NMR Spectroscopy as Basis for Characterization of Pluronic® F108 and Its Derivatives

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ABSTRACT: The hydroxyl end groups of Pluronic®F108 {a triblock copolymer surfactant of poly(ethylene glycol) and poly(propylene glycol) [PEG-PPG-PEG]} were modified into primary amine, sulfonic acid, and quaternary ammonium equivalents for use in affinity chromatography. NMR was used for monitoring the efficacy of modifications on intermediaries and final products. The primary amine equivalents were prepared via conversion of the hydroxyl groups to a tosylate, its displacement with an azide, followed by reduction to the primary amine. The sulfonic acid equivalents were prepared via hydroxyl group tosylation, the displacement of tosylate with thiol, and its oxidation to sulfonic acid. The conversion to trimethyl ammonium was achieved via hydroxyl group tosylation, tosylate displacement by halide, and halide displacement with trimethylamine. © 2000 John Wiley & Sons, Inc. J Appl Polym Sci 78: 109–117, 2000

Key words: NMR spectroscopy; glycol triblock polymers; amine termini; sulfonic acid termini; quaternary ammonium termini

INTRODUCTION

Membranes are used for diverse purposes such as reverse osmosis,[1] ultrafiltration,[2] microfiltration,[3] immobilization of enzymes in bioreactors,[4–6] affinity chromatography,[7–9] and ion-exchange chromatography.[10,11] A serious problem in the use of membranes is fouling.[12,13] When fouling is irreversible the membrane has to be discarded, which becomes an expensive procedure, especially in ultrafiltration, bioreactors, and affinity chromatography. Noncovalent attachment of polymeric surfactants to the surface of lipophilic membranes was considered to circumvent this problem. This approach should render the membrane more hydrophilic, which can reduce fouling. Furthermore, when irreversible fouling does occur, the surfactant can be removed and replaced without discarding the membrane. Ligands and enzymes can also be attached to the hydrophilic termini of the surfactants, allowing for less expensive affinity chromatography and bioreactors.

Pluronic®F108 (BASF) is a triblock polymer of poly(ethylene glycol)-poly(propylene glycol)-poly(ethylene glycol) (PEG-PPG-PEG); it is a surfactant and has the ability to adsorb onto hydropho-

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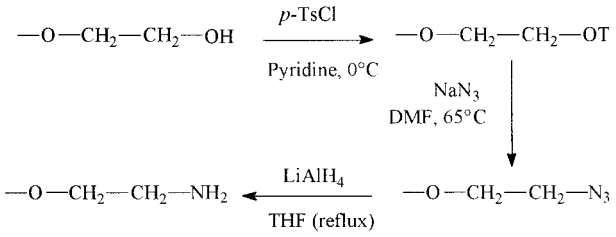
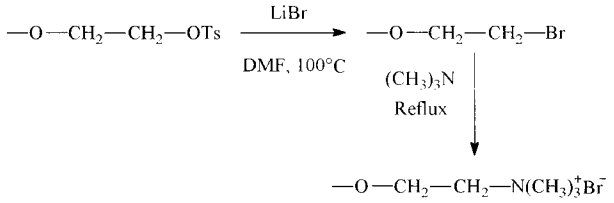


Scheme 1 The synthetic route for the preparation of primary amine equivalents from primary alcohols.



Scheme 2 The synthetic route for the preparation of quaternary ammonium equivalents from tosylates.

bic surfaces,[6,14,15] such as polysulfone, via the hydrophobic PP block while the hydrophilic end blocks are not adsorbed. The hydroxyl termini of Pluronic®F108 were converted into primary amine, cation, and anion to investigate the role of the terminal functional groups in the prevention or reduction of fouling of membranes. This also provides different species that can be attached to ligands and enzymes for bioreactors and affinity chromatography.

The molecular mass of Pluronic®F108 is 14,600 Da. The termini thus form an insignificant part of the polymer by mass. Efficient modification of the termini is therefore difficult to accomplish and monitor. Model compounds were used for developing the reactions before applying them to Pluronic®F108. Di(ethylene glycol) methyl ether (DEG) was selected as the first model compound. It simulates the first two ethylene oxide nodes with the hydroxyl terminus. Conversions and yields were easily determined by standard synthetic organic purification and characterization procedures. Hydroxyl terminated PEG with a molecular mass of 600 Da was used as a transition model compound between DEG and Pluronic®F108. It allowed the development of the reactions on a polymer, yet was more easily characterizable relative to Pluronic®F108.

