Supporting Information

Alkylation of Substituted Benzoic acids in a Continuous Flow Microfluidic Device: Kinetics and Linear Free Energy Relationships

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Table S1. Residence times versus flow rates in the 75 μm i.d, 3 m length capillary flow reactor

Flowrate ($\mu L.min^{-1}$)	150	75	37.5	18.75	12.5	9.375	7.5
Residence time (s)	5.3	10.6	21.2	42.4	63.6	84.8	106

Table S2. Internal standard peak area at different flow rates in a typical GC/MS experiment

Flow rate (μL. min^{-1})	TMB[a] peak area	DMB[b] peak area	Iodoanisole peak area
150	1011733	895986	943854
150	1058023	912141	984773
75	984080	919312	951730
75	1028007	925414	958760
37.5	1007530	918272	944272
37.5	1005388	926264	964276
18.75	1050252	946008	988435
18.75	1059301	936870	988676
12.5	1008086	918933	972378
12.5	1040201	929565	994153
9.375	1023249	926211	980643
9.375	1019407	926312	982046
7.5	1026044	923791	992671
7.5	1039291	922644	972631
7.5	858977	756139	824274

[a]TMB: 1,3,5-trimethoxybenzene; [b]DMB:1,4-dimethoxybenzene.

Table S3. Statistical analysis of internal standard intensities from table S2 data

	TMB[a]	DMB[b]	Iodoanisole	$\frac{\text{TMB}}{\text{TMB + DMB}}$	$\frac{\text{DMB}}{\text{TMB + DMB}}$
Average peak area	1014638	912258	962905	52.7 %	47.3 %
Standard deviation	47932	44574	41914	51.8 %	48.2 %
Standard deviation to Average peak area ratio %	4.7%	4.9%	4.4%	0.5%	0.5%

[a]TMB: 1,3,5-trimethoxybenzene; [b]DMB:1,4-dimethoxybenzene.

Table S4. Variation of reaction rate with temperature[a]

Solvent	Alkylating agent	Temperature (°C)							
		4	20	30	40	50	60	70	80
DMF	MeI	0.24±0.05	0.57±0.02	0.96±0.04	1.76±0.02	2.8	-	8.9±0.1	-
DMF	EtI	-	0.063±0.006	-	0.32	-	1.15±0.02	-	3.1±0.2
ACN	MeI	-	0.07±0.01	-	0.26±0.01	-	1.23±0.02	-	4.6
ACN	EtI	-	0.012	-	0.055±0.005	-	0.21±0.01	-	0.91±0.13

[a]Average and standard deviation when quoted for experiments performed in duplicate

Table S5. Compilation of substituent dependent parameters

Substituent	σ_m [1]	σ_p^+ [1]	σ_p^- [1]	Löwdin charges [2]			
				$Q_L(H)^a$	$Q_L(O^-)^a$	$Q_L(COO^-)^a$	$Q_L(COOH)^a$
$-NO_2$	0.71	0.79	1.27	0.1191	-0.3540	-0.7719	-0.0254
-CN	0.56	0.66	1.00	0.1182	-0.3567	-0.7768	-0.0312
-I	0.35	0.14	0.27				
-Br	0.39	0.15	0.25				
-Cl	0.37	0.11	0.19	0.1156	-0.3645	-0.7907	-0.0459
-F	0.34	-0.07	-0.03	0.1149	-0.3688	-0.7986	-0.0526
-H	0	0.00	0.00	0.1135	-0.3699	-0.8018	-0.0533
$-CH_3$	-0.07	-0.31	-0.17	0.1126	-0.3713	-0.8046	-0.0597
$-OCH_3$	0.12	-0.78	-0.26	0.1123	-0.3729	-0.8076	-0.0688
-OH	0.12	-0.92	-0.37	0.1150	-0.3637	-0.7956	-0.0471
$-NH_2$	-0.161	-1.30	-0.15				

a. For *para* substituent

Table S6. Correlations of reaction rates with Löwdin charges

Equation	R^2
$\log\frac{k_Y}{k_0}$= -16.31×Q_L(COOH) - 0.8835	0.9829
$\log\frac{k_Y}{k_0}$= -97.20×Q_L(H) + 11.11	0.9646
$\log\frac{k_Y}{k_0}$= -33.92×$Q_L(O^-)$ - 12.49	0.9763
$\log\frac{k_Y}{k_0}$= -18.08×$Q_L(COO^-)$ - 14.44	0.9746

Table S7. Relative V_{min} values of substituted benzoic acids[a]

Substituent	V_{ortho}	V_{meta}	V_{para}
$-NO_2$	1.53	10.67	10.98
-CN	8.88	8.79	9.71
-Br	3.85	4.21	4.12
-Cl	1.49	4.47	4.25
-F	1.89	3.11	2.54
-H	0.00	0.00	0.00
$-CH_3$	-0.72	-1.30	-1.76
$-OCH_3$	-4.40	-1.02	-3.21
-OH	5.03	0.02	-2.17
$-NH_2$	-3.16	-3.76	-6.12

