.36	0.75	9.88	1.20	9.85
1.12	8.91	0.82	9.42	0.77	9.97	1.24	9.99
1.15	8.97	0.84	9.47	0.79	10.08	1.27	10.11
1.19	9.03	0.86	9.52	0.81	10.19	1.30	10.24
1.23	9.10	0.88	9.58	0.83	10.32	1.33	10.40
1.27	9.16	0.90	9.63	0.85	10.47	1.35	10.51
1.31	9.22	0.92	9.69	0.87	10.64	1.37	10.63
1.36	9.30	0.94	9.75	0.89	10.81	1.39	10.74
1.41	9.37	0.96	9.81	0.91	10.98	1.41	10.84
1.46	9.44	0.98	9.88	0.925	11.09	1.43	10.94
1.51	9.51	1.00	9.95	0.94	11.19	1.45	11.03
1.56	9.59	1.02	10.02	0.955	11.27	1.47	11.10
1.61	9.66	1.04	10.11	0.97	11.34	1.49	11.17
1.66	9.74	1.06	10.18	0.99	11.43	1.52	11.25
1.71	9.81	1.08	10.27	1.01	11.51	1.55	11.32
1.76	9.90	1.10	10.38	1.03	11.57	1.58	11.39
1.81	9.99	1.12	10.49	1.05	11.63	1.62	11.45
1.86	10.08	1.14	10.63	1.08	11.70	1.66	11.51
1.92	10.21	1.16	10.77	1.11	11.77	1.71	11.58
1.98	10.35	1.18	10.91	1.15	11.85	1.76	11.63
2.04	10.50	1.20	11.06	1.19	11.92	1.81	11.68
2.09	10.64	1.22	11.17	1.24	11.99	1.86	11.72
2.13	10.76	1.24	11.27	1.29	12.05	1.91	11.76
2.17	10.87	1.26	11.37	1.34	12.1	1.97	11.8
2.20	10.95	1.28	11.46	1.39	12.15	2.03	11.84
2.23	11.03	1.30	11.52	1.44	12.19	2.09	11.87
2.27	11.13	1.32	11.58			2.15	11.9
2.31	11.22	1.34	11.64			2.21	11.93
2.35	11.30	1.37	11.71			2.28	11.96

2.39	11.37	1.41	11.80			2.35	11.99
2.43	11.43	1.46	11.88			2.42	12.02
2.47	11.49	1.51	11.96				
2.51	11.54	1.56	12.02				
2.56	11.60	1.61	12.07				
2.61	11.65	1.66	12.12				
2.66	11.69	1.71	12.16				
2.71	11.74						
2.76	11.77						
2.81	11.81						
2.87	11.85						
2.93	11.88						
2.99	11.91						
3.05	11.94						
3.11	11.97						
3.17	11.99						
Titration E		Titration F		Titration G		Titration H	
mL NaOH 0.151 M	pH	mL NaOH 0.185 M	pH	mL NaOH 0.139 M	pH	mL NaOH 0.139 M	pH
0	1.51	0	2.12	0	2.07	0	2.04
0.02	1.53	0.010	2.13	0.02	2.08	0.04	2.06
0.04	1.53	0.030	2.15	0.05	2.09	0.09	2.08
0.07	1.55	0.045	2.17	0.09	2.10	0.15	2.10
0.11	1.56	0.060	2.19	0.14	2.12	0.23	2.13
0.16	1.58	0.075	2.21	0.20	2.14	0.32	2.16
0.22	1.60	0.090	2.24	0.27	2.16	0.41	2.20
0.28	1.62	0.105	2.26	0.35	2.20	0.50	2.24
0.34	1.64	0.120	2.29	0.43	2.23	0.59	2.28
0.40	1.67	0.135	2.31	0.52	2.27	0.68	2.33
0.46	1.69	0.150	2.34	0.61	2.31	0.77	2.38
0.52	1.72	0.165	2.37	0.70	2.37	0.86	2.44
0.58	1.75	0.180	2.40	0.79	2.43	0.95	2.51
0.64	1.78	0.195	2.43	0.88	2.49	1.03	2.58
0.70	1.81	0.21	2.47	0.97	2.57	1.10	2.65
0.76	1.84	0.22	2.49	1.05	2.65	1.16	2.72
0.82	1.88	0.23	2.52	1.13	2.75	1.21	2.79
0.88	1.91	0.24	2.55	1.21	2.87	1.26	2.88
0.94	1.95	0.25	2.58	1.28	3.03	1.31	2.98
1.00	2.00	0.26	2.62	1.33	3.18	1.35	3.08
1.06	2.04	0.27	2.65	1.36	3.30	1.38	3.18
1.12	2.10	0.28	2.69	1.38	3.41	1.40	3.26
1.18	2.16	0.29	2.73	1.40	3.55	1.42	3.36
1.24	2.22	0.30	2.78	1.41	3.65	1.44	3.48
1.28	2.27	0.31	2.83	1.42	3.76	1.455	3.60
1.32	2.33	0.32	2.89	1.43	3.92	1.47	3.77
1.36	2.39	0.33	2.96	1.44	4.16	1.48	3.92

1.4	2.46	0.34	3.05	1.45	4.66	1.49	4.16
1.44	2.55	0.35	3.15	1.46	5.96	1.50	4.65
1.48	2.65	0.36	3.29	1.47	6.59	1.51	5.76
1.51	2.75	0.37	3.48	1.48	6.92	1.52	6.48
1.54	2.87	0.38	3.81	1.49	7.15	1.53	6.85
1.57	3.04	0.39	5.51	1.50	7.31	1.54	7.09
1.59	3.19	0.40	7.66	1.51	7.45	1.55	7.28
1.60	3.30	0.41	8.07	1.52	7.55	1.56	7.43
1.61	3.44	0.42	8.31	1.53	7.65	1.57	7.54
1.62	3.63	0.43	8.48	1.54	7.73	1.58	7.64
1.63	3.93	0.44	8.62	1.55	7.80	1.59	7.73
1.64	4.58	0.45	8.73	1.565	7.89	1.605	7.83
1.65	5.27	0.46	8.83	1.58	7.97	1.62	7.92
1.66	6.41	0.47	8.92	1.595	8.03	1.635	8.00
1.67	6.97	0.48	9.01	1.61	8.10	1.65	8.06
1.68	7.28	0.49	9.08	1.625	8.16	1.67	8.15
1.69	7.46	0.50	9.16	1.64	8.20	1.69	8.22
1.70	7.60	0.51	9.23	1.66	8.27	1.71	8.29
1.71	7.71	0.52	9.30	1.68	8.32	1.735	8.34
1.72	7.81	0.53	9.37	1.70	8.38	1.76	8.41
1.73	7.89	0.54	9.44	1.72	8.42	1.785	8.46
1.74	7.96	0.55	9.5	1.74	8.46	1.81	8.52
1.75	8.02	0.56	9.57	1.77	8.52	1.84	8.57
1.765	8.10	0.57	9.64	1.80	8.58	1.87	8.63
1.78	8.17	0.58	9.71	1.83	8.63	1.90	8.68
1.795	8.23	0.59	9.78	1.86	8.68	1.94	8.74
1.81	8.29	0.60	9.86	1.89	8.72	1.98	8.8
1.83	8.35	0.61	9.94	1.93	8.78	2.03	8.87
1.85	8.41	0.62	10.03	1.97	8.83	2.08	8.93
1.87	8.46	0.63	10.12	2.01	8.88	2.13	8.99
1.90	8.54	0.64	10.22	2.06	8.94	2.18	9.05
1.93	8.60	0.65	10.33	2.11	9.00	2.24	9.12
1.96	8.66	0.66	10.44	2.17	9.06	2.30	9.18
1.99	8.72	0.67	10.56	2.23	9.13	2.36	9.24
2.02	8.77	0.68	10.68	2.29	9.18	2.43	9.31
2.05	8.82	0.69	10.79	2.35	9.24	2.50	9.38
2.08	8.87	0.70	10.89	2.41	9.3	2.57	9.44
2.11	8.91	0.71	10.98	2.47	9.36	2.64	9.51
2.14	8.95	0.72	11.07	2.53	9.41	2.71	9.58
2.19	9.01	0.73	11.14	2.59	9.47	2.78	9.65
2.24	9.07	0.74	11.20	2.66	9.54	2.85	9.72
2.29	9.13	0.75	11.26	2.725	9.60	2.92	9.79
2.34	9.19	0.76	11.30	2.79	9.66	2.99	9.87
2.4	9.25	0.77	11.35	2.855	9.73	3.06	9.95
2.46	9.31	0.78	11.4	2.92	9.80	3.13	10.04
2.52	9.38	0.79	11.44	2.985	9.87	3.19	10.12

2.58	9.44	0.80	11.48	3.05	9.94	3.25	10.20
2.65	9.51	0.815	11.53	3.11	10.02	3.30	10.29
2.72	9.58	0.83	11.58	3.17	10.10	3.34	10.35
2.80	9.66	0.85	11.63	3.22	10.17	3.38	10.42
2.88	9.74	0.87	11.69	3.27	10.24	3.42	10.49
2.96	9.83	0.89	11.73	3.32	10.32	3.46	10.57
3.04	9.92	0.91	11.78	3.37	10.41	3.50	10.65
3.12	10.02	0.93	11.81	3.42	10.51	3.54	10.73
3.20	10.13	0.96	11.87	3.46	10.59	3.58	10.81
3.28	10.25	1.00	11.93	3.50	10.67	3.62	10.89
3.36	10.40	1.04	11.98	3.54	10.76	3.66	10.97
3.44	10.59	1.08	12.03	3.58	10.84	3.70	11.05
3.50	10.76	1.12	12.08	3.62	10.93	3.74	11.12
3.54	10.89	1.16	12.12	3.66	11.01	3.78	11.19
3.56	10.95	1.20	12.15	3.70	11.09	3.82	11.25
3.60	11.09	1.24	12.19	3.74	11.16	3.86	11.31
3.64	11.22	1.28	12.22	3.78	11.23	3.90	11.37
3.68	11.33			3.82	11.29	3.94	11.42
3.72	11.43			3.86	11.34	3.98	11.47
3.76	11.52			3.91	11.41	4.03	11.53
3.80	11.59			3.96	11.46	4.08	11.58
3.85	11.68			4.01	11.51	4.14	11.63
3.90	11.74			4.06	11.56	4.20	11.68
3.96	11.82			4.12	11.61	4.27	11.73
4.02	11.88			4.18	11.66	4.34	11.78
4.10	11.96			4.24	11.70	4.41	11.82
4.18	12.02			4.31	11.74	4.49	11.87
4.26	12.08			4.38	11.79	4.57	11.91
4.34	12.12			4.45	11.82	4.65	11.95
4.42	12.16			4.52	11.86	4.73	11.98
4.50	12.20			4.59	11.89	4.81	12.01
4.58	12.24			4.67	11.92		
				4.75	11.95		
				4.83	11.98		
				4.91	12.01		

Table S2. Logβ values of cumulative stability constants from Hyperquad fitting of AcEn titrations.

