

Supporting Information

Simultaneous Determination of Interfacial Molarities of Amide Bonds, Carboxylate Groups, and Water by Chemical Trapping in Micelles of Amphiphiles Containing Peptide Bond Models

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Section S1. Synthesis and/or purification procedures for the preparation of arenediazonium ion, dediazonation products, amino acid amphiphiles and other related products, and their ^1H NMR spectra, respectively.

a. Synthetic routes for some of the products, 16-ArNH₂, 16-ArN₂⁺, 16-ArOH, 16-ArNHAc, 16-ArF, 16-ArBr and 16-ArInd, have been published. For detailed information, please refer to the literature cited in **Scheme 4**.

b. 1-*n*-Hexadecyl-3,5-dimethylbenzene, 16-ArH. Using a slightly modified method published by Kornblum, *et al.*,^{1,2} 200 mg of 16-ArN₂⁺ dissolved in 5.0 mL THF was added dropwise to a solution of 951 mg of hypophosphorous acid (H₃PO₂, 50% w/w) dissolved in 5.0 mL distilled water under ice bath. After 5 min the ice bath was removed the ice bath and the mixture was stirred overnight. Excess THF was evaporated and 10 mL×3 hexane (HPLC grade) aliquots were added to extract the remaining reaction mixture. The combined aliquots of hexane solution were dried by Na₂SO₄ and hexane evaporated to give a white solid. The solid was further purified by column chromatography eluted by hexanes and 86 mg (54%) of white crystals were obtained. Mw (calcd.): 330.6 g mol⁻¹. ^1H NMR (300 MHz, CDCl₃): δ ppm 0.86 (3H, t, $J=8.0$ Hz), 1.28 (26H, br s), 1.57 (2H, br), 2.24 (6H, s), 2.55 (2H, t, $J=8.0$ Hz), 6.80 (2H, s), 7.26 (1H, s, overlapped by CHCl₃ at 7.26). See ^1H NMR spectrum, **Figure S1b**.

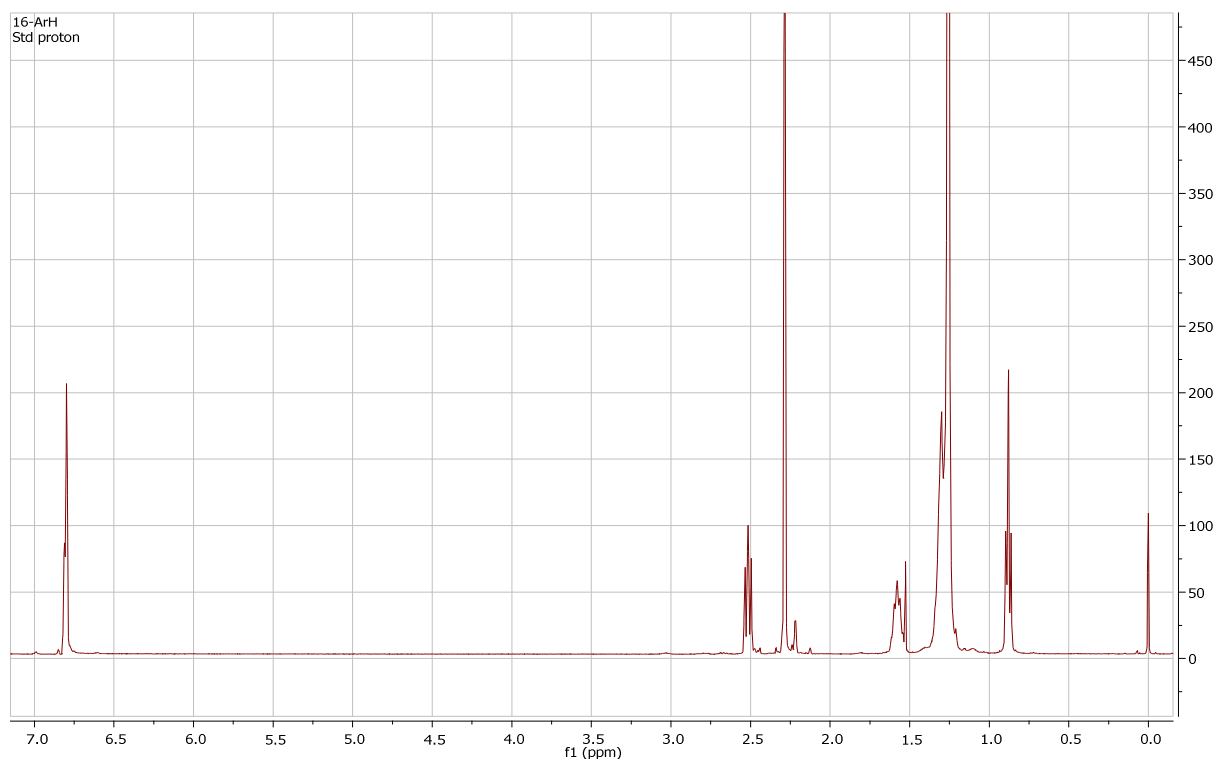


Figure S1b. ^1H -NMR Spectrum for 16-ArH.

c. 4-*n*-Hexadecyl-2,6-dimethylphenyllaurate, 16-ArEC₁₂. *N,N'*-Diisopropylcarbodiimide (DIC) (55.9 μ L, 0.357 mmol, 1.5 eq.) and then DMAP (14.5 mg, 0.5 eq.) was added to a solution of 16-ArOH (82.6 mg, 0.238 mmol) and dodecanoic acid (95.5 mg, 2 eq.) in dichloromethane (5.0 mL). The mixture was stirred at r.t. overnight. The solid product was removed by filtration and the filtrate was evaporated to give a white solid. This solid was dissolved in EtOAc, which was washed successively with saturated Na₂CO₃, NH₄Cl and NaCl solution dried over Na₂SO₄ and the EtOAc evaporated. The product was purified via column chromatography using 5% ethyl acetate/hexanes and recrystallized from methanol. 84 mg (67%) of pure compound was obtained. Mw (calcd.): 528.9 g mol⁻¹. ¹H NMR (300 MHz, CDCl₃): δ ppm 0.87 (6H, t, J=6.5 Hz), 1.36 (b, s, 42H), 1.54 (2H, m), 1.77 (2H, m), 2.11 (6H, s), 2.54 (2H, t, J=7.6 Hz), 2.58 (2H, t, J=7.6 Hz), 6.86 (s, 2H). See ¹H NMR spectrum, **Figure S1c**.

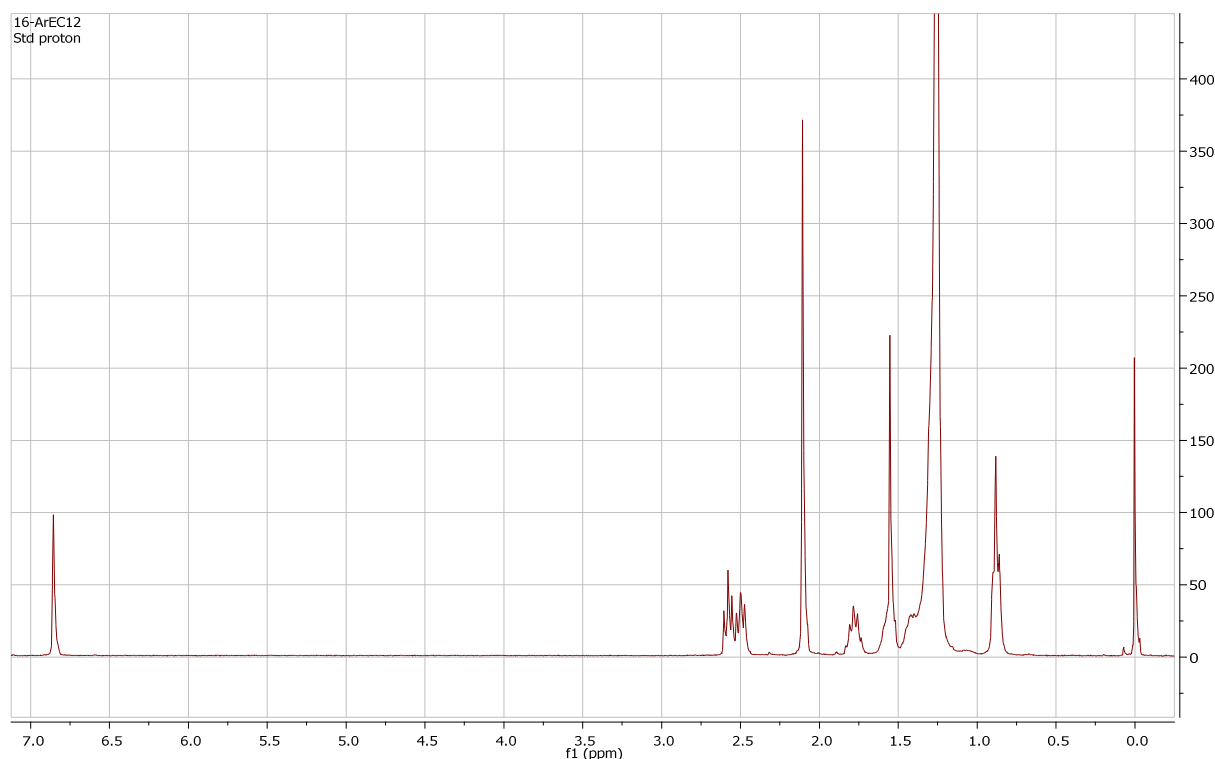


Figure S1c. ¹H-NMR Spectrum for 16-ArEC₁₂.