[a]Data from reference [3]

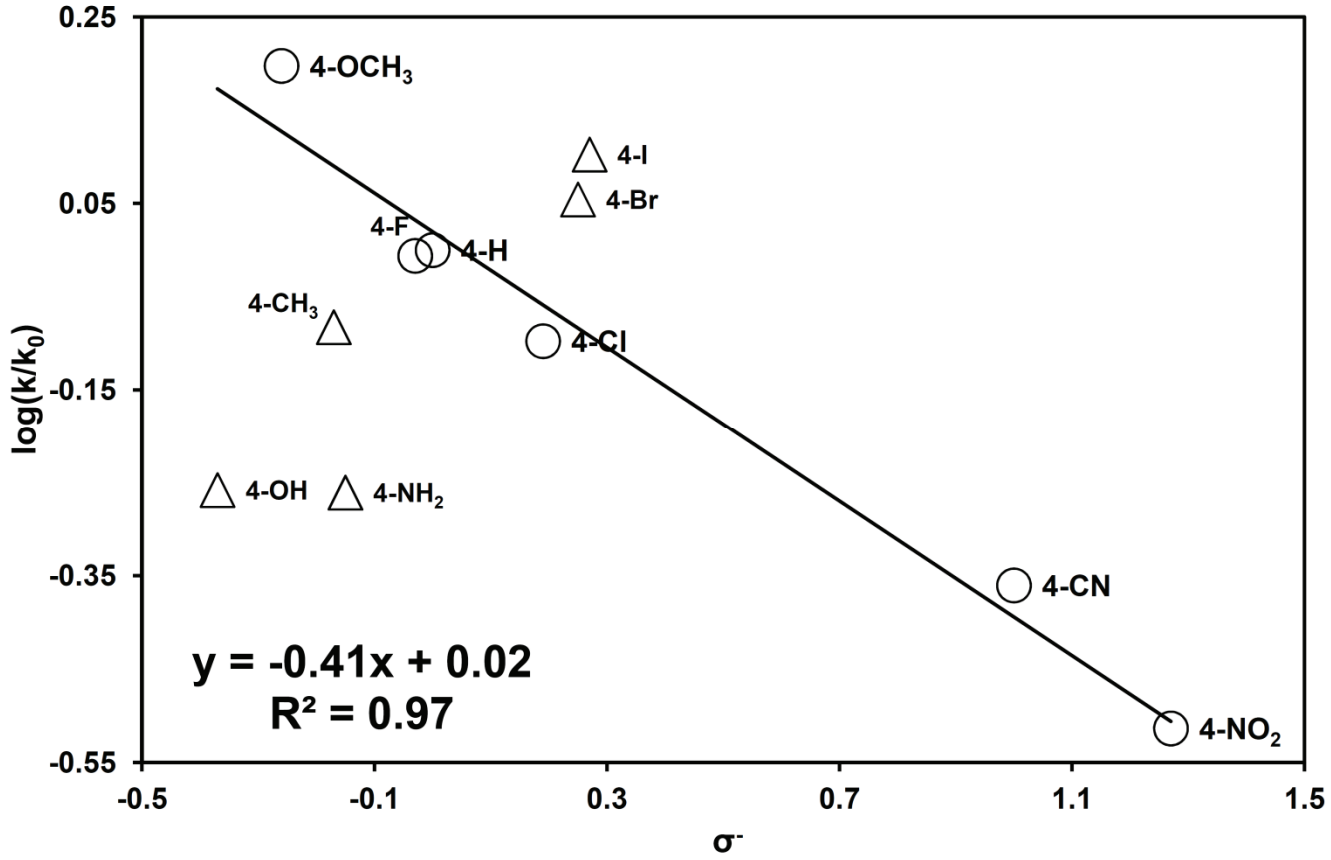

Figure S1. Rate constant for the alkylation of benzoic acids by iodomethane versus σ^- in the presence of TMGN and in DMF at 20 °C.