Log β	Value	Standard deviation
AcEnH	9.3674	0.0061
H-1	-14.1033	0.0073

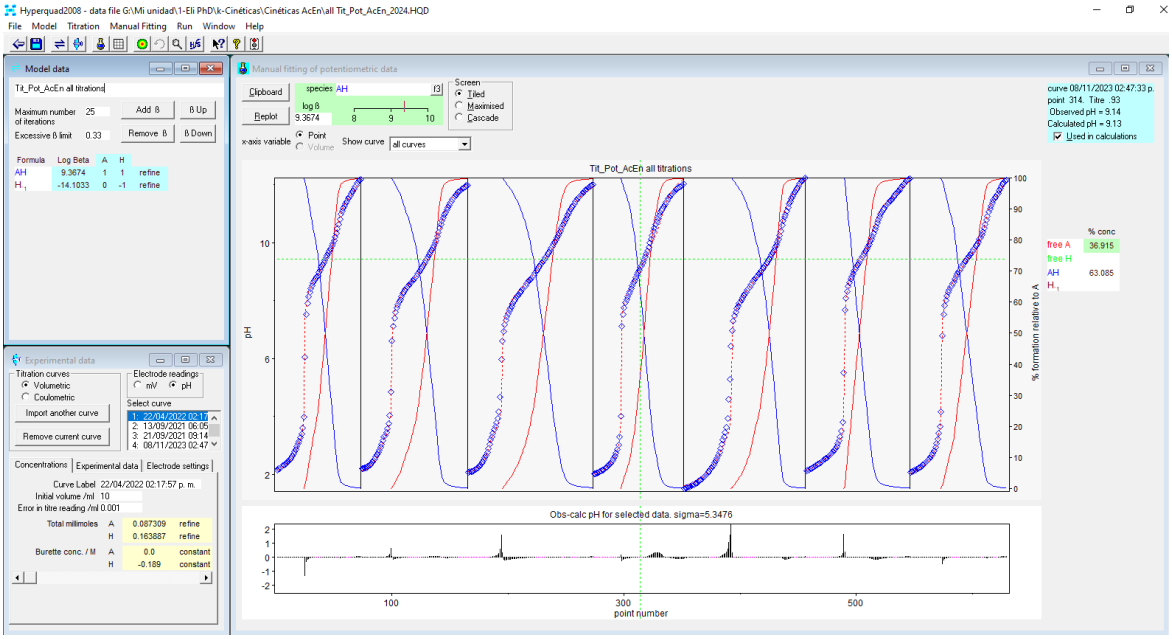


Fig. S1. Simultaneous fitting of AcEn titration curves in Hyperquad.

II. Potentiometric titrations of dendrimers

All potentiometric titrations were performed in an initial volume of 5 mL of solution containing the appropriate amount of each dendrimer by weight, in a thermostated cell at 25.0±0.1°C, under a continuous flow of nitrogen. Freshly standardized NaOH and HCl solutions were used as titrants, as indicated in the columns, and the ionic strength was maintained constant 100 mM using NaCl.

Table S3. Potentiometric titration G0 2.5 mM. (A) NaOH 5 mM added, (B) HCl 16.8 mM added.

Titration A		Titration B	
mL HCl 0.226 M	pH	mL NaOH 0.266 M	pH
0.00	11.66	0.00	3.20
0.01	11.62	0.01	3.42
0.02	11.56	0.02	3.67
0.03	11.50	0.03	4.41
0.04	11.43	0.04	5.67
0.05	11.34	0.05	6.15
0.06	11.25	0.06	6.55
0.07	11.13	0.07	6.93
0.08	10.98	0.08	7.31
0.09	10.78	0.09	7.65
0.10	10.54	0.10	7.85
0.11	10.30	0.11	8.09

0.12	10.08	0.12	8.22
0.13	9.90	0.13	8.39
0.14	9.75	0.14	8.54
0.15	9.61	0.15	8.64
0.16	9.48	0.16	8.81
0.17	9.37	0.17	8.94
0.18	9.25	0.18	9.06
0.19	9.14	0.19	9.19
0.20	9.04	0.20	9.31
0.21	8.93	0.21	9.44
0.22	8.82	0.22	9.58
0.23	8.72	0.23	9.73
0.24	8.60	0.24	9.86
0.25	8.48	0.25	10.08
0.26	8.36	0.26	10.32
0.27	8.19	0.27	10.57
0.28	8.03	0.28	10.81
0.29	7.84	0.29	11.00
0.30	7.61	0.3	11.15
0.31	7.33	0.31	11.26
0.32	6.99	0.32	11.35
0.33	6.67	0.33	11.43
0.34	6.36	0.34	11.5
0.35	6.01	0.35	11.56
0.36	5.41	0.36	11.61
0.37	4.20	0.37	11.65
0.38	3.69		
0.39	3.40		
0.40	3.20		

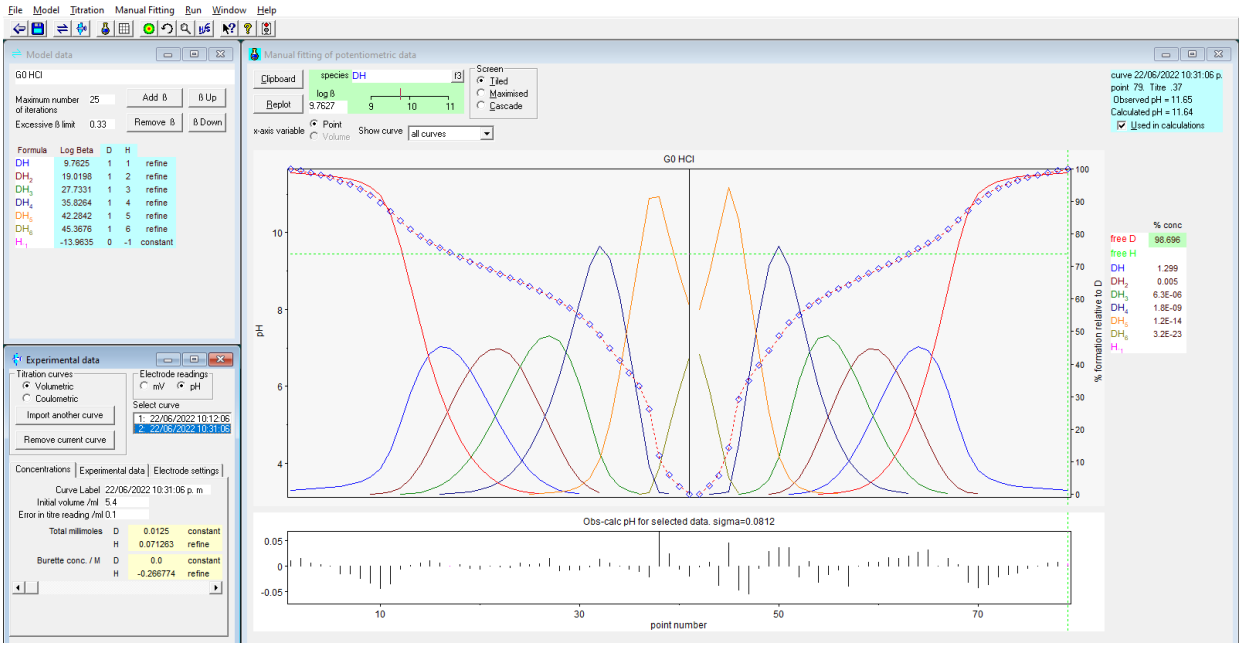


Fig. S2. Simultaneous fitting of PAMAM-NH_2 G0 dendrimer titration curves in Hyperquad.

Table S4. Logβ values of cumulative stability constants from Hyperquad fitting of PAMAM-NH_2 G0 dendrimer titrations.

Log β	Value	Standard deviation
DH	9.7625	0.0194
DH_2	19.0198	0.0152
DH_3	27.7331	0.0214
DH_4	35.8264	0.0286
DH_5	42.2842	0.0533
DH_6	45.3676	0.0891
H-1	-13.9635	

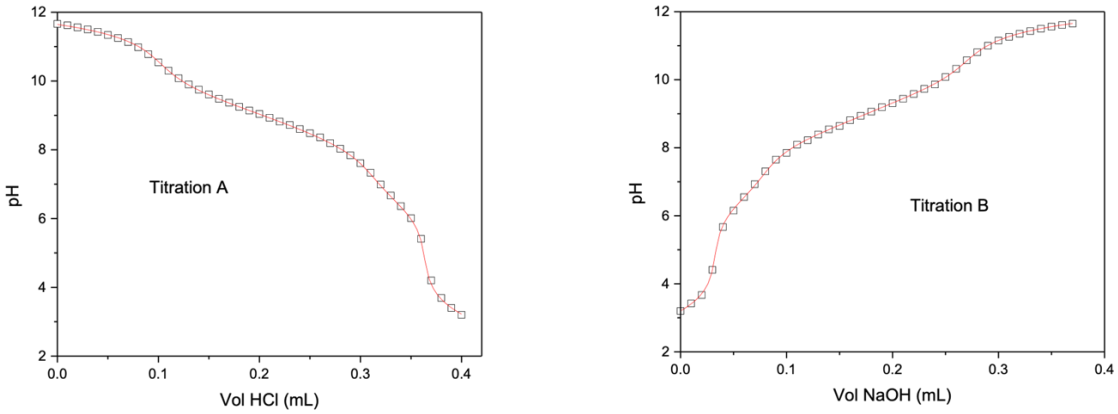


Fig. S3. Experimental (open squares) and calculated (continuous line) titration curves with Hyperquad stability constants for PAMAM-NH_2 dendrimer G0

Table S5. Potentiometric titrations G1 1.25 mM. (A) NaOH 5 mM added, (B) HCl 16.8 mM added, (C) NaOH 5 mM added, (D) HCl 19.47 mM added.