d. 4-*n*-Hexadecyl-2,6-dimethylphenyl-*N*-lauroylsarcosinate, 16-ArSE. DIC (67.8 μ L, 0.433 mmol) and then DMAP (17.62 mg, 0.5 eq) was added to a solution of 16-ArOH (100 mg, 0.289 mmol) and *N*-lauroylsarcosine (156 mg, 2 eq.) in dichloromethane (5.0 mL). The mixture was stirred at r.t. overnight, the precipitate filtered out and the filtrate evaporated to give a white solid. The solid was dissolved in EtOAc, which was washed successively with saturated Na₂CO₃, NH₄Cl and NaCl solution, and dried over Na₂SO₄. Evaporation of the solvent yielded 120 mg (69%) of white solid that was purified

by column chromatography using 15% ethyl acetate/hexanes, and recrystallization from methanol. Mw (calcd.): 600.0 g mol⁻¹. ¹H NMR (300 MHz, CDCl₃): δ ppm 0.88 (6H, t, J=6.5 Hz), 1.28 (b, s, 42H), 1.5-1.7 (4H, m), 2.09 (6H, s), 2.39 (2H, t, J=7.6 Hz), 2.50 (2H, t, J=7.9 Hz), 3.12 (s, 3H), 4.35 (s, 2H), 6.86 (s, 2H). See ¹H NMR spectrum, **Figure S1d**.

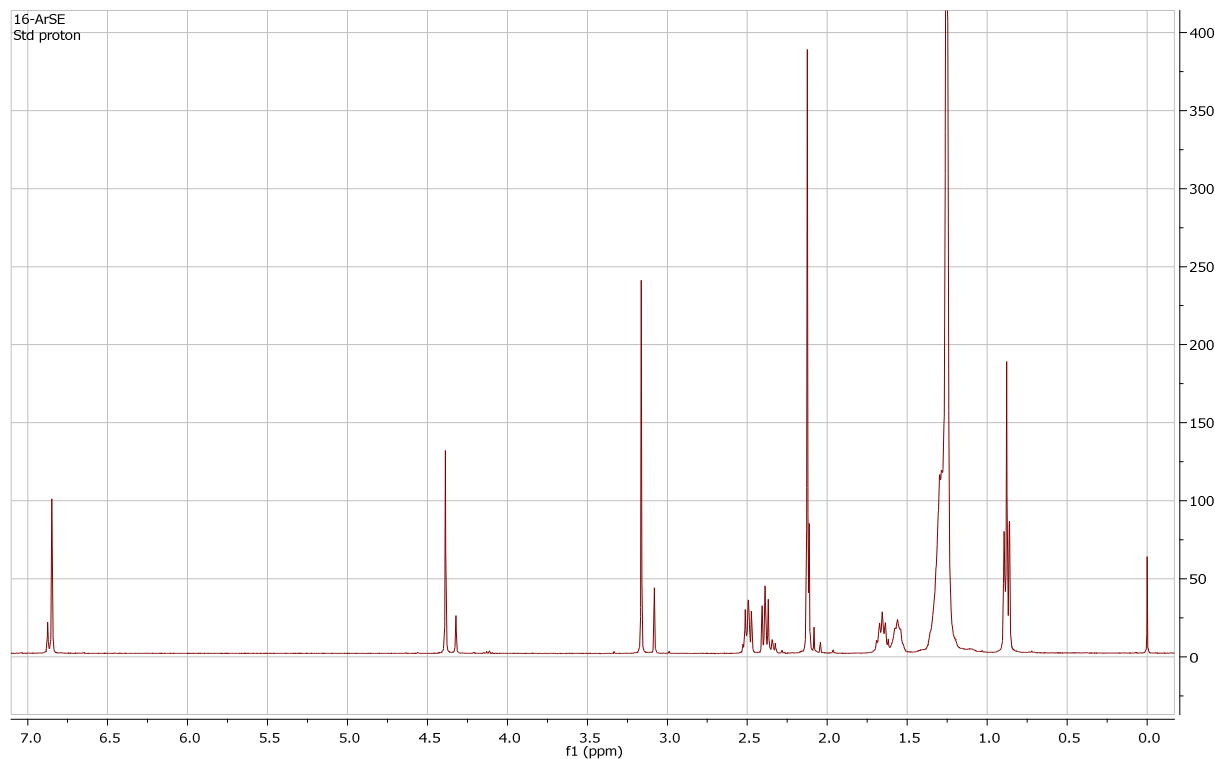


Figure S1d. ¹H-NMR Spectrum for 16-ArSE.

e. 4-*n*-Hexadecyl-2,6-dimethylphenyl-*N*-lauroylglycinate, 16-ArGE. DIC (67.8 μL, 0.433 mmol) and DMAP (17.62 mg, 0.5 eq.) were added to a solution of 16-ArOH (100 mg, 0.289 mmol) and *N*-lauroylglycine (156 mg, 2 eq.) in dichloromethane (DCM) (5.0 mL). The mixture was stirred at r.t. overnight, solid removed by filtration and the filtrate evaporated to give a white solid. The solid was dissolved in EtOAc, which was washed successively with saturated Na₂CO₃, NH₄Cl and NaCl solution, dried over Na₂SO₄ and the EtOAc evaporated. 30 mg (17%) of white solid was obtained after column chromatography using 10% ethyl acetate/hexanes. Mw (calcd.): 585.9 g mol⁻¹. ¹H NMR (300 MHz, CDCl₃): δ ppm 0.88 (6H, t, J=6.7 Hz), 1.27 (b, s, 42H), 1.56 (2H, m), 1.64 (2H, m), 2.12 (6H, s), 2.28 (2H, t, J=7.5 Hz), 2.50 (2H, t, J=8.0 Hz), 4.35 (t, 2H, J=5.1 Hz), 5.99 (1H, b), 6.87 (s, 2H). See ¹H NMR spectrum, **Figure S1e**.

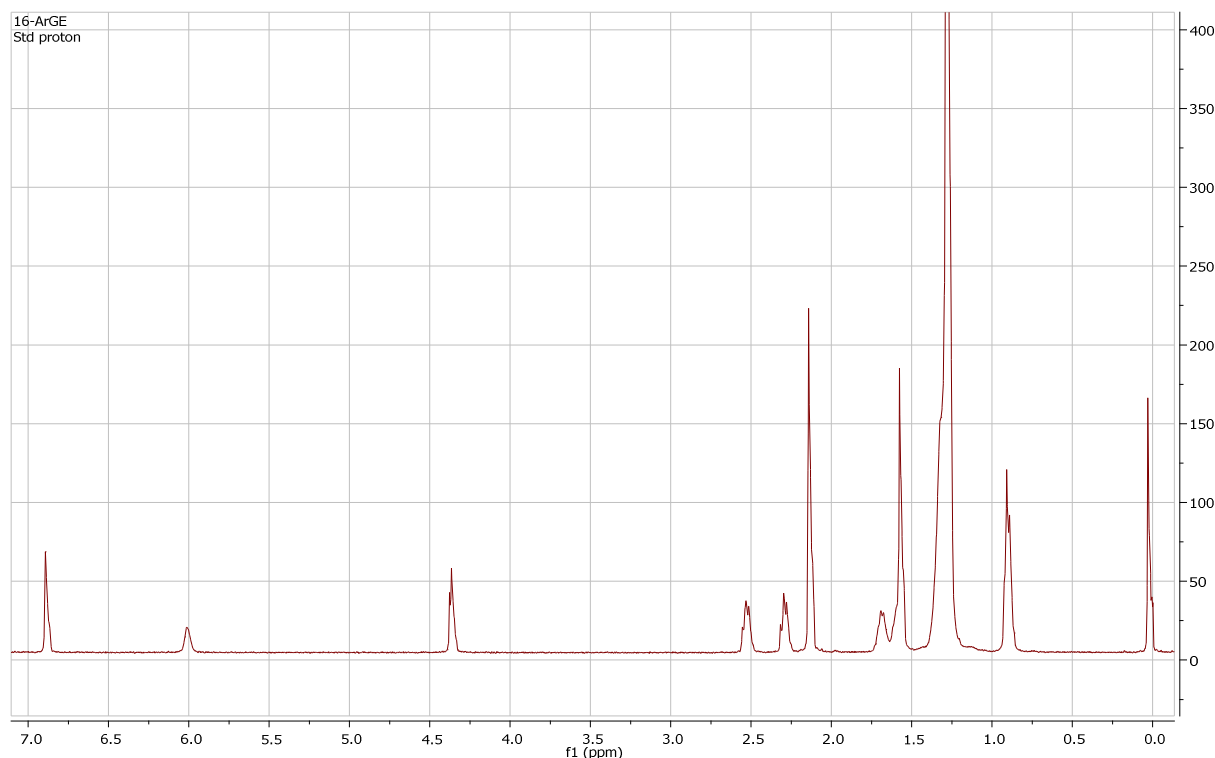


Figure S1e. ^1H -NMR Spectrum for 16-ArGE.

f. Sodium *N*-lauroylglycinate, SLG. Lauroyl chloride (5.00 mL, 21.19 mmol) was added to the suspension of methyl glycinate·HCl (2.93 g, 23.33 mmol) in DCM (70 mL). Dropwise addition of triethylamine (13.0 mL, 57.2 mmol) gave a thick suspension that was filtered after 30 min and the solid product was washed with DCM. The DCM filtrate was washed with 1.0 M HCl (30 mL) and brine, dried, and concentrated to afford a white solid. The solid was dissolved in DCM and precipitated with hexane, filtered and dried to give white lauroyl glycinate (LG-ester) (2.54 g, 44.2%). NaOH, (1 M, 18 mL) was mixed with a solution of LG-ester (2.51 g, 9.24 mmol) in ethanol (90 mL) and stirred at room temp overnight. The ethanol was removed by evaporation and the remaining solution was acidified with aqueous 1.0 M HCl to give white precipitate that was filtered, washed with water, and air dried. Recrystallization from MeCN gave white *N*-lauroyl glycinic acid (LG-acid) (2.1 g, 88.3%). A suspension of LG-acid (1.007 g, 3.91 mmol) in water (10 mL) was titrated with 1.0 M NaOH aqueous solution (3.91 mL) to form a clear solution. The solution was freeze-dried to afford a white solid. Recrystallization of the solid with MeOH gave white SLG (0.85 g, 76.7%). Mw (calcd.): 279.4 g mol⁻¹. ^1H NMR (D₂O): δ ppm 0.73 (3H, t, J=7.0 Hz), 1.15 (16H, bs), 1.46 (2H, m), 2.17 (2H, t, J=7.7 Hz), 3.62 (2H, s). The signal for the proton on NH was not observed. See **Figure S1f**.