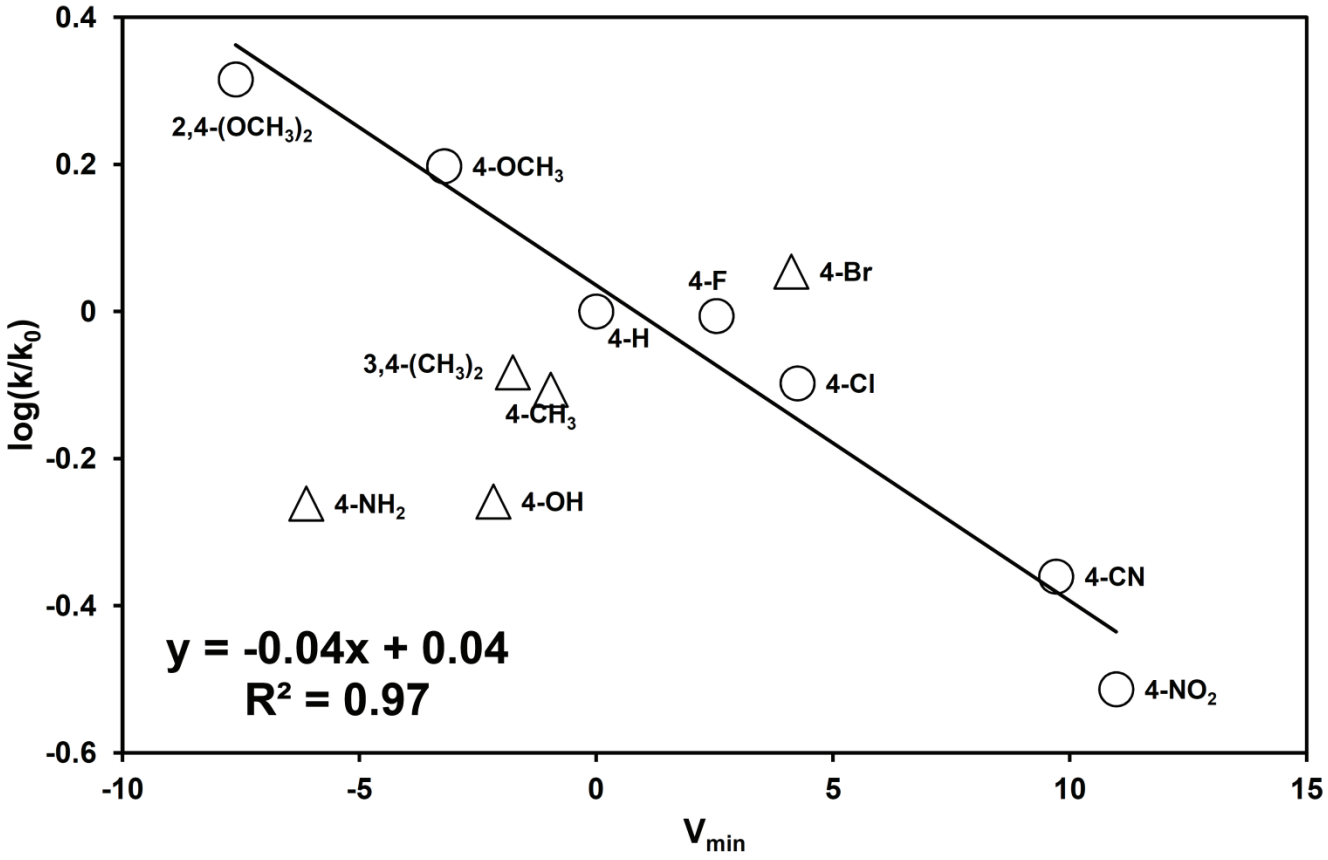

Figure S2. Rate constant for the alkylation of benzoic acids by iodomethane versus the electrostatic potential minimum, V_{min} in the presence of TMGN and in DMF at 20°C.