Titration A		Titration B		Titration C		Titration D	
mL HCl 0.226 M	pH	mL NaOH 0.266 M	pH	mL HCl 0.226 M	pH	mL NaOH 0.266 M	pH
0	11.69	0	2.86	0	11.53	0	2.89
0.01	11.64	0.01	3.02	10	11.48	0.01	3.03
0.02	11.59	0.02	3.25	20	11.42	0.02	3.21
0.03	11.53	0.03	3.65	30	11.36	0.03	3.50
0.04	11.46	0.04	4.44	40	11.28	0.04	4.05
0.05	11.38	0.05	5.00	50	11.19	0.05	4.70
0.06	11.29	0.06	5.38	60	11.07	0.06	5.07
0.07	11.17	0.07	5.62	70	10.91	0.07	5.32
0.08	11.02	0.08	5.92	80	10.70	0.08	5.54
0.09	10.80	0.09	6.18	90	10.46	0.09	5.73
0.10	10.52	0.10	6.46	100	10.21	0.10	5.92
0.11	10.21	0.11	6.77	110	10.01	0.11	6.12
0.12	9.95	0.12	7.10	120	9.84	0.12	6.32
0.13	9.73	0.13	7.51	130	9.69	0.13	6.56
0.14	9.54	0.14	7.85	140	9.56	0.14	6.82
0.15	9.39	0.15	8.10	150	9.45	0.15	7.17
0.16	9.22	0.16	8.29	160	9.33	0.16	7.51
0.17	9.07	0.17	8.46	170	9.22	0.17	7.83
0.18	8.92	0.18	8.66	180	9.11	0.18	8.06
0.19	8.76	0.19	8.85	190	9.01	0.19	8.23
0.20	8.60	0.20	8.98	200	8.91	0.20	8.39
0.21	8.42	0.21	9.15	210	8.80	0.21	8.53
0.22	8.23	0.22	9.30	220	8.68	0.22	8.66

0.23	8.02	0.23	9.49	230	8.56	0.23	8.78
0.24	7.76	0.24	9.70	240	8.43	0.24	8.90
0.25	7.43	0.25	9.94	250	8.31	0.25	9.01
0.26	7.06	0.26	10.21	260	8.15	0.26	9.12
0.27	6.71	0.27	10.55	270	7.97	0.27	9.23
0.28	6.41	0.28	10.78	280	7.77	0.28	9.35
0.29	6.16	0.29	10.98	290	7.52	0.29	9.47
0.30	5.96	0.30	11.15	300	7.21	0.30	9.60
0.31	5.74	0.31	11.26	310	6.91	0.31	9.75
0.32	5.52	0.32	11.35	320	6.66	0.32	9.93
0.33	5.26	0.33	11.44	330	6.45	0.33	10.12
0.34	4.85	0.34	11.50	340	6.25	0.34	10.35
0.35	4.21			350	6.08	0.35	10.59
0.36	3.63			360	5.92	0.36	10.80
0.37	3.32			370	5.75	0.37	10.97
0.38	3.10			380	5.58	0.38	11.10
0.39	2.96			390	5.39	0.39	11.20
0.40	2.80			400	5.16	0.40	11.28
				410	4.89	0.41	11.34
				420	4.42	0.42	11.40
				430	3.78	0.43	11.45
				440	3.38	0.44	11.50
				450	3.16	0.45	11.53
				460	3.01		
				470	2.89		

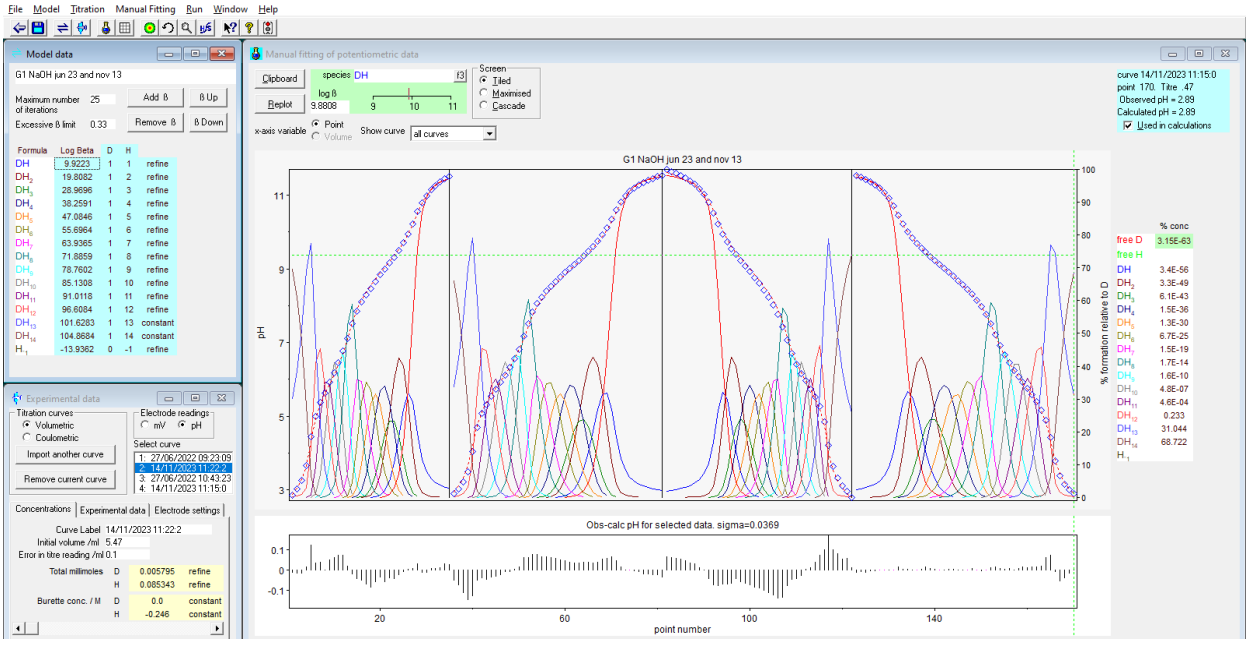


Fig. S4. Simultaneous fitting of PAMAM-NH_2 G1 dendrimer titration curves in Hyperquad.

Table S6. Logβ values of cumulative stability constants from Hyperquad fitting of PAMAM-NH_2 G1 dendrimer titrations.

Log β	Value	Standard deviation
DH	9.9223	0.2351
DH_2	19.8082	0.2096
DH_3	28.9696	0.6324
DH_4	38.2591	0.4683
DH_5	47.0846	0.5133
DH_6	55.6964	0.3518
DH_7	63.9365	0.2577
DH_8	71.8859	0.1513
DH_9	78.7602	0.1533
DH_{10}	85.1308	0.196
DH_{11}	91.0118	0.1482
DH_{12}	96.6084	0.1665
DH_{13}	101.6283	0.095
DH_{14}	104.8684	0.1704
H-1	-13.9362	0.0077

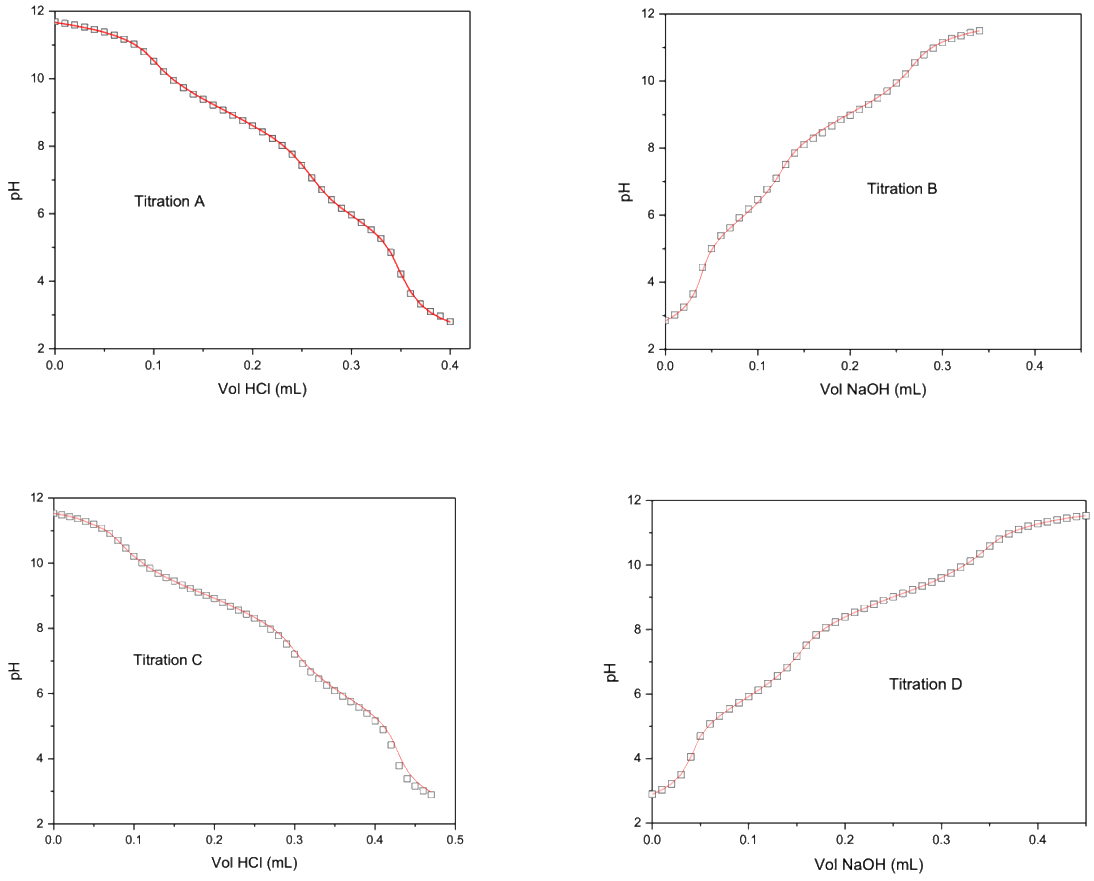


Fig. S5. Experimental (open squares) and calculated (continuous line) titration curves with Hyperquad stability constants for PAMAM-NH_2 dendrimer G1

Table S7. Potentiometric titrations G3. (A) 0.625 mM, NaOH 5 mM added; (B) 0.579 mM, 16.8 mM HCl added; (C) 0.3125 mM, NaOH 5 mM added; (D) 0.289 mM, 16.8 mM HCl added.