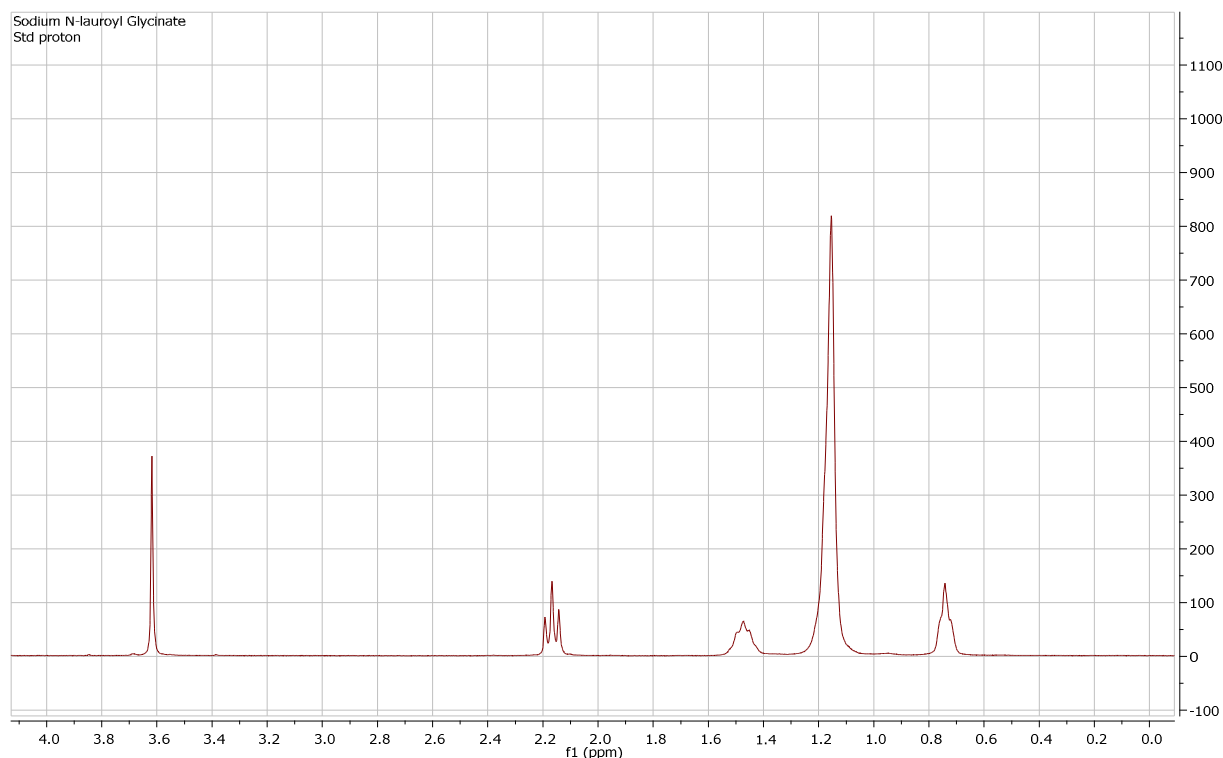


Figure S1f. ^1H -NMR spectrum for sodium *N*-lauroyl glycinate.

g. Purification of SLS, its ^1H -NMR and its cmc determination in buffer. Sodium *N*-lauroylsarcosinate (Aldrich) was dissolved in HPLC grade hot MeOH. Undissolved solid was removed by filtration on a Büchner funnel, the filtrate cooled to room temperature, and then placed into an ice bath for 15 minutes. The white crystals were collected on a Büchner funnel, washed with small amounts of cold Et₂O and dried under oven. This process was repeated three times. ^1H NMR spectrum, **Figure S1g-1**. ^1H NMR (D₂O): δ ppm 0.70 (3H, t, $J=7.0$ Hz), 1.16 (16H, bs), 1.45 (2H, m), 2.14 and 2.29 (2 sets, 2H, t, $J=7.7$ Hz), 2.77 and 2.93 (2 sets, 2H, s), 3.80 (2 sets, overlapped, 2H, s). Note that the spectrum is free of extraneous signals, including the signal for sodium laurate, **Figure S1g-2**, at $\delta = 2.05$ ppm.

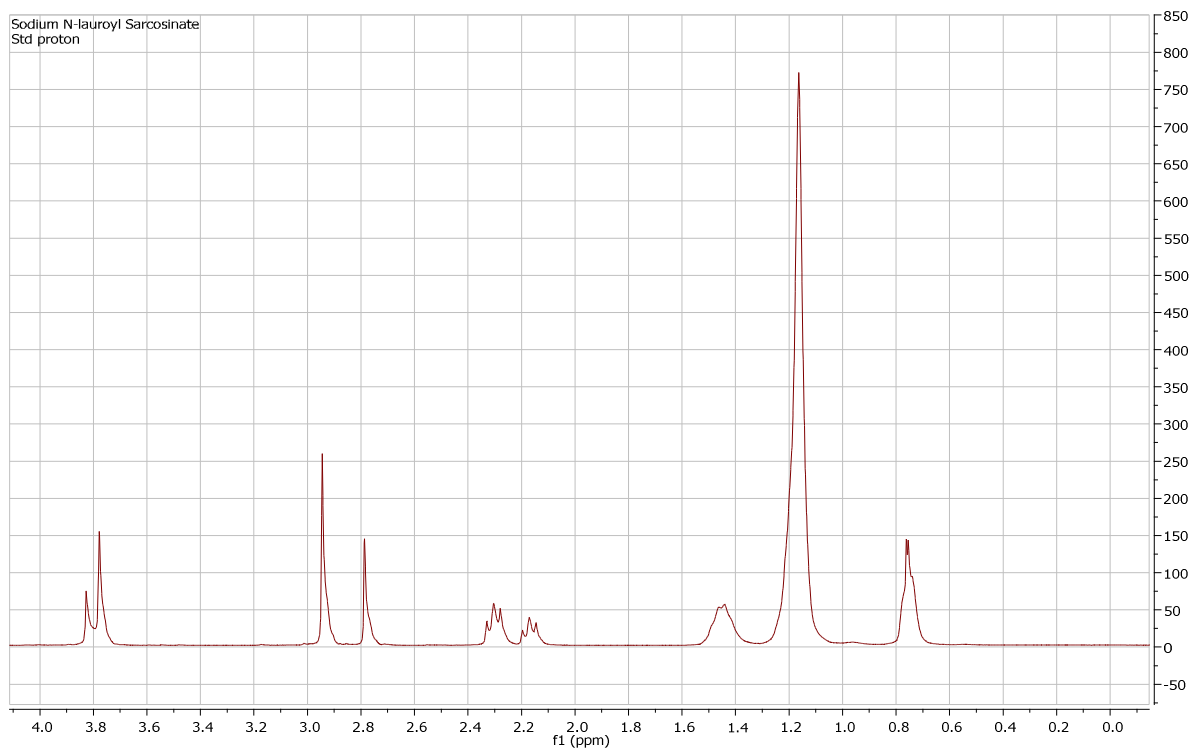


Figure S1g-1. ^1H -NMR spectrum for sodium *N*-lauroyl sarcosinate.