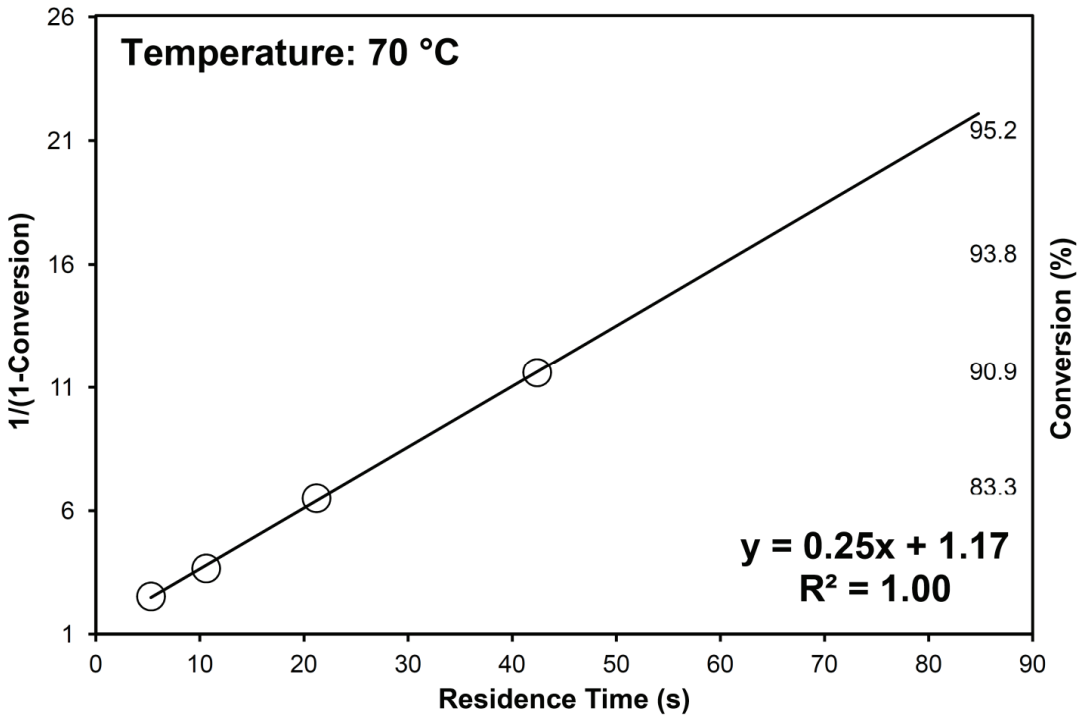

Figure S3. Second order kinetics plot of benzoic acid alkylation by iodomethane in the presence of TMGN and in DMF at 70°C.

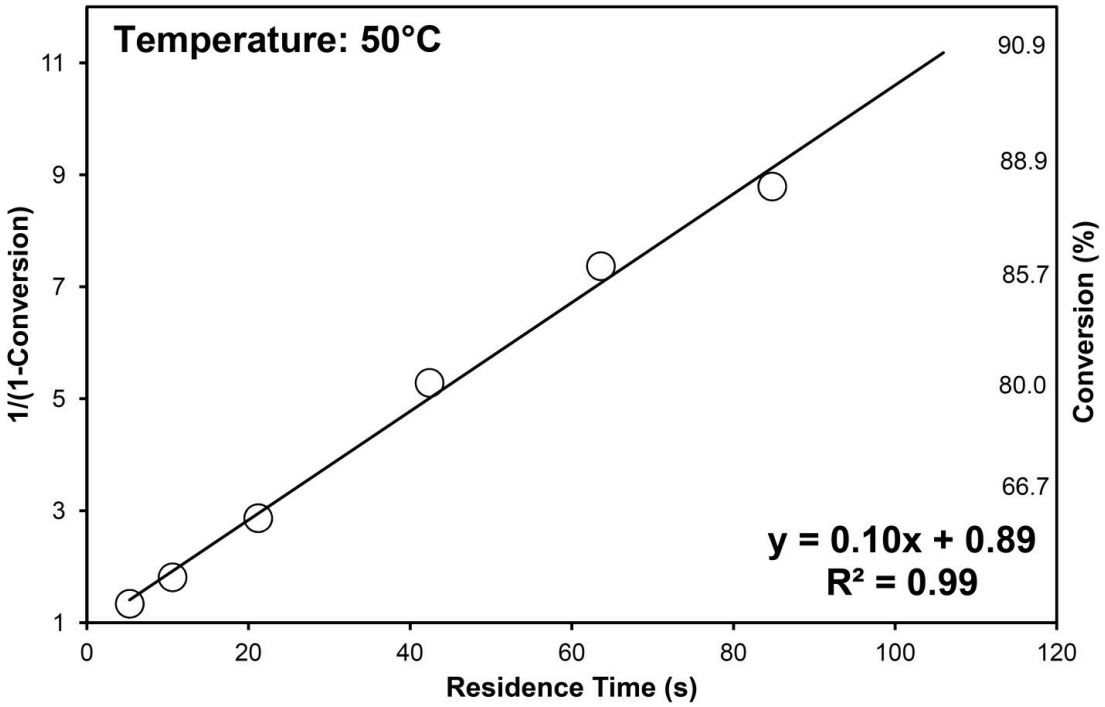

Figure S4. Second order kinetics plot of benzoic acid alkylation by iodomethane in the presence of TMGN and in DMF at 50°C.