Titration A		Titration B		Titration C		Titration D	
mL HCl 0.226 M	pH	mL NaOH 0.266 M	pH	mL HCl 0.226 M	pH	mL NaOH 0.266 M	pH
0	11.65	0	2.75	0	11.67	0	2.94
0.01	11.60	0.01	2.89	0.01	11.62	0.01	3.14
0.02	11.54	0.02	3.07	0.02	11.56	0.02	3.47
0.03	11.47	0.03	3.35	0.03	11.50	0.03	4.02
0.04	11.39	0.04	3.70	0.04	11.42	0.04	4.47
0.05	11.30	0.05	4.02	0.05	11.34	0.05	4.76
0.06	11.19	0.06	4.26	0.06	11.24	0.06	4.94
0.07	11.05	0.07	4.43	0.07	11.11	0.07	5.09
0.08	10.88	0.08	4.56	0.08	10.93	0.08	5.25
0.09	10.69	0.09	4.68	0.09	10.70	0.09	5.41
0.10	10.51	0.10	4.79	0.10	10.42	0.10	5.57
0.11	10.33	0.11	4.89	0.11	10.16	0.11	5.69
0.12	10.19	0.12	4.97	0.12	9.93	0.12	5.82
0.13	10.06	0.13	5.04	0.13	9.74	0.13	5.97
0.14	9.94	0.14	5.12	0.14	9.57	0.14	6.15
0.15	9.85	0.15	5.20	0.15	9.42	0.15	6.30
0.16	9.75	0.16	5.28	0.16	9.28	0.16	6.52
0.17	9.67	0.17	5.35	0.17	9.16	0.17	6.80
0.18	9.59	0.18	5.42	0.18	9.04	0.18	7.08
0.19	9.52	0.19	5.49	0.19	8.92	0.19	7.49
0.2	9.45	0.20	5.56	0.20	8.80	0.20	7.83
0.21	9.38	0.21	5.62	0.21	8.68	0.21	8.07
0.22	9.31	0.22	5.70	0.22	8.55	0.22	8.24
0.23	9.25	0.23	5.77	0.23	8.41	0.23	8.41
0.24	9.19	0.24	5.84	0.24	8.26	0.24	8.57
0.25	9.13	0.25	5.91	0.25	8.10	0.25	8.71
0.26	9.07	0.26	5.98	0.26	7.92	0.26	8.85
0.27	9.01	0.27	6.07	0.27	7.70	0.27	8.98
0.28	8.96	0.28	6.13	0.28	7.45	0.28	9.13
0.29	8.90	0.29	6.21	0.29	7.15	0.29	9.25
0.30	8.84	0.30	6.30	0.30	6.87	0.30	9.38
0.31	8.79	0.31	6.38	0.31	6.67	0.31	9.52
0.32	8.73	0.32	6.47	0.32	6.47	0.32	9.67
0.33	8.67	0.33	6.59	0.33	6.30	0.33	9.82
0.34	8.61	0.34	6.72	0.34	6.15	0.34	10.03
0.35	8.55	0.35	6.86	0.35	6.01	0.35	10.25
0.36	8.49	0.36	7.02	0.36	5.90	0.36	10.51
0.37	8.43	0.37	7.19	0.37	5.77	0.37	10.75
0.38	8.37	0.38	7.37	0.38	5.64	0.38	10.90

0.39	8.30	0.39	7.54	0.39	5.51	0.39	11.06
0.40	8.23	0.40	7.69	0.40	5.39	0.40	11.16
0.41	8.16	0.41	7.82	0.41	5.25	0.41	11.26
0.42	8.08	0.42	7.92	0.42	5.11	0.42	11.33
0.43	8.00	0.43	8.02	0.43	4.95	0.43	11.40
0.44	7.91	0.44	8.12	0.44	4.76	0.44	11.45
0.45	7.82	0.45	8.21	0.45	4.52	0.45	11.49
0.46	7.74	0.46	8.29	0.46	4.18		
0.47	7.63	0.47	8.37	0.47	3.71		
0.48	7.51	0.48	8.45	0.48	3.33		
0.49	7.38	0.49	8.52	0.49	3.10		
0.50	7.24	0.50	8.59	0.50	2.94		
0.51	7.10	0.51	8.65				
0.52	6.96	0.52	8.71				
0.53	6.84	0.53	8.78				
0.54	6.72	0.54	8.84				
0.55	6.62	0.55	8.89				
0.56	6.53	0.56	8.95				
0.57	6.44	0.57	9.00				
0.58	6.35	0.58	9.06				
0.59	6.28	0.59	9.12				
0.60	6.21	0.60	9.18				
0.61	6.13	0.61	9.24				
0.62	6.07	0.62	9.30				
0.63	6.01	0.63	9.37				
0.64	5.95	0.64	9.44				
0.65	5.89	0.65	9.52				
0.66	5.84	0.66	9.60				
0.67	5.78	0.67	9.69				
0.68	5.73	0.68	9.78				
0.69	5.68	0.69	9.86				
0.70	5.62	0.70	9.97				
0.71	5.57	0.71	10.09				
0.72	5.51	0.72	10.23				
0.73	5.45	0.73	10.39				
0.74	5.40	0.74	10.55				
0.75	5.34	0.75	10.71				
0.76	5.29	0.76	10.88				
0.77	5.24	0.77	11.02				
0.78	5.17	0.78	11.13				
0.79	5.11	0.79	11.23				
0.80	5.05	0.80	11.31				
0.81	4.98	0.81	11.38				
0.82	4.89	0.82	11.44				
0.83	4.82	0.83	11.49				
0.84	4.73	0.84	11.54				

0.85	4.63	0.85	11.58				
0.86	4.53	0.86	11.62				
0.87	4.39	0.87	11.66				
0.88	4.24	0.88	11.69				
0.89	4.05						
0.90	3.78						
0.91	3.48						
0.92	3.21						
0.93	3.01						
0.94	2.86						
0.95	2.75						

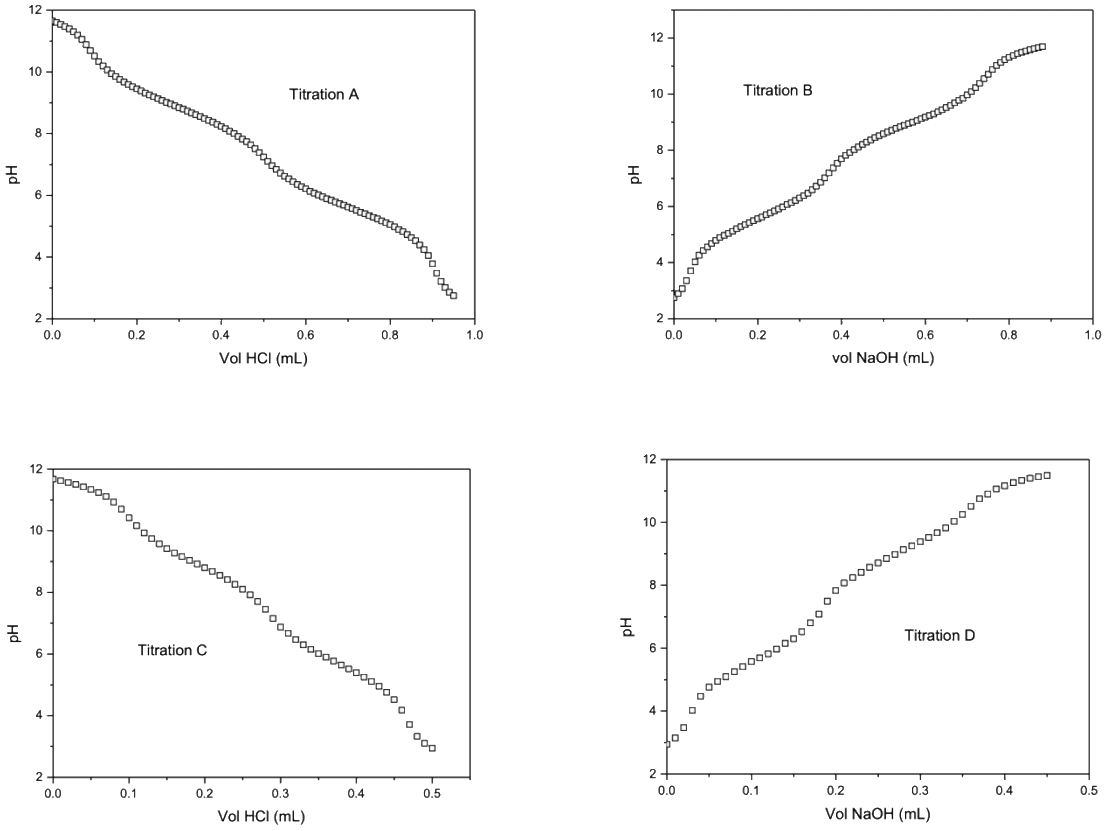


Fig. S6. Experimental acid and base titration curves for PAMAM-NH_2 dendrimer G3

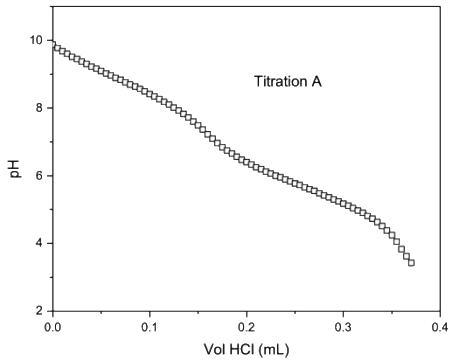
Table S8. Potentiometric titrations of G4. (A) G4 0.176 mM; (B) G4 0.16 mM; (C) G4 0.066 mM, NaOH 5.0 mM added; (D) G4 0.062 mM, HCl 0.017 mM added. (E) G4 0.0329 mM, NaOH 5.0 mM added; (F) G4 0.032 mM, HCl 0.017 mM added; (G) G4 0.066 mM, NaOH 5.0 mM added; (H) G4 0.062 mM, HCl 0.013 mM added.