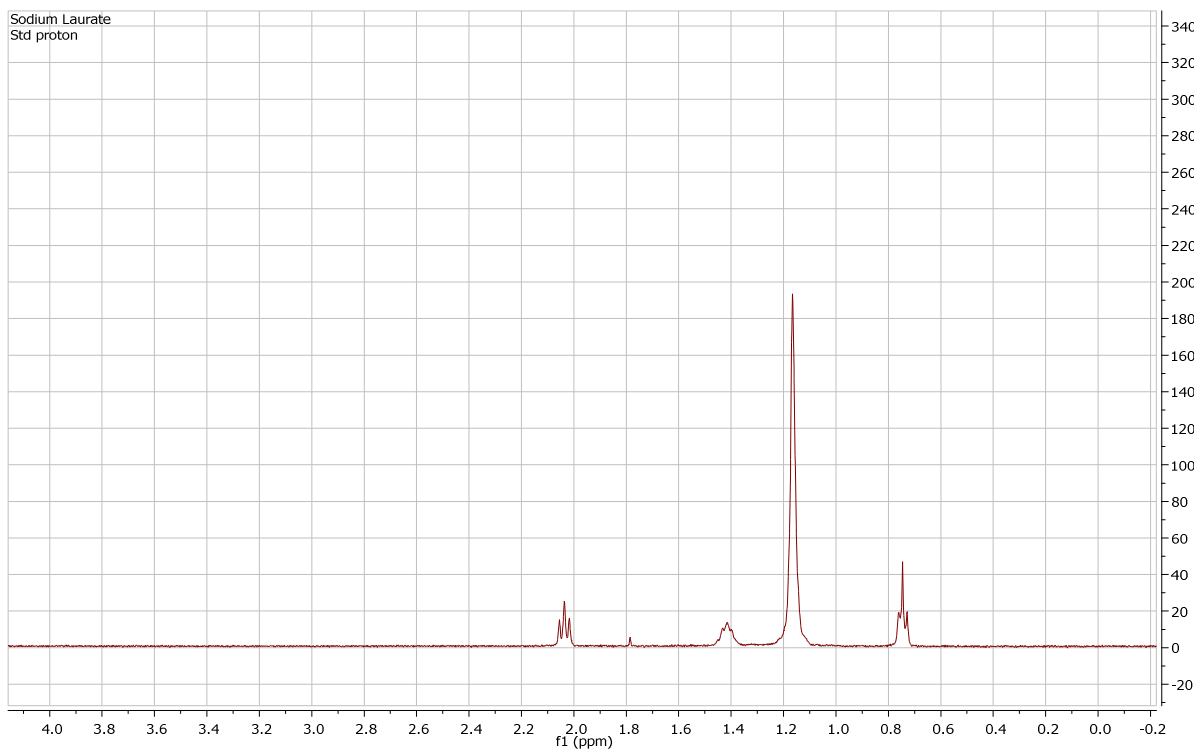


Figure S1g-2. ^1H -NMR spectrum for sodium laurate.

Section S2. Calibration curves for reaction products.

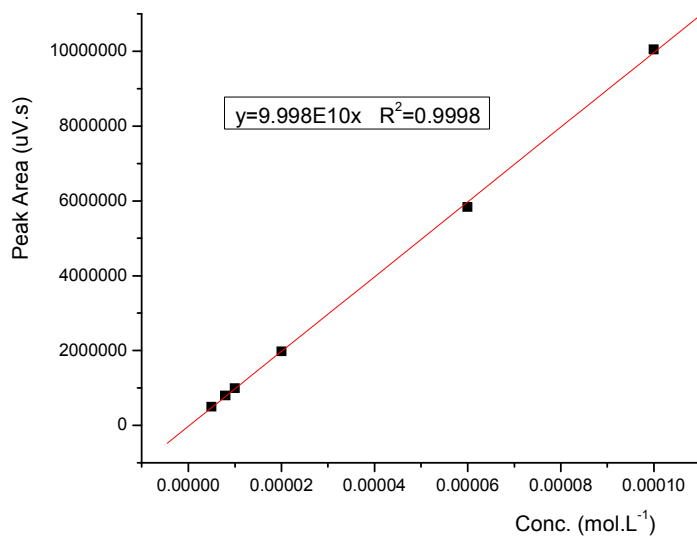


Figure S2a. Calibration curve for 16-ArOH.

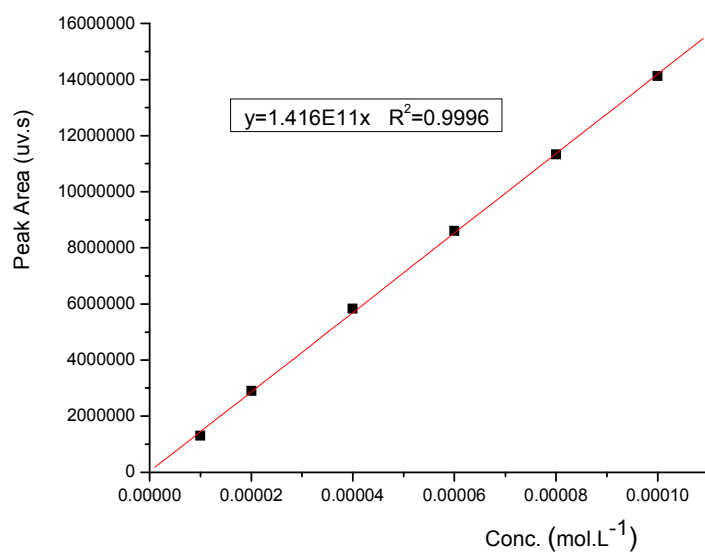


Figure S2b. Calibration curve for 16-ArNHAc.

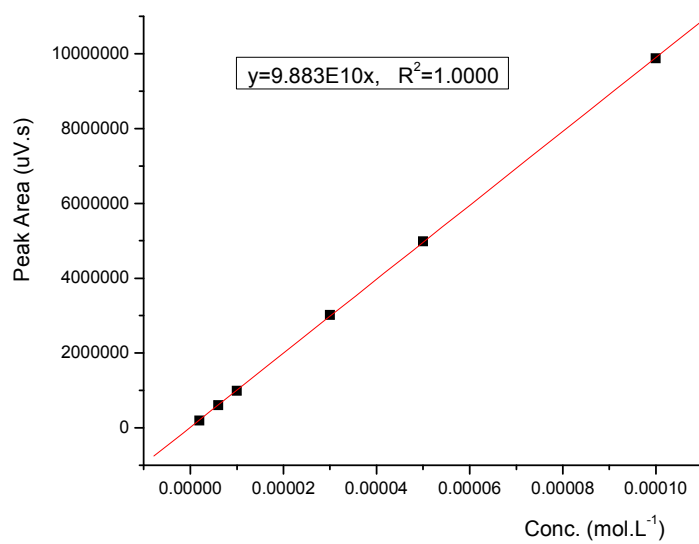


Figure S2c. Calibration curve for 16-ArH.

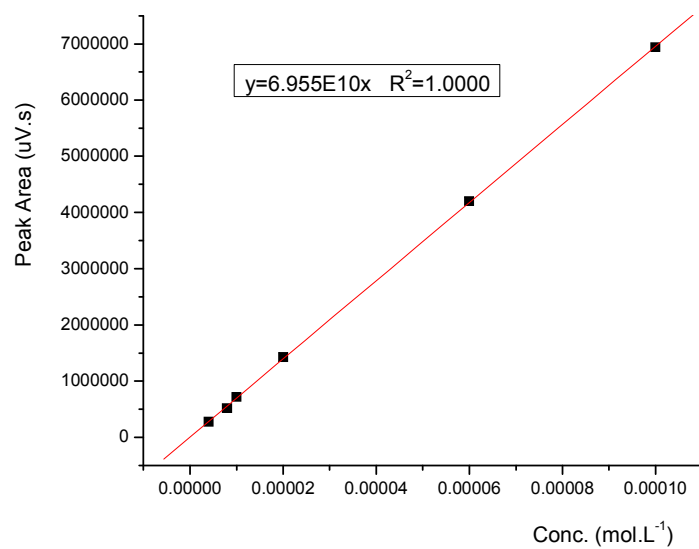


Figure S2d. Calibration curve for 16-ArF.

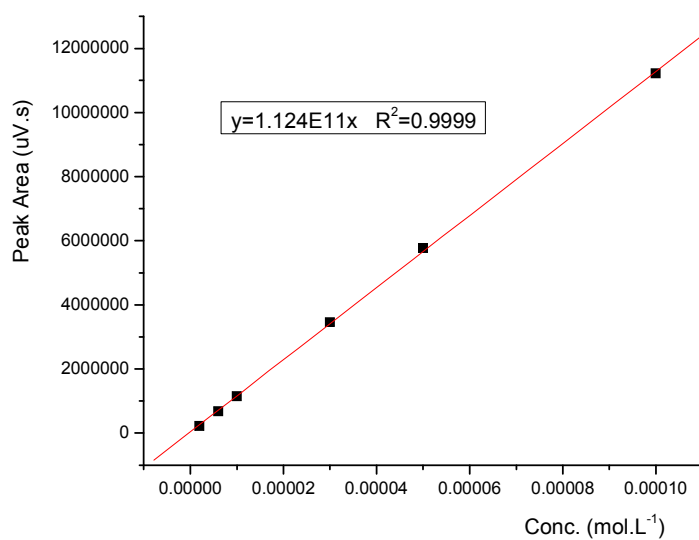


Figure S2e. Calibration curve for 16-ArSE.

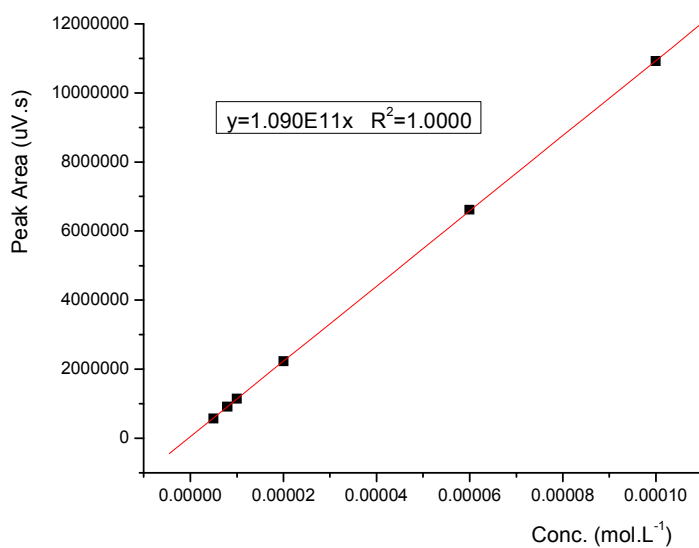


Figure S2f. Calibration curve for 16-ArGE.