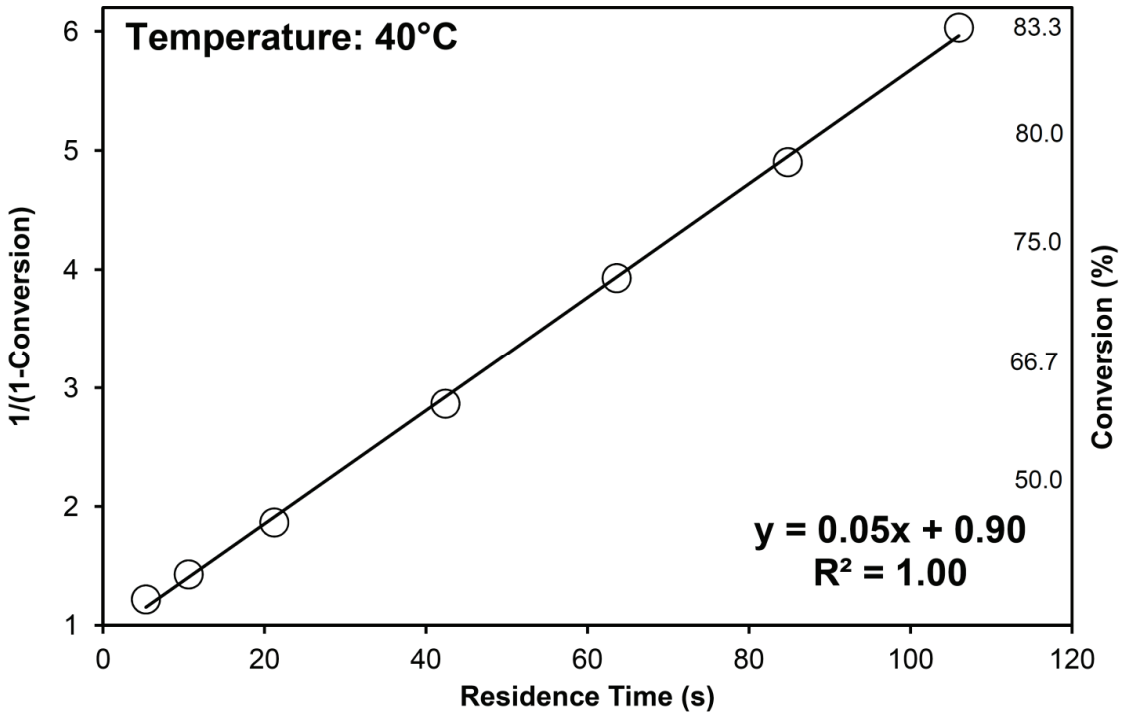

Figure S5. Second order kinetics plot of benzoic acid alkylation by iodomethane in the presence of TMGN and in DMF at 40°C.

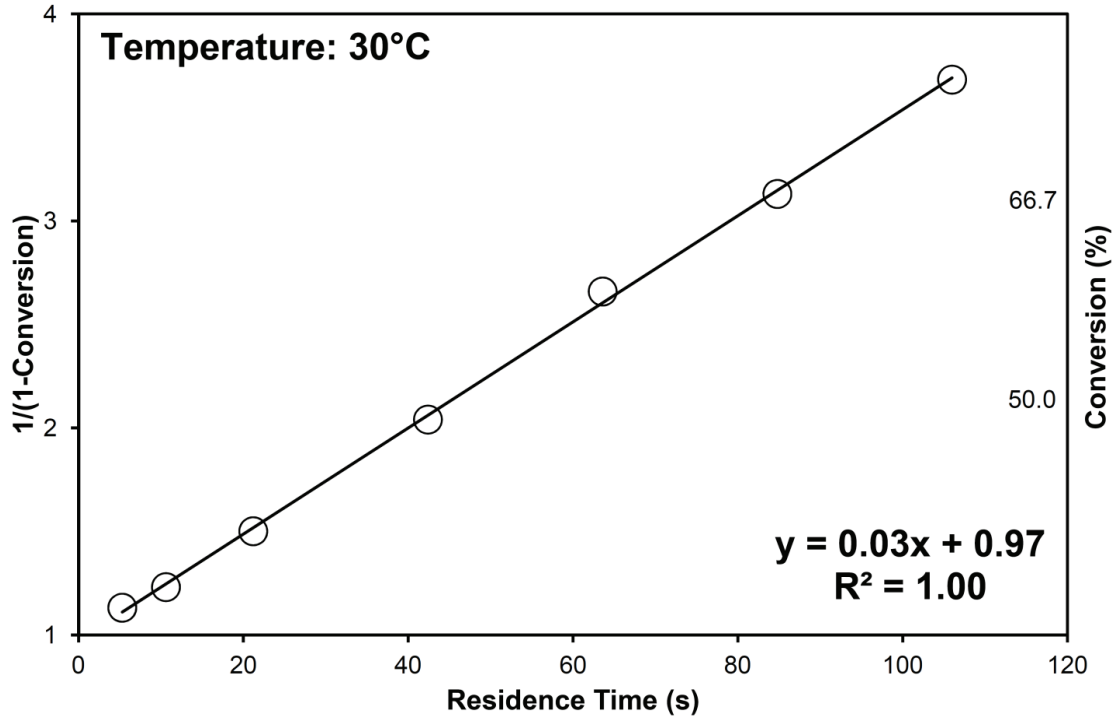

Figure S6. Second order kinetics plot of benzoic acid alkylation by iodomethane in the presence of TMGN and in DMF at 30°C.