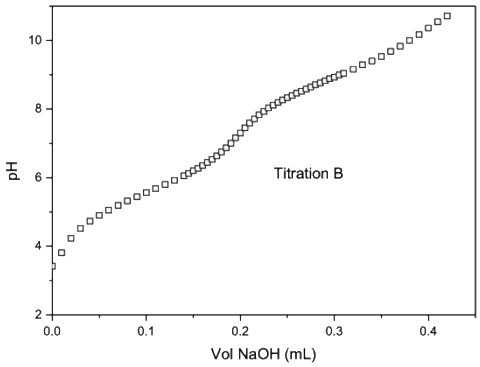
Titration A		Titration B		Titration C		Titration D	
mL HCl 0.229 M	pH	mL NaOH 0.232 M	pH	mL HCl 0.226 M	pH	mL NaOH 0.266 M	pH
0.00	9.87	0.00	3.42	0.00	11.61	0.00	2.24
0.005	9.77	0.01	3.81	0.01	11.56	0.01	2.28
0.010	9.68	0.02	4.23	0.02	11.50	0.02	2.35
0.015	9.60	0.03	4.52	0.03	11.44	0.03	2.41
0.020	9.51	0.04	4.73	0.04	11.36	0.04	2.48
0.025	9.44	0.05	4.9	0.05	11.27	0.05	2.57
0.030	9.37	0.06	5.05	0.06	11.15	0.06	2.70
0.035	9.3	0.07	5.19	0.07	11.00	0.07	2.85
0.040	9.22	0.08	5.32	0.08	10.80	0.08	3.06
0.045	9.16	0.09	5.44	0.09	10.51	0.09	3.44
0.050	9.09	0.10	5.56	0.10	10.12	0.10	4.16
0.055	9.02	0.11	5.68	0.11	9.75	0.11	4.65
0.060	8.96	0.12	5.80	0.12	9.45	0.12	5.01
0.065	8.89	0.13	5.92	0.13	9.17	0.13	5.32
0.070	8.83	0.14	6.05	0.14	8.92	0.14	5.61
0.075	8.76	0.145	6.12	0.15	8.67	0.15	5.92
0.080	8.69	0.150	6.20	0.16	8.42	0.16	6.23
0.085	8.63	0.155	6.27	0.17	8.14	0.17	6.68
0.090	8.56	0.160	6.35	0.18	7.81	0.18	7.30
0.095	8.49	0.165	6.44	0.19	7.39	0.19	7.84
0.100	8.41	0.170	6.53	0.20	6.89	0.20	8.24
0.105	8.34	0.175	6.63	0.21	6.49	0.21	8.55
0.110	8.26	0.180	6.75	0.22	6.19	0.22	8.83
0.115	8.18	0.185	6.87	0.23	5.94	0.23	9.15
0.120	8.10	0.190	7.00	0.24	5.71	0.24	9.48
0.125	8.01	0.195	7.16	0.25	5.48	0.25	9.89
0.130	7.92	0.200	7.30	0.26	5.23	0.26	10.35
0.135	7.82	0.205	7.45	0.27	4.96	0.27	10.72
0.140	7.72	0.210	7.59	0.28	4.61	0.28	10.95
0.145	7.60	0.215	7.71	0.29	4.11	0.29	11.11
0.150	7.49	0.220	7.83	0.30	3.50	0.30	11.23
0.155	7.36	0.225	7.93	0.31	3.11	0.31	11.33
0.160	7.22	0.230	8.03	0.32	2.88	0.32	11.41
0.165	7.09	0.235	8.11	0.33	2.75	0.33	11.48
0.170	6.96	0.240	8.19	0.34	2.63	0.34	11.53
0.175	6.84	0.245	8.26	0.35	2.53	0.35	11.58

0.180	6.74	0.250	8.33	0.36	2.46	0.36	11.63
0.185	6.65	0.255	8.39	0.37	2.39	0.37	11.66
0.190	6.56	0.260	8.46	0.38	2.33		
0.195	6.47	0.265	8.52	0.39	2.28		
0.200	6.40	0.270	8.58	0.40	2.24		
0.205	6.33	0.275	8.64				
0.210	6.25	0.280	8.71				
0.215	6.19	0.285	8.76				
0.220	6.12	0.290	8.82				
0.225	6.06	0.295	8.88				
0.230	6.00	0.300	8.93				
0.235	5.95	0.305	8.99				
0.240	5.89	0.310	9.04				
0.245	5.83	0.320	9.16				
0.250	5.77	0.330	9.29				
0.255	5.72	0.340	9.40				
0.260	5.66	0.350	9.53				
0.265	5.60	0.360	9.68				
0.270	5.55	0.370	9.83				
0.275	5.48	0.380	10.00				
0.280	5.42	0.390	10.17				
0.285	5.36	0.400	10.36				
0.290	5.30	0.410	10.54				
0.295	5.24	0.420	10.71				
0.300	5.17						
0.305	5.11						
0.310	5.04						
0.315	4.97						
0.320	4.90						
0.325	4.81						
0.330	4.73						
0.335	4.63						
0.340	4.51						
0.345	4.38						
0.350	4.24						
0.355	4.05						
0.360	3.83						
0.365	3.62						
0.370	3.42						

Titration E		Titration F		Titration G		Titration H	
mL HCl 0.226 M	pH	mL NaOH 0.266 M	pH		pH	mL NaOH 0.266 M	pH
0	11.65	0	2.79	0	11.58	0	2.74
0.01	11.59	0.01	2.93	0.01	11.53	0.01	2.88
0.02	11.53	0.02	3.19	0.02	11.47	0.02	3.08
0.03	11.47	0.03	3.9	0.03	11.39	0.03	3.41

0.04	11.39	0.04	5.07	0.04	11.31	0.04	4.06
0.05	11.3	0.05	5.77	0.05	11.20	0.05	4.66
0.06	11.2	0.06	6.86	0.06	11.05	0.06	5.04
0.07	11.05	0.07	8.21	0.07	10.85	0.07	5.35
0.08	10.84	0.08	8.99	0.08	10.56	0.08	5.64
0.09	10.50	0.09	9.71	0.09	10.13	0.09	5.93
0.10	9.92	0.10	10.46	0.10	9.73	0.10	6.27
0.11	9.35	0.11	10.80	0.11	9.40	0.11	6.74
0.12	8.78	0.12	10.99	0.12	9.10	0.12	7.35
0.13	8.10	0.13	11.10	0.13	8.81	0.13	7.88
0.14	7.08	0.14	11.23	0.14	8.50	0.14	8.27
0.15	6.30	0.15	11.32	0.15	8.18	0.15	8.59
0.16	5.71	0.16	11.41	0.16	7.78	0.16	8.89
0.17	5.08	0.17	11.48	0.17	7.31	0.17	9.18
0.18	4.25	0.18	11.55	0.18	6.79	0.18	9.50
0.19	3.48	0.19	11.60	0.19	6.40	0.19	9.87
0.20	3.17	0.20	11.65	0.20	6.10	0.20	10.31
0.21	2.94			0.21	5.84	0.21	10.68
0.22	2.79			0.22	5.58	0.22	10.92
				0.23	5.36	0.23	11.09
				0.24	5.07	0.24	11.21
				0.25	4.74	0.25	11.30
				0.26	4.26	0.26	11.38
				0.27	3.63	0.27	11.44
				0.28	3.24	0.28	11.50
				0.29	3.01	0.29	11.55
				0.30	2.85	0.30	11.59
				0.31	2.74		





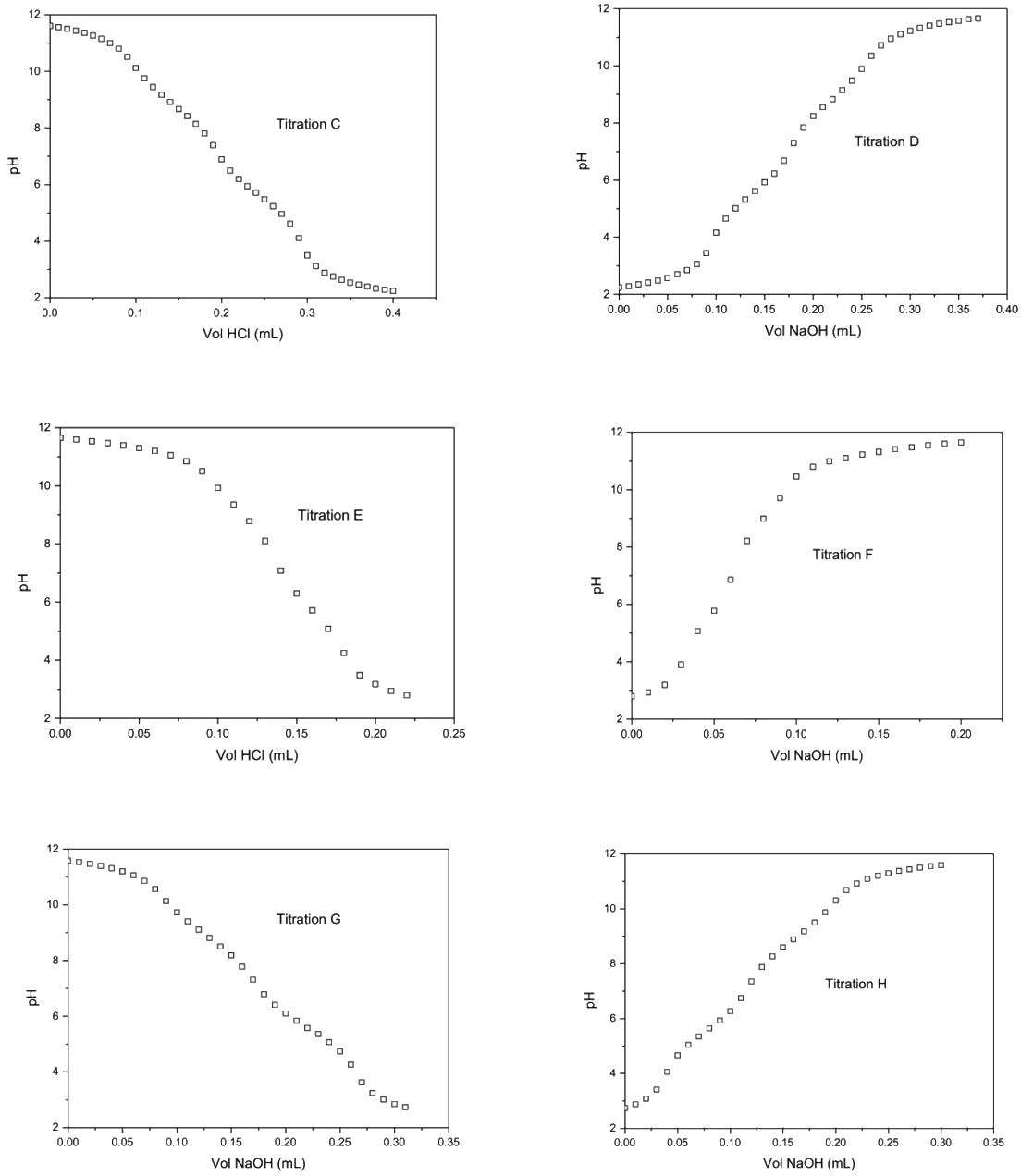


Fig. S7. Experimental acid and base titration curves for PAMAM-NH_2 dendrimer G4

Table S9. pK_a values for dendrimers G0 and G1 obtained in this work, values previously reported in Ref. 1 and predicted values by using *ACD pK_a* software using both available algorithms, *Classic* and *Galas*.

	pK_a G0				pK_a G1			
	This work	Cakara et al.[1]	ACD classic	ACD GALAS	This work	Cakara et al.[1]	ACD classic	ACD GALAS
DH	9.76±0.02	9.70	9.6±0.1	9.8±0.4	9.92±0.24	9.95	9.9±0.1	10.1±0.4
DH_2	9.26±0.02	9.26	9.2±0.1	9.4±0.4	9.89±0.21	9.70	9.5±0.1	9.7±0.4
DH_3	8.65±0.02	8.74	8.8±0.1	9.1±0.4	9.16±0.63	9.25	9.3±0.1	9.3±0.4
DH_4	8.09±0.03	8.31	8.4±0.1	8.6±0.4	9.29±0.46	9.19	9.1±0.1	9.2±0.4
DH_5	6.46±0.05	6.68	7.6±0.5	6.0±0.6	8.83±0.16	8.78	8.9±0.1	9.2±0.4
DH_6	3.08±0.09	3.15	3.6±0.5	2.8±0.8	8.61±0.40	8.68	8.7±0.1	9.2±0.4
DH_7					8.24±0.15	8.30	8.7±0.1	8.8±0.4
DH_8					7.95±0.23	7.96	8.6±0.1	8.3±0.4
DH_9					6.87±0.08	7.10	8.3±0.1	6.7±0.6
DH_{10}					6.67±0.16	6.36	8.3±0.1	5.4±0.6
DH_{11}					5.88±0.20	5.95	8.1±0.1	4.8±0.6
DH_{12}					6.00±0.12	5.55	7.7±0.1	3.3±0.7
DH_{13}					5.02±0.05	5.10	7.7±0.5	
DH_{14}					3.24±0.10	3.07	3.7±0.5	

III. Kinetics of aminolysis reactions

The progress of the aminolysis reactions between AcEn or PAMAM dendrimers with NPA and DNFB as substrates was followed by UV-Vis spectroscopy under various conditions. Time-dependent spectra and kinetic absorbance profiles are shown for AcEn with NPA at different concentrations (Fig. S8), and with DNFB at various pH values (Fig. S9). Similarly, the reactivity of dendrimer G1 with NPA (Fig. S10) and DNFB (Fig. S11) was monitored as a function of pH. In all cases, characteristic spectral changes were observed over time, confirming product formation.