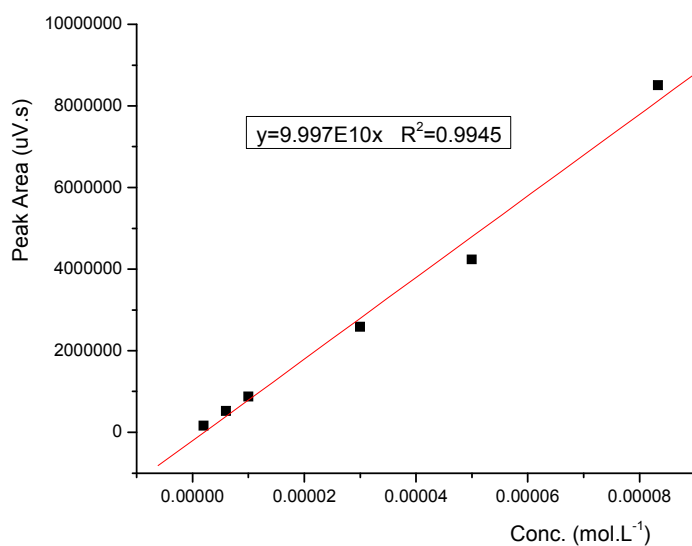


Figure S2g. Calibration curve for 16-ArEC₁₂.

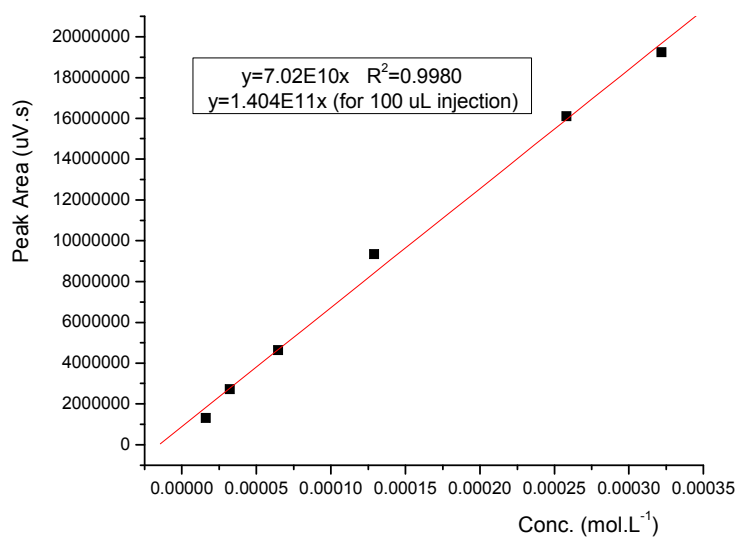


Figure S2h. Calibration curve for 16-ArInd.

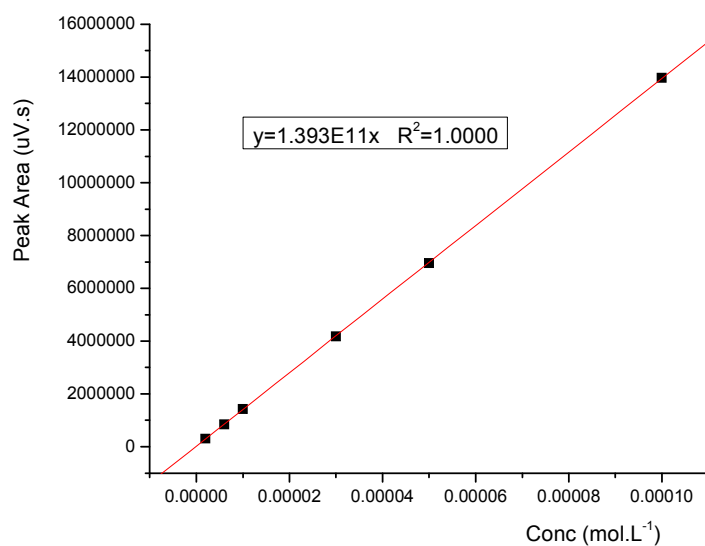


Figure S2i. Calibration curve for 16-ArBr.

Table S2a. Equations used to fit HPLC calibration curves for dediazonation products.^a

Reaction Product	Calibration Equation ^b	R ²
16-ArOH	$y=9.998 \times 10^{10}x$	0.9998
16-ArNHAc	$y=1.416 \times 10^{11}x$	1.0000
16-ArH	$y=9.883 \times 10^{10}x$	1.0000
16-ArF	$y=6.955 \times 10^{10}x$	1.0000
16-ArSE	$y=1.124 \times 10^{11}x$	0.9999
16-ArGE	$y=1.090 \times 10^{11}x$	1.0000
16-ArEC ₁₂	$y=9.997 \times 10^{10}x$	0.9945
16-ArInd	$y=1.404 \times 10^{11}x$	0.9980
16-ArBr	$y=1.393 \times 10^{11}x$	1.0000

a.HPLC Eluting solvent: *i*-PrOH/MeOH, 36%/64% (v/v), or 45%/55% (v/v). Flow rate: 0.40 mL/min. b.Units: **y**-peak area (μV.s), **x**-concentration (molarity), and **R²** (correlation coefficient). The **y** intercept values are very small and not used in the calculations.

Section S3. Sample HPLC chromatograms and HPLC peak areas, observed and normalized yields of chemical trapping with CTAB, SLS and SLG, and the retention times for each product from chemical trapping experiments with SLS and SLG.

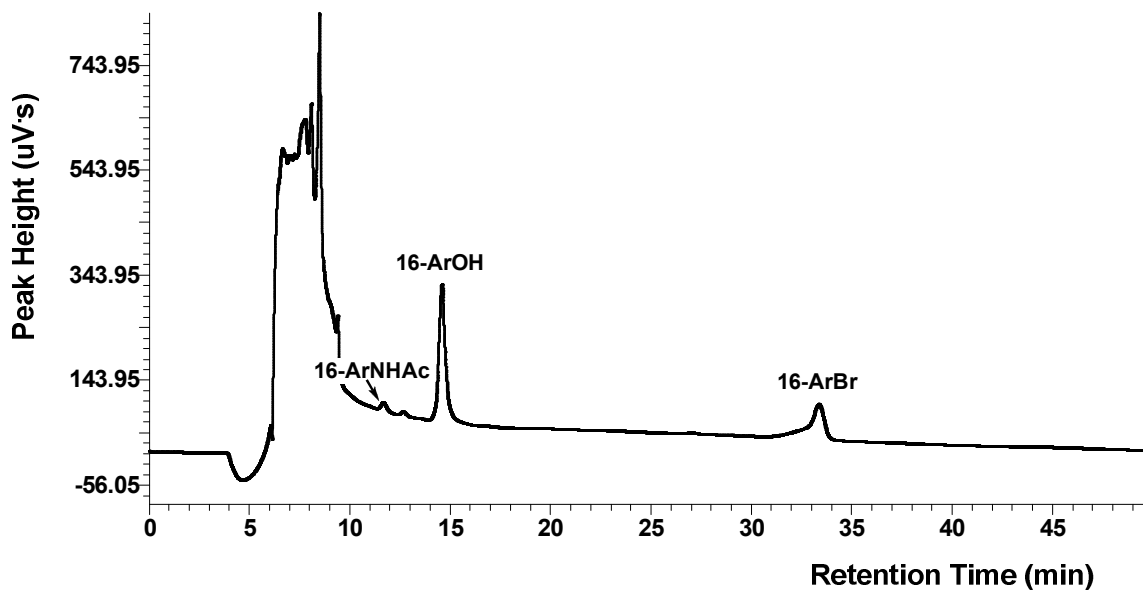


Figure S3a. HPLC chromatogram for dediazonation of 1×10^{-4} M 16-ArN_2^+ in 0.197 M CTAB aqueous solution.

Table S3a. HPLC Peak Areas and Observed and Normalized Yields for the Reaction of 16-ArN_2^+ (1×10^{-4} M) with 0.197 M CTAB micelles in Water at $40 \pm 0.1^\circ\text{C}$ with a Reaction Time of about 6 hours.

Reaction Product	10^5 Peak Area ($\mu\text{V}\cdot\text{s}$)	Observed Yields ^a (%)	Normalized Yields ^b (%)
16-ArNHAc	2.93	2.00	2.04
16-ArOH	66.64	66.70	68.13
16-ArBr	40.63	29.20	29.83
Total		97.90	100

a. Calibration curves for these products are in **Table 1**.

b. Normalized Yield: $\%16\text{-ArX}^b = (\%16\text{-ArX}^a / \text{Total Observed Yield}) \times 100\%$ (X = NH_4Ac , OH, Br).