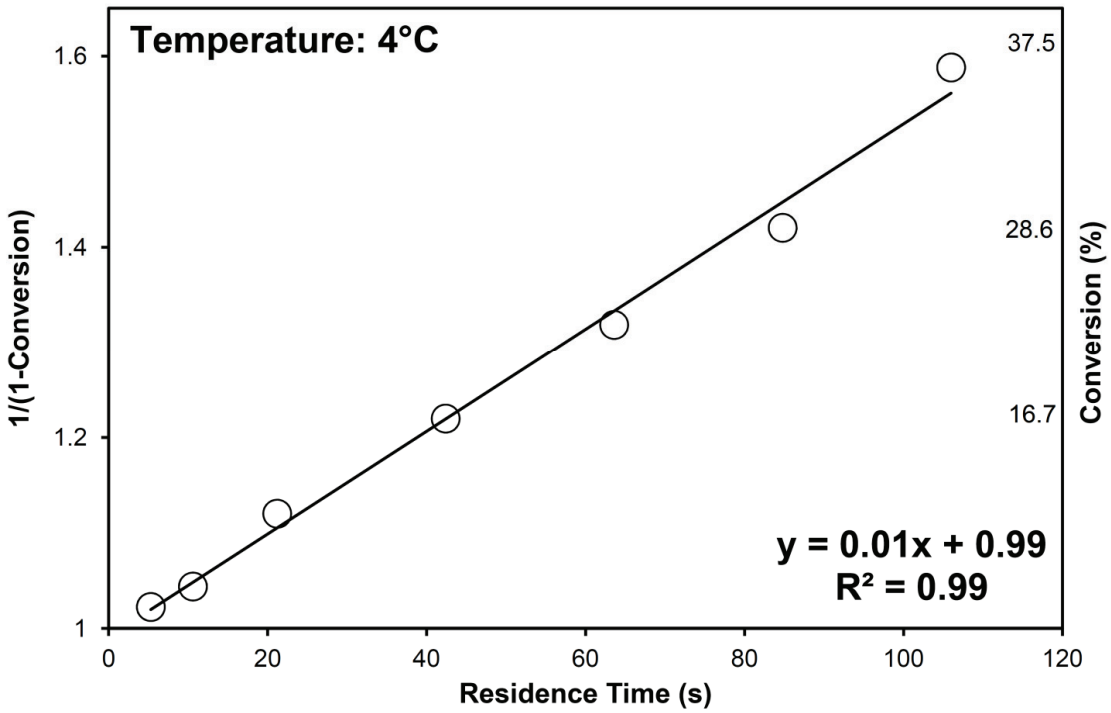

Figure S7. Second order kinetics plot of benzoic acid alkylation by iodomethane in the presence of TMGN and in DMF at 4°C.