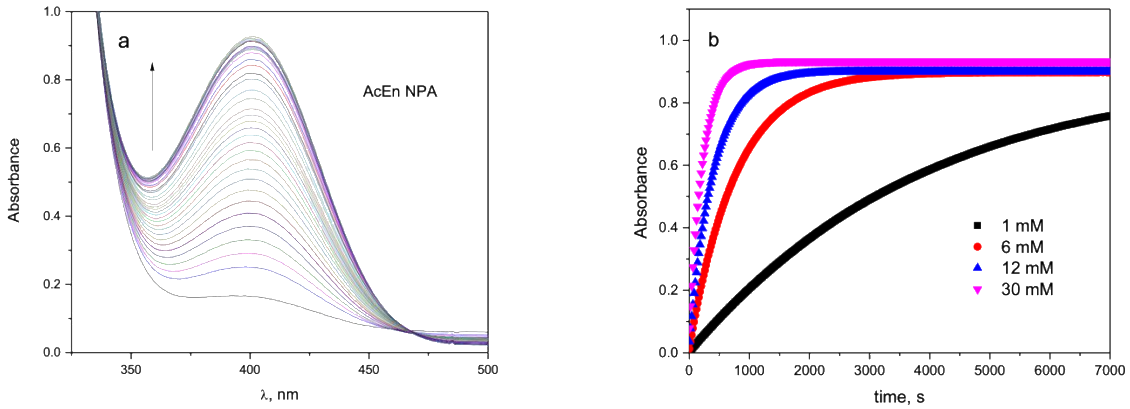


Fig. S8. (a) UV–vis spectra of the reaction between 12 mM AcEn and 0.05 mM NPA at pH 8.5, recorded over time. (b) Kinetic absorbance profiles as a function of time for the reaction of 0.05 mM NPA with varying AcEn concentrations at pH 8.5.

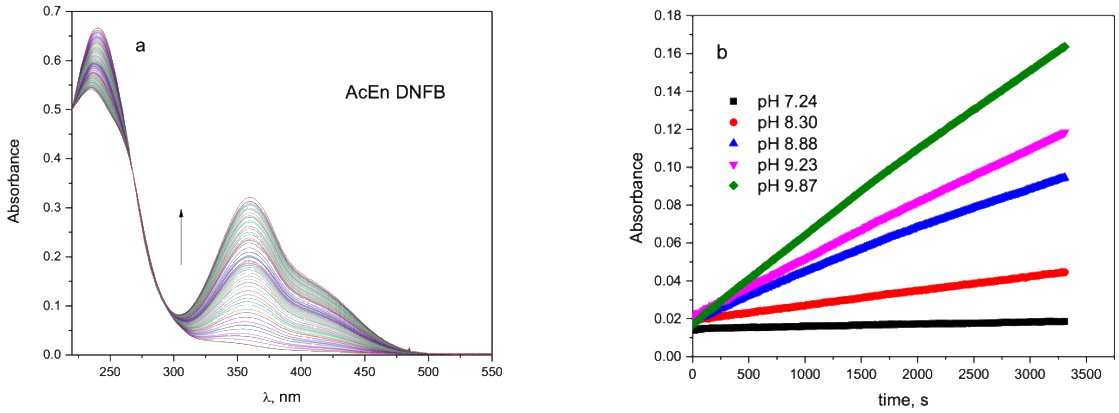


Fig. S9. (a) UV–vis spectra of the reaction between 0.5 mM AcEn and DNFB at pH 9.0, recorded over time. (b) Kinetic absorbance profiles as a function of time for the reaction of 0.5 mM AcEn with DNFB at various pH values.

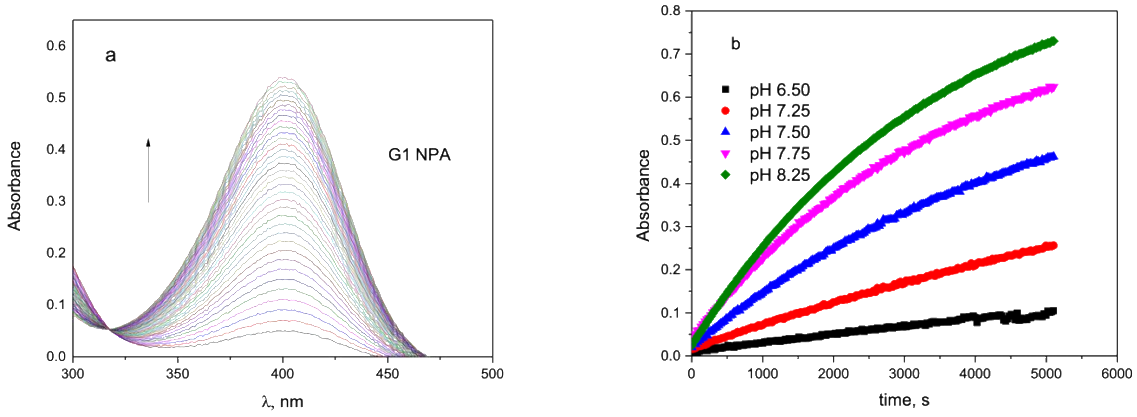


Fig. S10. (a) UV–vis spectra of the reaction between 0.5 mM G1 and NPA at pH 8.25, recorded over time. (b) Kinetic absorbance profiles as a function of time for the reaction of 0.5 mM G1 with NPA at various pH values.

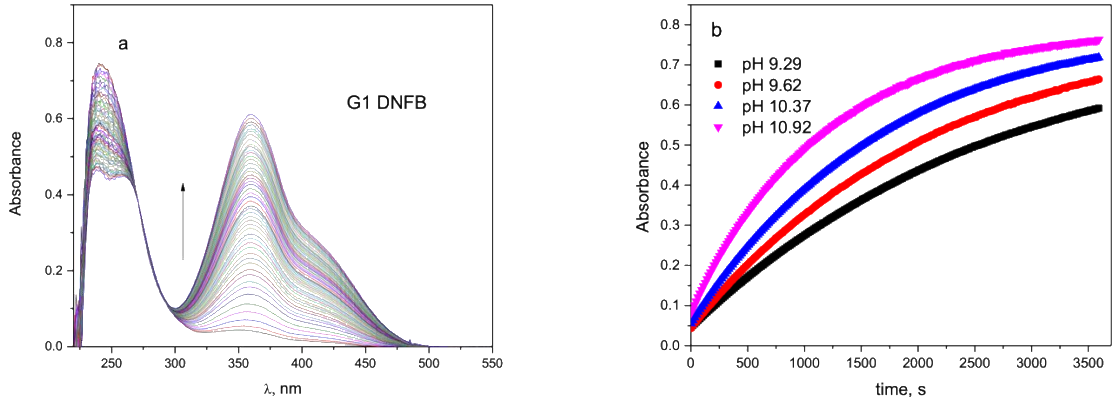


Fig. S11. (a) UV–vis spectra of the reaction between 0.5 mM G1 and DNFB at pH 9.62, recorded over time. (b) Kinetic absorbance profiles as a function of time for the reaction of 0.5 mM G1 with DNFB at various pH values.

In order to ensure the reproducibility of our rate constants each kinetic run was performed 3 times and 2-3 series of data varying the pH or concentration values within the same range were measured, and the average values intercalated; also different batches of purchased dendrimers were employed. The observed rate constants were analyzed together for a global fitting. Fig. S12 shows the fitting of two series of observed first-order rate constants, k_{1obs} s^{-1}, for NPA aminolysis by the dendrimer G4 as a function of pH with standard deviation bars used to represent the error.

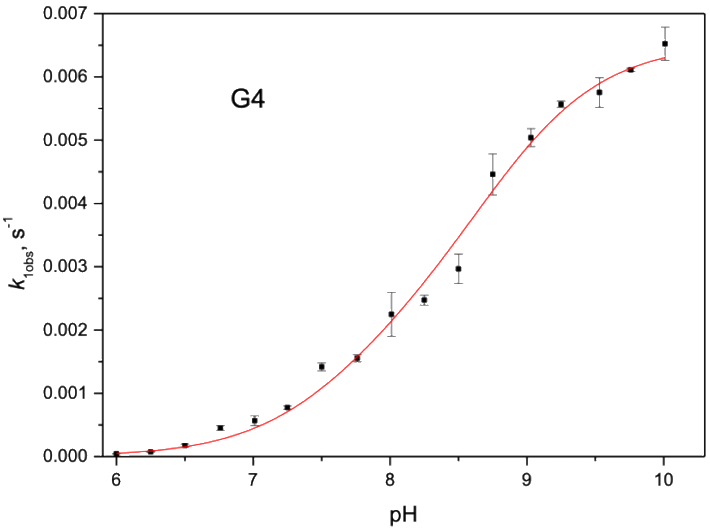


Fig. S12. Average values of observed first-order rate constants, k_{1obs} s^{-1}, for NPA aminolysis by the dendrimer G4 0.1 mM as a function of pH. Standard deviation values are shown as error bars.

To confirm the formation of the 2,4-dinitrophenylamine reaction product between AcEn and DNFB, rather than the nucleophilic substitution product DNP resulting from reaction with OH^-, UV-Vis spectra were recorded after each reaction was completed. Standard additions of DNP were performed to distinguish it from the hydrolysis product; however, the resulting spectra were too similar to allow clear differentiation (Fig. S.11 a,b). Therefore, in a separate experiment, the pH was lowered to acidic conditions after reaction completion. Under these conditions, the spectrum of the AcEn product remained largely unchanged, whereas the spectrum of DNP (formed in the presence of OH^-) showed a characteristic blue shift upon protonation (Figure S.13 c,d). A similar behavior was observed for the substitution products of dendrimers G0 and G1 (Fig. S13 e,f), whose spectra were also unaffected by the acid addition, confirming the presence of the 2,4-dinitrophenylamine product rather than DNP.