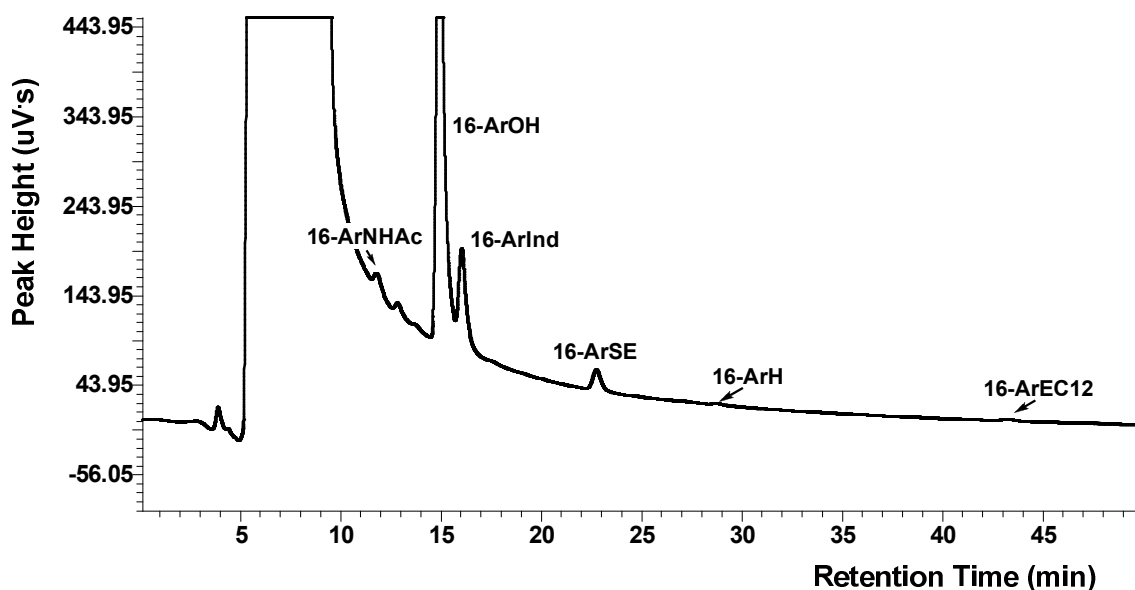


Figure S3b. HPLC chromatogram for dediazotization of 2×10^{-4} M 16-ArN_2^+ in 0.098 M SLS aqueous solution.

Table S3b-1. HPLC Peak Areas and Observed and Normalized Yields for the Reaction of 2×10^{-4} M 16-ArN_2^+ in 0.098 M SLS Aqueous Solution at $40 \pm 0.1^\circ\text{C}$ with a Reaction Time of 12 hours.

Reaction Product	10^4 Peak Area ($\mu\text{V}\cdot\text{s}$)	Observed Yields ^a (%)	Normalized Yields ^b (%)
16-ArNHAc	115.89	3.97	4.19
16-ArOH	1508.19	75.40	79.64
16-ArInd	358.47	12.77	13.49
16-ArSE	48.37	2.15	2.27
16-ArH	3.44	0.17	0.18
16-ArEC ₁₂	4.32	0.22	0.23
Total		94.68	100

a. Calibration curves are in **Table 1**.

b. Normalized Yields: $\%16\text{-ArX}^b = (\%16\text{-ArX}^a / \text{Total Observed Yield}) \times 100\%$ (X = NH₄Ac, OH, Ind, SE, H, EC₁₂).

Table S3b-2. HPLC Peak Areas and Observed and Normalized Yields for the Reaction of 2×10^{-4} M 16-ArN₂⁺ with 0.069 M SLS Aqueous Solution at $40 \pm 0.1^\circ\text{C}$ with a Reaction Time of 12 hours.

Reaction Product	10^4 Peak Area ($\mu\text{V}\cdot\text{s}$)	Observed Yields ^a (%)	Normalized Yields ^b (%)
16-ArNHAc	89.79	3.07	3.28
16-ArOH	1560.77	78.05	83.29
16-ArInd	270.49	9.64	10.29
16-ArSE	57.06	2.54	2.71
16-ArH	4.13	0.21	0.22
16-ArEC ₁₂	3.99	0.20	0.21
Total		93.71	100

a. Calibration curves are in **Table 1**.

b. Normalized Yield: $\%16\text{-ArX}^b = (\%16\text{-ArX}^a / \text{Total Observed Yield}) \times 100\%$ (X = NH₄Ac, OH, Ind, SE, H, EC₁₂).

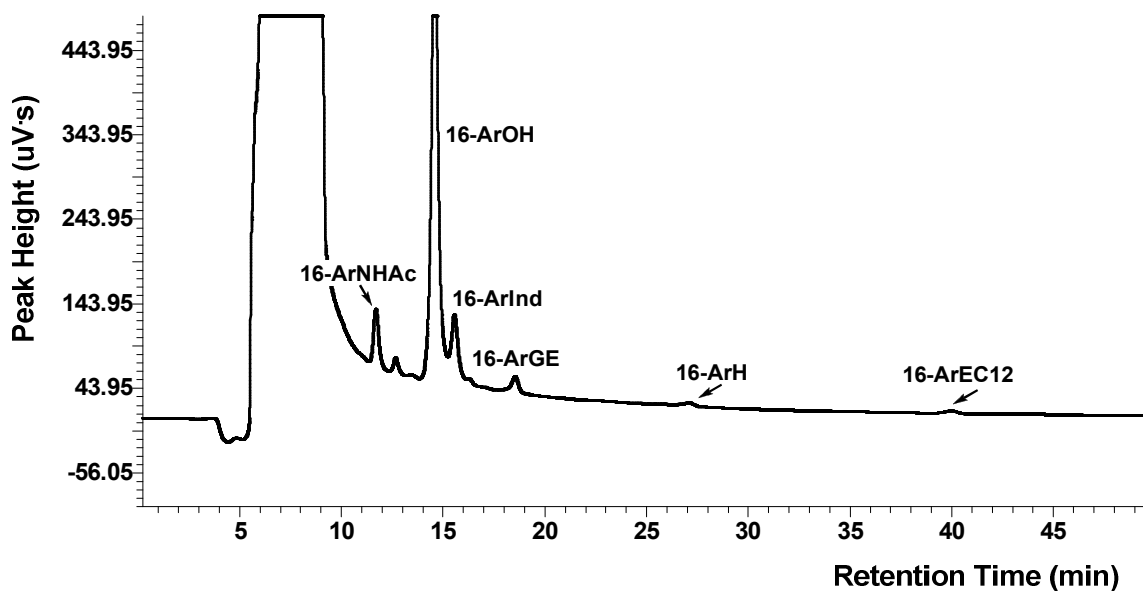


Figure S3c. HPLC chromatogram for dediazonation of 2×10^{-4} M 16-ArN₂⁺ in 0.098 M SLG aqueous solution.

Table S3c-1. HPLC Peak Areas and Observed and Normalized Yields for the Reaction of 2×10^{-4} M 16-ArN₂⁺ with 0.098 M SLG Aqueous Solution at $40 \pm 0.1^\circ\text{C}$ with a Reaction Time of 12 hours.

Reaction Product	10 ⁴ Peak Area ($\mu\text{V}\cdot\text{s}$)	Observed Yields ^a (%)	Normalized Yields ^b (%)
16-ArNHAc	128.79	4.41	4.88
16-ArOH	1498.70	74.95	82.85
16-ArInd	216.41	7.71	8.52
16-ArGE	49.66	2.28	2.52
16-ArH	6.21	0.31	0.34
16-ArEC ₁₂	15.93	0.80	0.88
Total		90.46	100

a. Calibration curves are in **Table 1**.

b. Normalized Yield: $\%16\text{-ArX}^b = (\%16\text{-ArX}^a / \text{Total Observed Yield}) \times 100\%$ (X = NH₄Ac, OH, Ind, GE, H, EC₁₂).

Table S3c-2. HPLC Peak Areas and Observed and Normalized Yields for the Reaction of 2×10^{-4} M 16-ArN₂⁺ with 0.069 M SLG Aqueous Solution at $40 \pm 0.1^\circ\text{C}$ with a Reaction Time of 12 hours.

Reaction Product	10 ⁴ Peak Area ($\mu\text{V}\cdot\text{s}$)	Observed Yields ^a (%)	Normalized Yields ^b (%)
16-ArNHAc	101.20	3.46	3.76
16-ArOH	1599.06	80.00	86.96
16-ArInd	135.53	4.83	5.25
16-ArGE	51.62	2.37	2.58
16-ArH	12.58	0.64	0.70
16-ArEC ₁₂	13.71	0.69	0.75
Total		92.00	100

a. Calibration curves are in **Table 1**.

b. Normalized Yield: $\%16\text{-ArX}^b = (\%16\text{-ArX}^a / \text{Total Observed Yield}) \times 100\%$ (X = NH₄Ac, OH, Ind, GE, H, EC₁₂).

Table S3d. The retention time ranges for each product from chemical trapping experiments with SLS and SLG.^a

Reaction Product	Retention Time ^b (min)
16-ArNHAc	12-13
16-ArOH	14-15
16-ArInd	15-16
16-ArGE	18-19
16-ArSE	21-22
16-ArH	26-27
16-ArEC₁₂	39-43

a. HPLC chromatograms of 100 μ L of samples were obtained in triplicate at $\lambda = 220$ nm, eluent 36%/64% v/v, *i*-PrOH/MeOH, flow rate: 0.40 mL/min.

b. Retention times obtained from chemical trapping results.

Section S4. Analysis of dediazonation kinetic data.