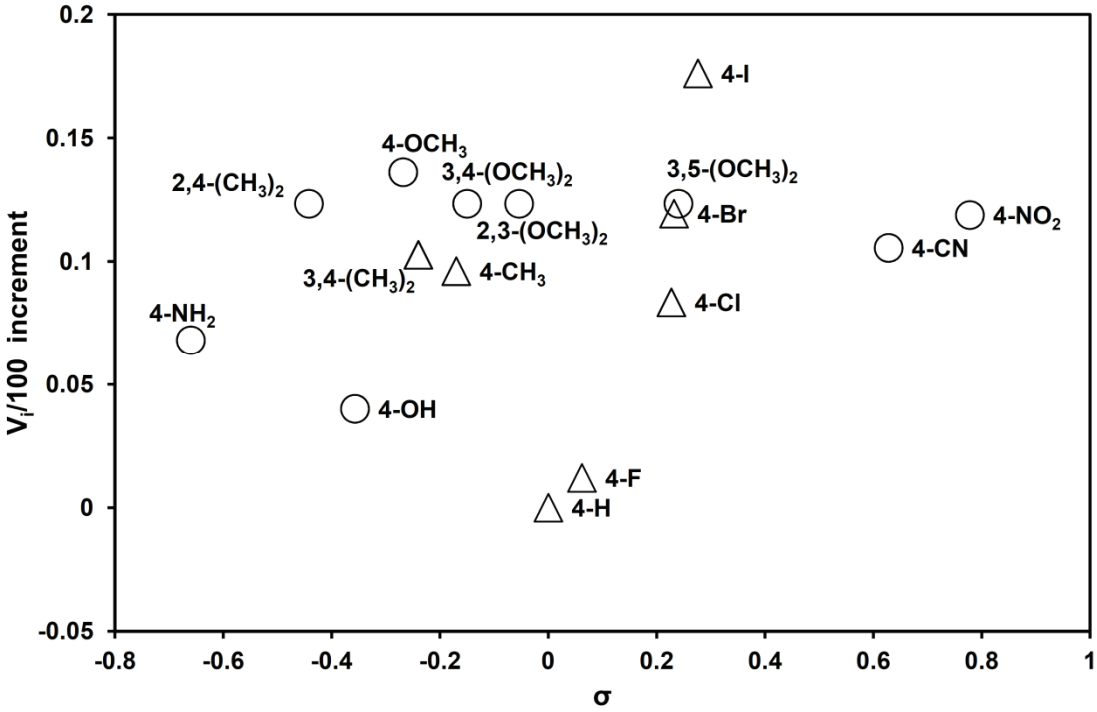

Figure S8. Kamlet-Taft V_i parameter substituent incremental value for aromatic compounds versus σ (data from Hickey et *al.*)[4]

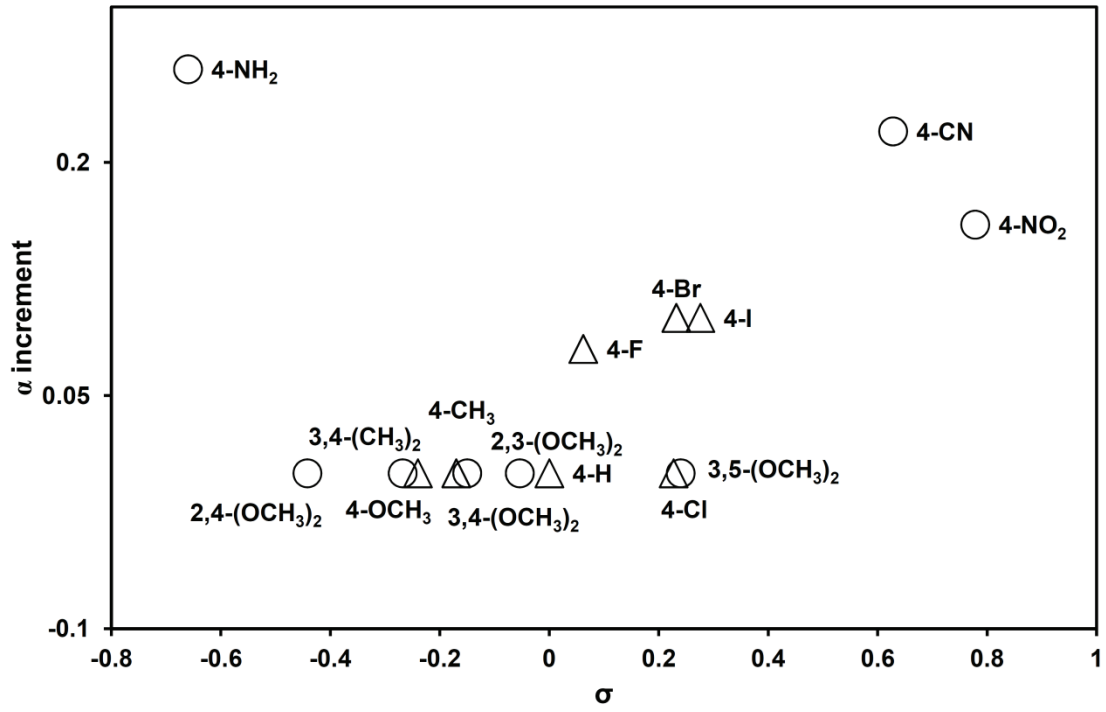

Figure S9. Kamlet-Taft α parameter substituent incremental value for aromatic compounds versus σ (data from Hickey et *al.*)[4]