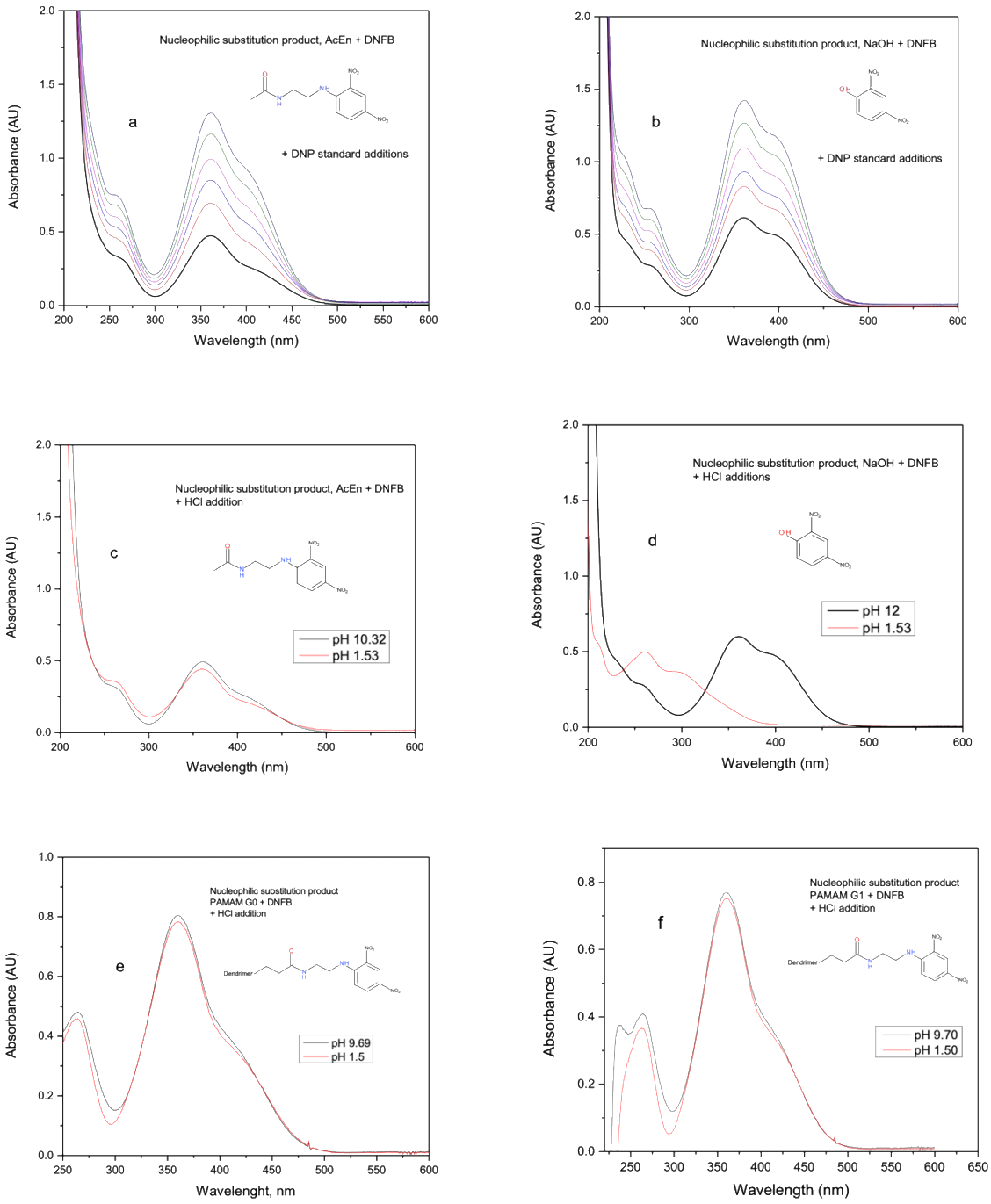
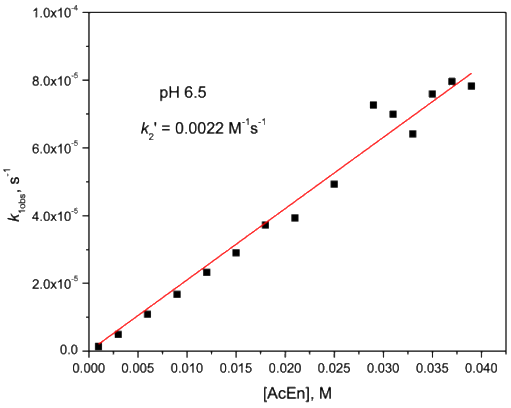
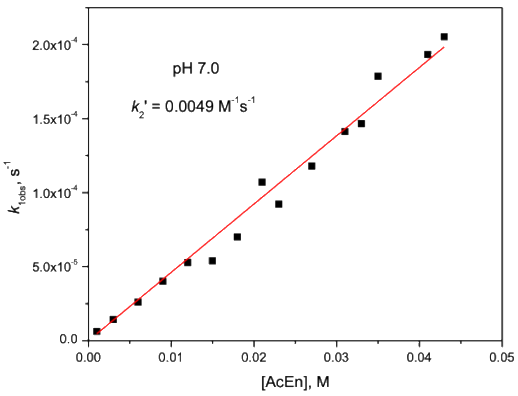
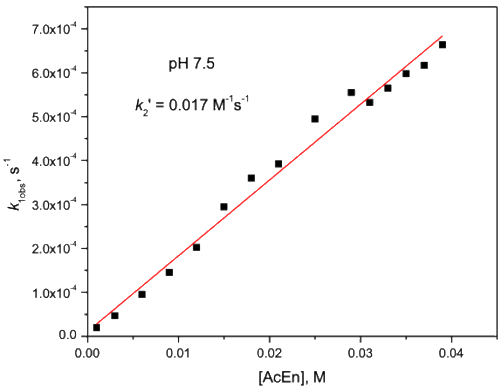
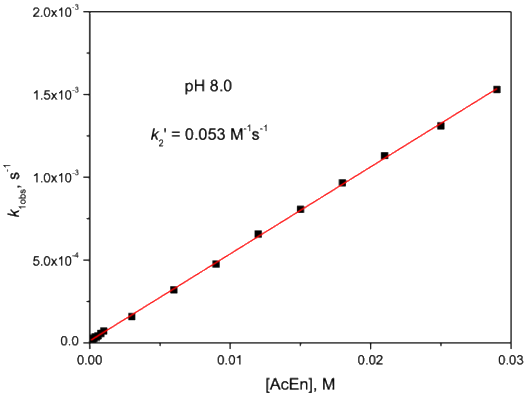


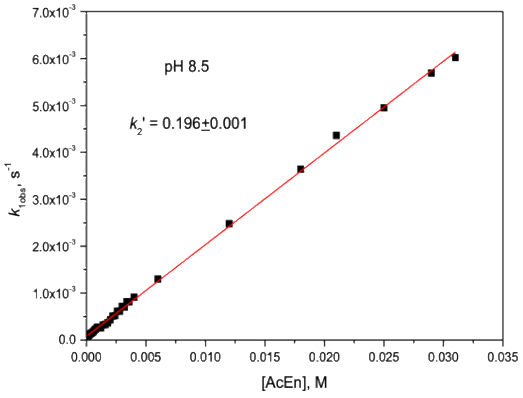
Fig. S13. UV-Vis spectra of DNFB nucleophilic substitution products: (a) AcEn, (b) NaOH, with standard additions of 2,4-dinitrophenol (DNP); (c) AcEn and (d) NaOH products at basic and acidic pH after HCl addition; (e) PAMAM G0 and (f) PAMAM G1 substitution products after HCl addition.