Figures S4a and **S4b** below show the absorbance versus time plots for the dediazonation of 16-ArN₂⁺ in SLS and SLG micelles at 40°C. The interfacial concentrations of the nucleophiles, H₂O, amide oxygen and carboxylate oxygen, etc., are in large excess, i.e. 16-ArN₂⁺ is the limiting reagent. Therefore, the reaction should be in the pseudo-first order and the rate of the reaction should only depend on the concentration of 16-ArN₂⁺. Values of k_{obs} were obtained by plotting the change in absorbance versus time, **Figures S4c-S4f**, using the integrated first order rate law, **Equation S4a**,^{3,4} where A_t is the absorbance at any time t , A_{∞} is the absorbance at infinite time, here ≥ 10 half-lives. The absorbance of 16-ArN₂⁺, A , at any time, t , is expressed as the difference in absorbance at time t (A_t), and B is the constant of integration.

$$-\ln (A_t - A_{\infty}) = k_{\text{obs}}t - B \quad (\text{S4a})$$

The half-life of the reaction was calculated from:

$$t_{1/2} = \frac{\ln 2}{k_{obs}} \quad (\text{S4b})$$

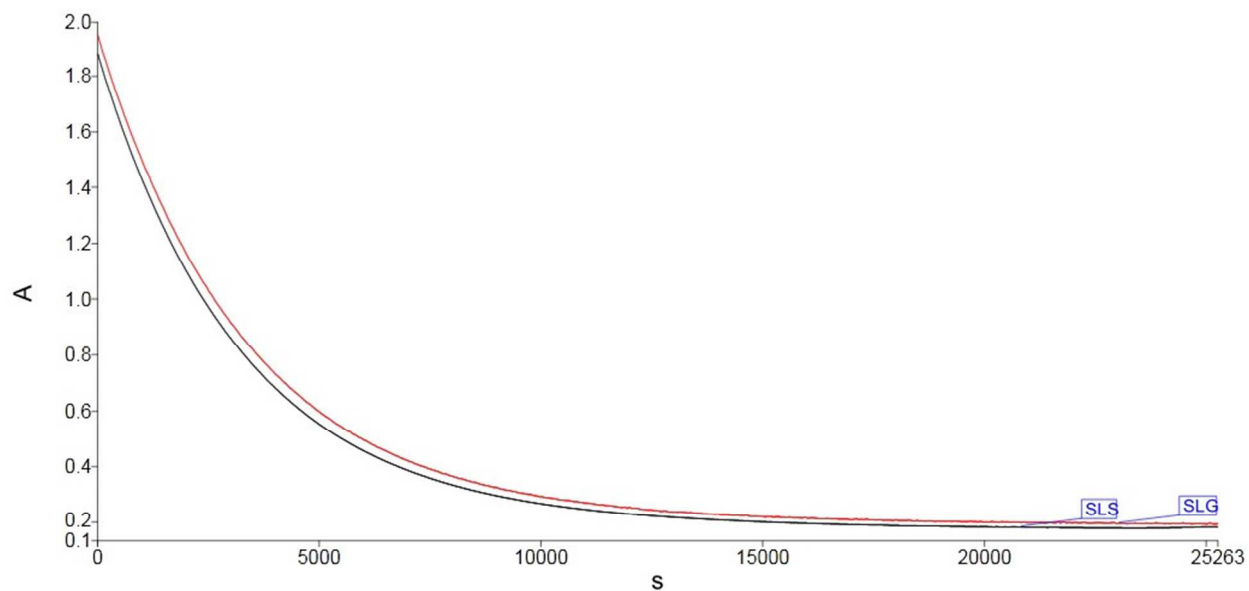


Figure S4a. Decrease in absorbance for dediazonation of 2×10^{-4} M 16-ArN₂⁺ in 0.098 M SLS (black line) and SLG (red line) micelles at 285.5 nm at 40°C and over 7 hours ($\geq 10 t_{1/2}$). Note: the x-axis label, S, stands for time (s) in seconds and the y-axis label, A, stands for absorbance.

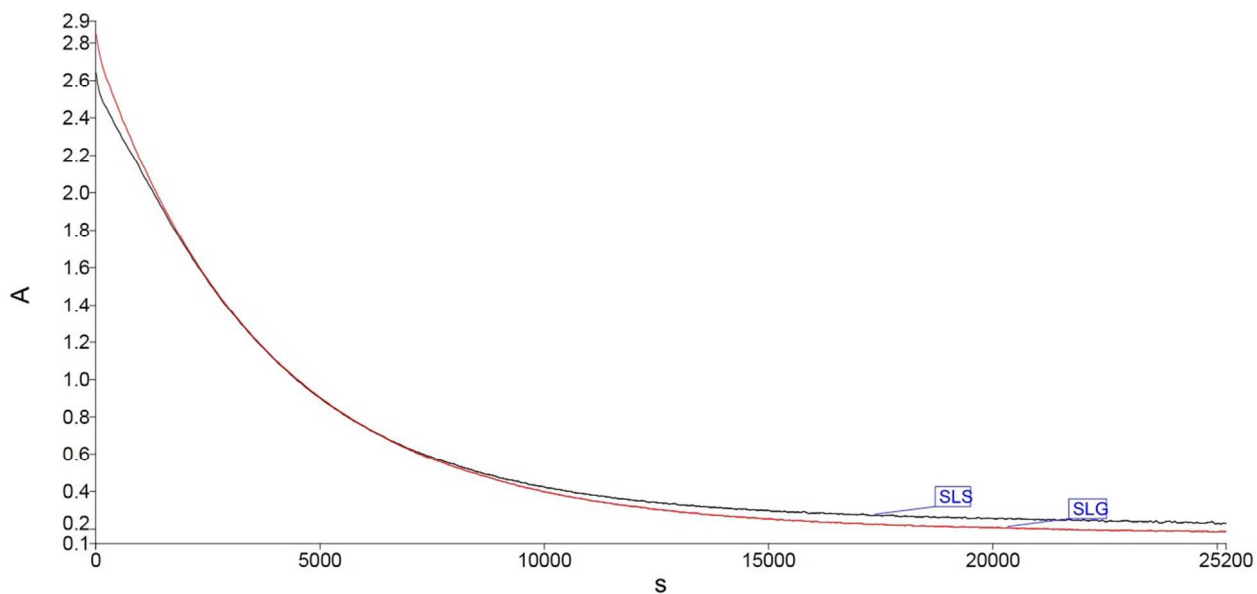


Figure S4b. Decrease in absorbance for dediazonation of 2×10^{-4} M 16-ArN₂⁺ in 0.069 M SLS (black line) and SLG (red line) micelles at 285.5 nm at 40°C and over 7 hours ($\geq 10 t_{1/2}$). Note: the x-axis label, S, stands for time (s) in seconds and the y-axis label, A, stands for absorbance.

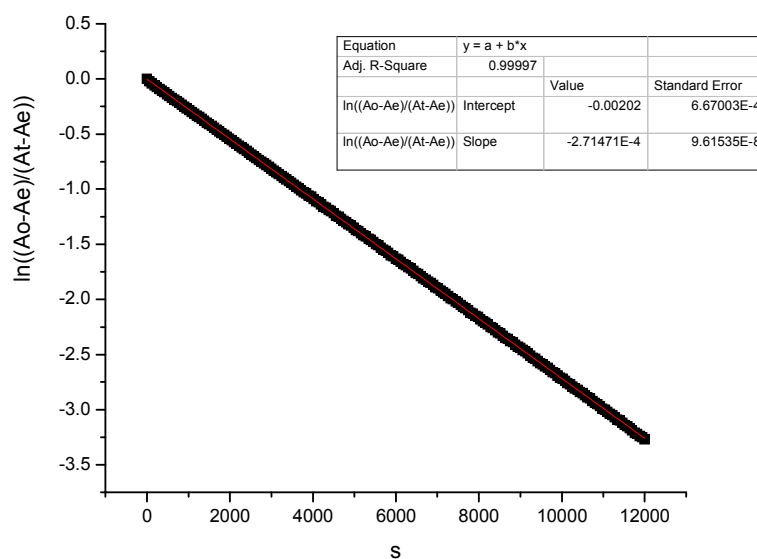


Figure S4c. Ln plot of UV absorbance for the dediazonation of 2×10^{-4} M 16-ArN₂⁺ in 0.098 M SLS. S stands for time in seconds.

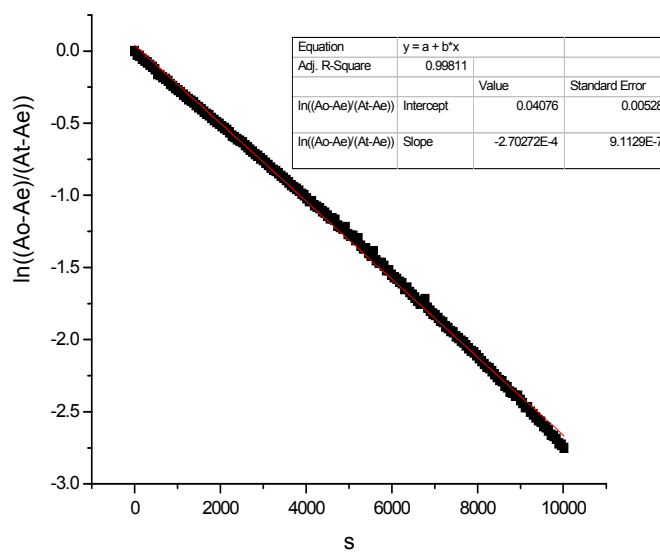


Figure S4d. Ln plot of UV absorbance for the dediazonation of 2×10^{-4} M 16-ArN₂⁺ in 0.098 M SLG. S stands for time in seconds.