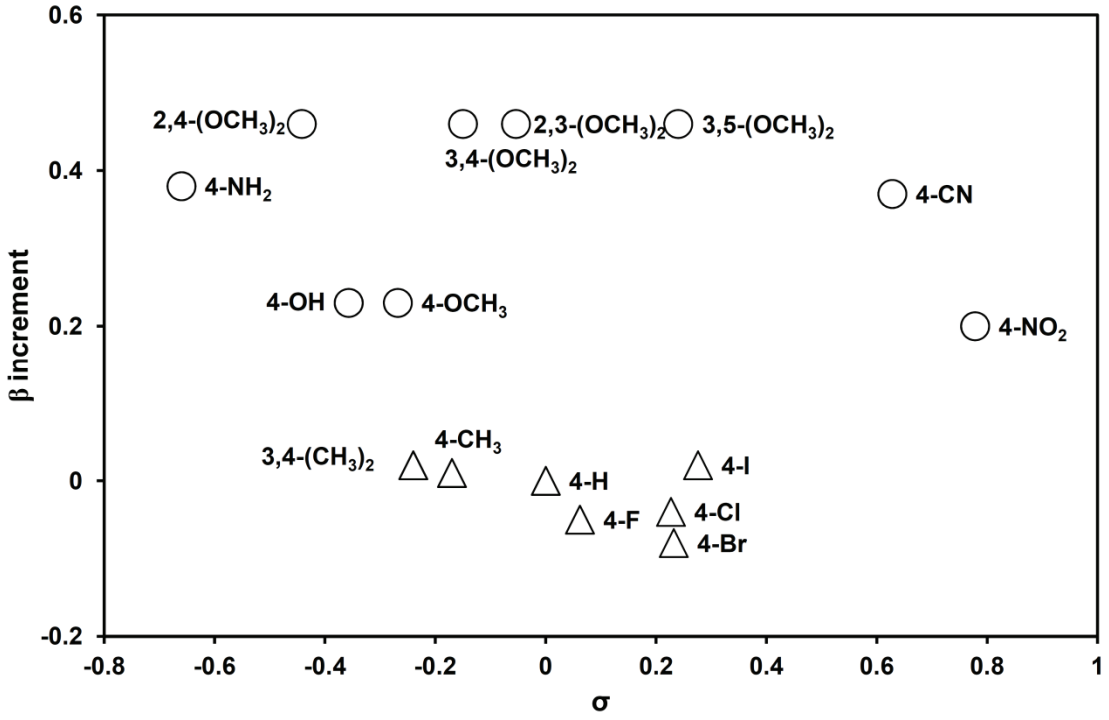

Figure S10. Kamlet-Taft β parameter[4] substituent incremental value for aromatic compounds versus σ (data from Hickey et *al.*)[4]

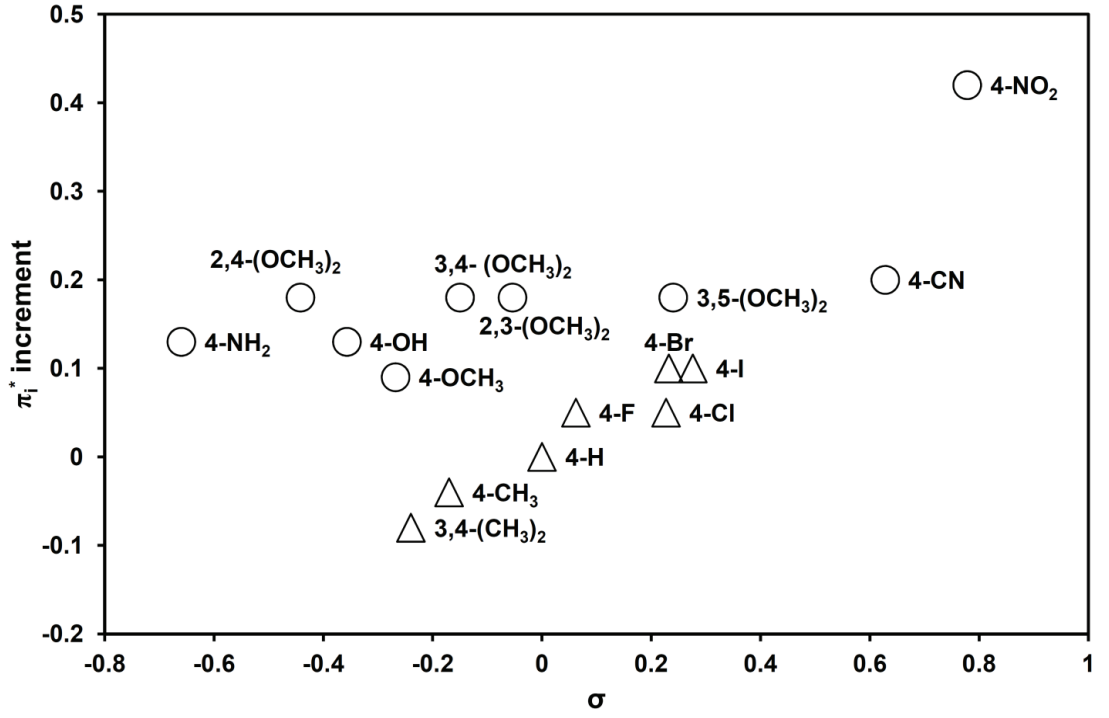

Figure S11. Kamlet-Taft π^* parameter[4] substituent incremental value for aromatic compounds versus σ (data from Hickey et *al.*)[4]

References

(1) Hansch, C.; Leo, A.; Taft, R. W., *Chem. Rev.* **1991,** *91*, 165.

(2) Hollingsworth, C. A.; Seybold, P. G.; Hadad, C. M., *Int. J. Quantum Chem.* **2002,** *90*, 1396.

(3) Sayyed, F. B.; Suresh, C. H., *New J. Chem.* **2009,** *33*, 2465.

(4) Hickey, J. P.; Passino-Reader, D. R., *Environ. Sci. Technol.* **1991,** *25*, 1753.