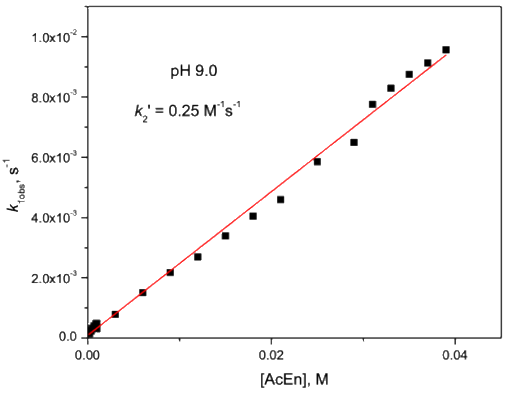

pH 6.5
k_2' = 0.0022 $M^{-1}s^{-1}$
k_{1obs}, s^{-1}
[AcEn], M


pH 7.0
k_2' = 0.0049 $M^{-1}s^{-1}$
k_{1obs}, s^{-1}
[AcEn], M


pH 7.5
k_2' = 0.017 $M^{-1}s^{-1}$
k_{1obs}, s^{-1}
[AcEn], M


pH 8.0
k_2' = 0.053 $M^{-1}s^{-1}$
k_{1obs}, s^{-1}
[AcEn], M


pH 8.5
k_2' = 0.196±0.001
k_{1obs}, s^{-1}
[AcEn], M


pH 9.0
k_2' = 0.25 $M^{-1}s^{-1}$
k_{1obs}, s^{-1}
[AcEn], M

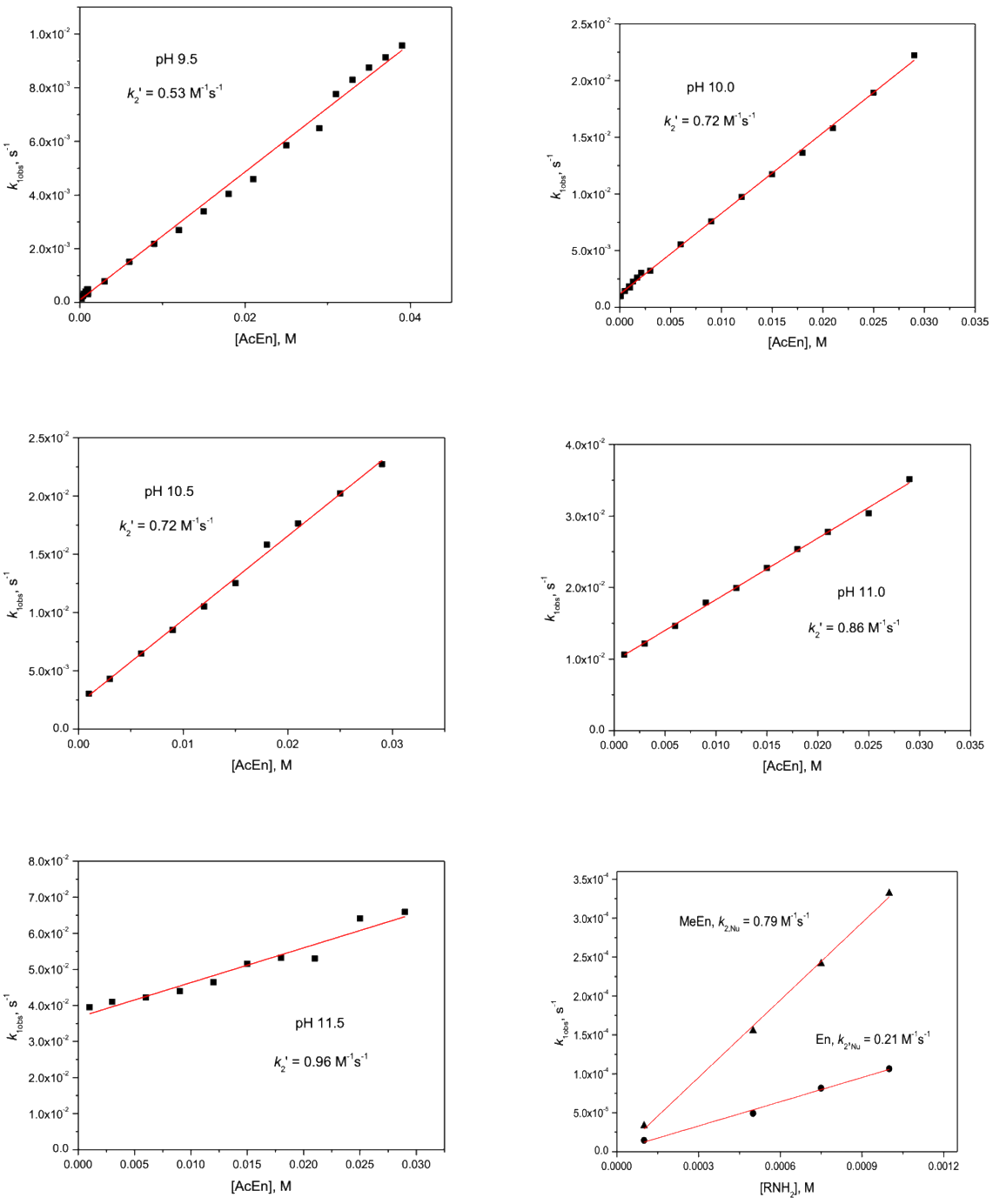


Fig. S14. Observed first-order rate constants for NPA cleavage, k_{1obs} s^{-1}, as a function of AcEn concentration in a range of 0.1-40 mM at various pH values and as a function of MeEn and En concentration at pH 10.0. Observed second-order rate constants, k_2' M^{-1}s^{-1}, were calculated from the linear fitting at each pH. In the case of MeEn and En, $k_{2,Nu}$ M^{-1}s^{-1}, was calculated by dividing this second-order rate constant by the free amine concentration at pH 10.0.

Table S10. Second-order rate constants (k_{2Nu}, $M^{-1}s^{-1}$) for reactions of NPA with primary amines in water at 25°C from Ref. 2

Amine	**pK_a**	**k_{2Nu}, $M^{-1}s^{-1}$**
$PhNH_2$	4.85	0.000183
$CF_3CH_2NH_2$	5.84	0.0007
EnH^+	7.42	0.093
GlyOEt	7.90	0.067
GlyGly	8.25	0.17
$MeOCH_2CH_2NH_2$	9.72	2.67
Gly	9.76	2.58
En	10.18	8.93
$PrNH_2$	10.89	16
$EtNH_2$	10.97	16
AcEn*	9.37	0.88

*This work

Table S11. Second-order rate constants (k_2, $M^{-1}s^{-1}$) for reactions of DNFB with amines in water.

Amine	**pK_a**	**k_{2Nu}, $M^{-1}s^{-1}$**	**Ref.**
Butylamine	10.60	0.43	3
Propylamine	10.54	0.37	4
N-MeEn	10.14	0.79	This work
En	9.98	0.21	This work
AcEn	9.37	0.31	This work
Glycine	9.76	0.142	4
Ethanolamine	9.5	0.098	4
Benzylamine	9.34	0.238	4
Glycinethylester	7.68	0.0267	4
Trifluoroethylamine	5.7	0.0017	4

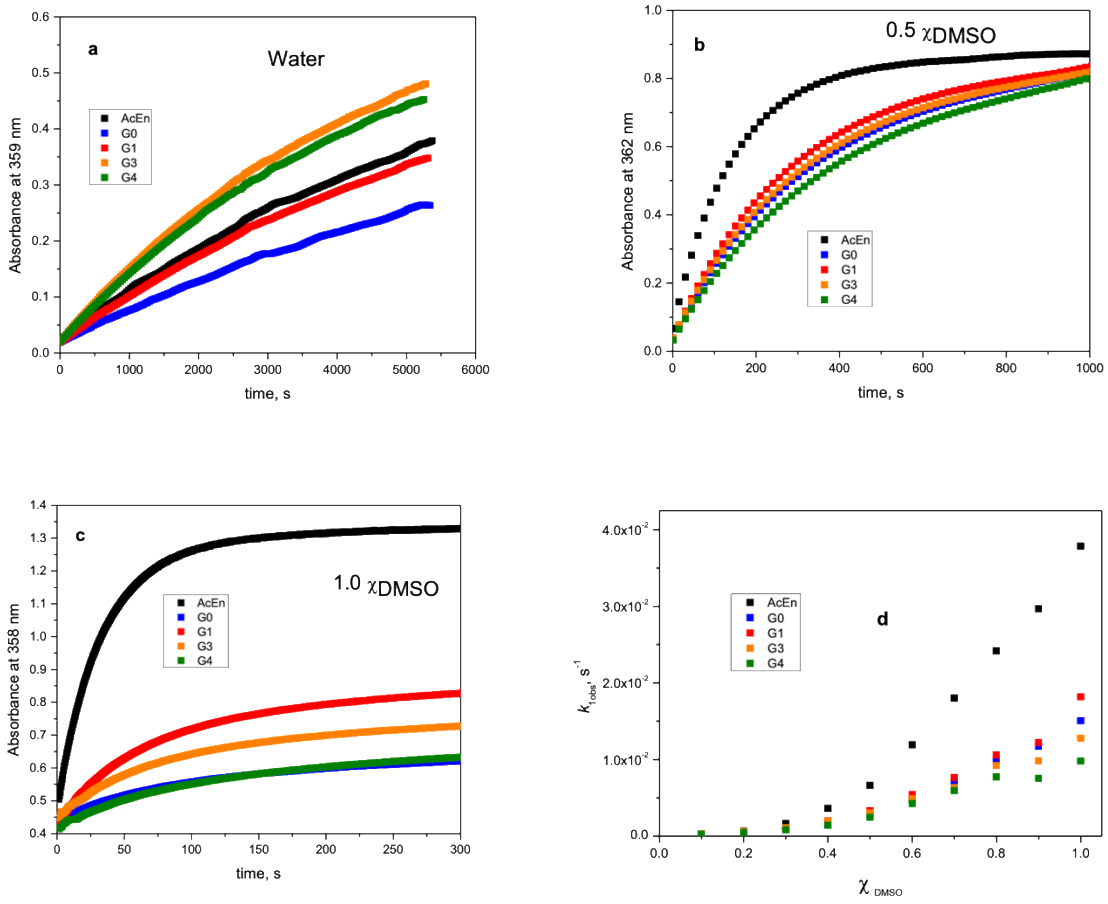


Fig. S15. Reaction of 1.0 mM total amine concentration of AcEn and PAMAM-NH_2 dendrimers G0, G1, G3 and G4 with DNFB at various DMSO molar fractions. Kinetic absorbance profiles as a function of time in (a) water, (b) 0.5 χ_{DMSO} and (c) 1.0 χ_{DMSO}. (d) Observed first-order rate constants, k_{1obs} s^{-1}, for DNFB cleavage as a function of molar fraction of DMSO.

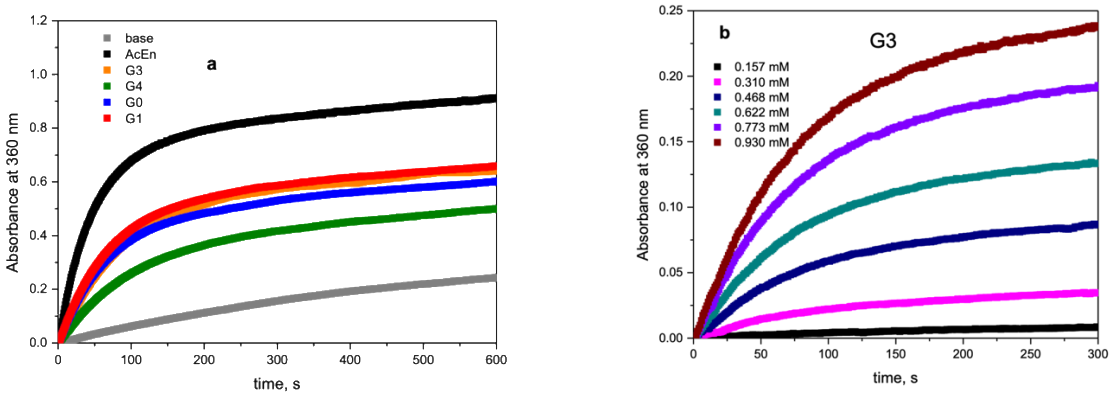


Fig. S16. Kinetic absorbance profiles as a function of time for the reaction of AcEn and PAMAM dendrimers with DNFB in DMSO in the presence of a ternary amine base to neutralize the released HF. (a) AcEn and dendrimers G0, G1, G3 and G4 0.05 mM of total primary amine concentration in the presence of triethylamine 1.0 mM. (b) Different concentrations of PAMAM G3 dendrimer in the presence of pyridine 1.0 mM.

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[1] D. Cakara, J. Kleimann, M. Borkovec, *Macromolecules*, 2003, **36**, 4201–4207.
[2] W. P. Jencks, M. Gilchrist, *J. Am. Chem. Soc.*, 1968, **90**, 2622–2637.
[3] I. H. Um, L. R. Im, J. S. Kang, S. S. Bursey, J. M. Dust, *J. Org. Chem.* 2012, **77**, 9738 − 9746.
[4] R. Ormazábal-Toledo, R. Contreras, R. A. Tapia, P. R. Campodónicoc, *Org. Biomol. Chem.*, 2013, **11**, 2302–2309.