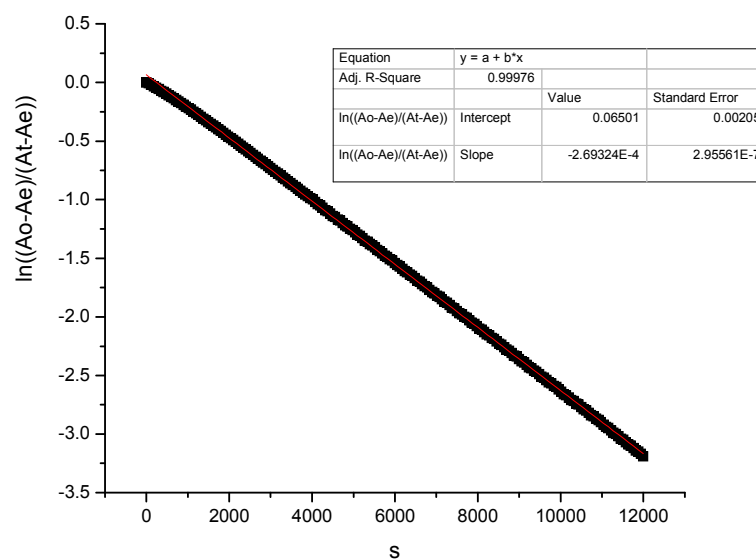


Figure S4e. Ln plot of UV absorbance for the dediazonation of 2×10^{-4} M 16-ArN₂⁺ in 0.069 M SLS. S stands for time in seconds.

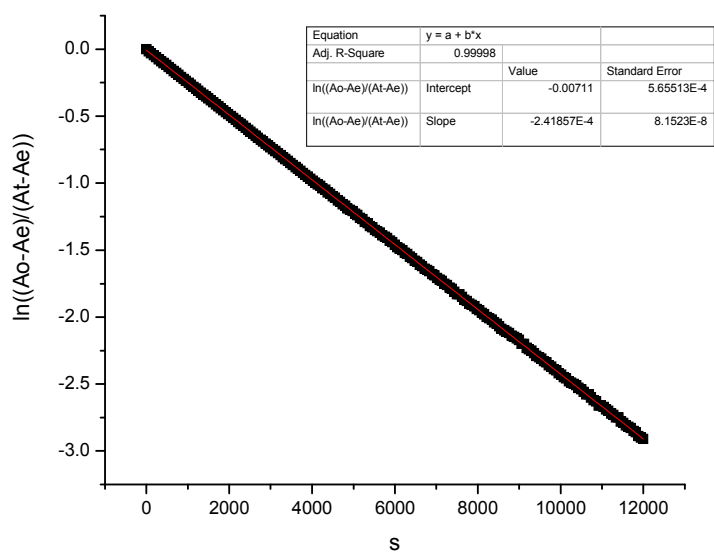
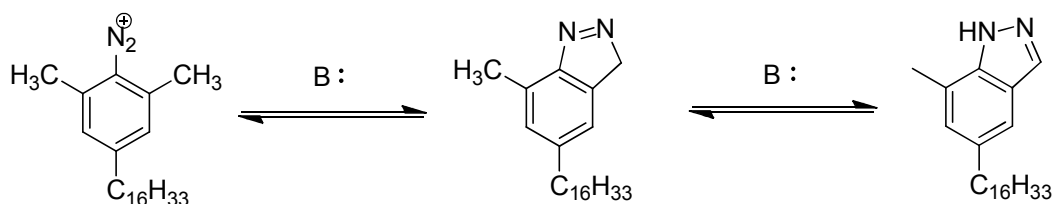


Figure S4f. Ln plot of UV absorbance for the dediazonation of 2×10^{-4} M 16-ArN₂⁺ in 0.069 M SLG. S stands for time in seconds.

Section S5. Proposed general base catalyzed pathway for indazole formation.



Scheme S5a. Proposed general base, **B:**, catalyzed formation of 5-*n*-Hexadecyl-7-methyl-1H-indazole (**16-ArInd**). The general base is assumed to be the carboxylate groups of SLG and SLS.

Section S6. Selectivity of the dediazonation reaction toward the amide oxygen and the carboxylate group.

The selectivity of the dediazonation reaction toward the amide O, compared to water (w) was determined previously.⁵ The percent yield of imido ester intermediate (16-ArOI), the immediate product from trapping by the amide nitrogen, was impossible to measure due to the rapid hydrolysis. The phenol product, 16-ArOH, from hydrolysis of the intermediate, is also not easy to measure because its corresponding peak in the HPLC chromatograms cannot be separated from the one for phenol formed by trapping with interfacial H₂O directly, **Scheme 3**. Published studies described the application of H₂O¹⁸ isotopic method, conjunct with GC/MS and HPLC, to determine the percent yield of short chain phenol (1-ArOH, the short chain analogue of the long chain phenol, 16-ArOH) from the hydrolysis.⁵ The selectivity was determined in aqueous *N*-methylacetamide and *N,N*-methylacetamide solutions, and at 2 different amide concentrations, respectively, by applying **Equation 2**. The results are summarized in **Table S6a**. Note that an average value of the estimated selectivity was used to calculate the interfacial molarities. Selectivity toward the carboxylate O, compared to water (w), was determined in aqueous glycine solutions, **Table S6b**. Note that an average value of the estimated selectivity was used to calculate interfacial molarities.

Table S6a. Average selectivities determined from dediazonation from 1-ArN_2^+ in the presence of aqueous amides two different water/amide, N_w/N_A , molar ratios at 40°C .⁵

Amide	N_w/N_A	S_w^O ^a
<i>N</i> -methylacetamide	2	0.63
	4	0.64
<i>N, N</i> -dimethylacetamide	2	0.62
	4	0.63

a. Average Value of $S_w^O = 0.63$.

Table S6b. Normalized yields for 1-ArN_2^+ dediazonation in aqueous glycine and the selectivity of carboxylate Group at 40°C .⁶

[Gly] (M)	1-ArOG(%)	1-ArOH(%)	$S_w^{(\text{COO}^-)}$ ^b
2.70	4.85	95.15	0.87
1.48	3.00	97.00	1.05
0.78	1.58	98.42	1.09

b. Average value of $S_w^{(\text{COO}^-)} = 1.00$.

Section S7. Analysis of 16-ArEC₁₂ and 16-ArOH_n yields from hydrolysis of 16-ArOI from acetamides based on results published previously.⁵

The dediazonation reaction with 1-ArN_2^+ was run in concentrated aqueous acetamide *N*-methylacetamide solutions, a model compound for the hydrolysis of the imido ester from SLG, and in *N, N*-dimethylacetamide solutions, a model compound for the formation and hydrolysis of the imido ester from SLS, at 2.0 M and 4.0 M, respectively in the presence and absence of 43.84% H_2^{18}O . Note that the labeled 1-ArOH is obtained only during direct reaction of H_2^{18}O with 1-ArN_2^+ , i.e., the hydrolysis of the imido ester intermediate gives only unlabeled 1-ArOH, **Scheme 3**. This yield difference was analyzed by GC/MS (M and M+2 peaks) to determine the yield of 1-ArOH from reaction of 1-ArN_2^+ with water (1-

ArOH_w) and the yield of 1-ArOH by hydrolysis (1-ArOH_h). The total yields of the imido ester intermediate in the reactions are: 1-ArOI = 1-ArOAc + 1-ArOH_h, where 1-ArOH_h is corrected for the amount of 1-ArOH produced during the reaction of 1-ArN₂⁺ with water (1-ArOH_w).

The yield of 16-ArOH_h was obtained by assuming that the 16-ArOH_h/16-ArEC₁₂ yield ratio in SLG and SLS micelles is the same as the 1-ArOH_h/16-ArEC₁₂ yield ratio from aqueous acetamides. The product yields were further modified by assuming that the total yield of the competitively formed products, 16-ArOH, 16-ArSE or 16-ArGE, and 16-ArEC₁₂ is 100%, where %16-ArOH = %16-ArOH_w + %16-ArOH_h and %16-ArOI = %16-ArEC₁₂ + %16-ArOH_h (see **Table 8**). (Note that %16-ArOH_w stands for the percent yield of the phenol product by trapping with water, i.e., by subtracting the amount of phenol formed by hydrolysis of the imido ester intermediate %16-ArOH_h from the total.)

Section S8. References

- (1) Kornblum, N.; Cooper, G.; Taylor, J. Chemistry of diazo compounds. ii. Evidence for a free radical chain mechanism in the reduction of diazonium salts by hypophosphorous acid *J. Am. Chem. Soc.* **1950**, *72*, 3013-3021.
- (2) Kornblum, N.; Kelley, A.; Cooper, G. Chemistry of diazo compounds. iii. Reduction of diazonium salts by phosphorous acid *J. Am. Chem. Soc.* **1952**, *74*, 3074-3076.
- (3) Laidler, K. J. *Chemical kinetics*; Harper & Row: New York, 1987.
- (4) Zuman, P.; Patel, R. *Techniques in organic reaction kinetics*; John Wiley & Sons: New York, 1984.
- (5) Romsted, L. S.; Zhang, J.; Zhuang, L. Mechanism of reaction of an arenediazonium ion in aqueous solutions of acetamide, *N*-methylacetamide and *N,N*-dimethylacetamide. Development of a novel reagent for chemically tagging peptide bonds at aggregate interfaces. *J. Am. Chem. Soc.* **1998**, *120*, 10046-10034.
- (6) Zhuang, L. Ph.D. Thesis, Rutgers, the State University of New Jersey, 1998.