Several analytical techniques were considered to characterize the Pluronic®F108 derivatives and ascertain the yields of the reactions and to characterize and quantify the terminal functional group by-products. These include electrospray mass spectrometry (ESMS), acoustic IR, and NMR spectroscopy. ^{13}C-NMR (75 MHz) proved to be the most effective means of analyzing the success of each reaction for two reasons:

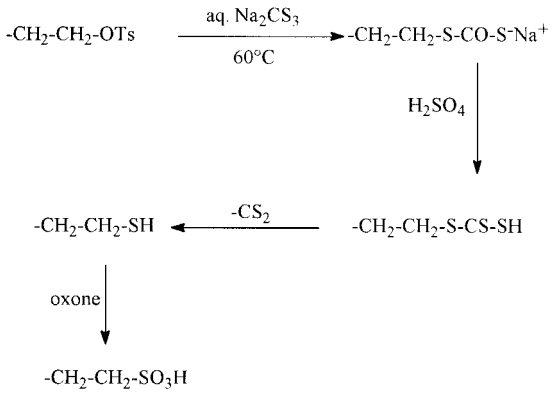
- at 75 MHz the dispersion is high enough to observe the terminus functionality and to distinguish it from the signals that issue from the bulk of the polymer and from other terminus functionalities that may be present that are due to incomplete or undesired reactions; and
- an extremely good correlation was found between the chemical shifts of the signals associated with the same functionality on the model compounds, allowing for the unambiguous empirical assignment of the functional group signals, even when they were of very low intensity.

^{1}H-NMR also proved to be useful in the cases where peaks were distinct from each other, thus allowing integration and semiquantification.

EXPERIMENTAL

NMR spectra were obtained using a Varian VXR 300 spectrometer operating at 299.9 MHz for the observation of ^{1}H and 75.42 MHz for the observation of ^{13}C.

All spectra were recorded at 25°C in either $CDCl_3$ or DMSO-d_6 as the lock solvent using tetramethylsilane at δ 0.0 as the internal reference.



Scheme 3 The synthetic route for the preparation of sulfonic acid equivalents form tosylates.

Table I ^{1}H-NMR Chemical Shifts (δ) of DEG and Its Derivatives in $CDCl_3$ at 25°C

Proton	DEG X = OH	DEG-Tosylate X = OTs	DEG-Azide X = N_3	Amino-DEG X = NH_2	DEG-Thiol X = SH	DEG-Sulf. Acid[a] X = SO_3H	DEG-Bromide X = Br	DEG-Ammonium X = $N(CH_3)_3Br$
—C**H**$_2$X	3.72–3.75	4.172	3.408	2.895	2.713	2.739	3.482	4.001
—C**H**$_2$CH$_2$X	3.59–3.64	3.690	3.673	3.519	3.623	3.621	3.815	3.980
O—(C**H**$_2$)$_2$—O	3.55–3.69	3.46–3.60	3.55–3.67	3.54–3.64	3.54–3.65	3.36–3.54	3.55–3.69	3.52–3.70
OCH_3	3.400	3.348	3.397	3.394	3.394	3.238	3.395	3.358
m-Ts-H	—	7.340	—	—	—	—	—	—
o-Ts-H	—	7.800	—	—	—	—	—	—
Ts-CH_3	—	2.446	—	—	—	—	—	—
NH_2	—	—	—	1.627	—	—	—	
SH	—	—	—	—	1.579	—	—	—
$^+N(CH_3)_3$	—	—	—	—	—	—	—	3.481
OH	2.790	—	—	—	—	—	—	—

[a] DMSO-d_6 was used as the solvent.

Table II ^{1}H-NMR Chemical Shifts (δ) of PEG and Its Derivatives in $CDCl_3$ at 25°C

Proton	PEG X = OH	PEG-Tosylate X = OTs	PEG-Azide X = N_3	Amino-PEG X = NH_2	PEG-Thiol X = SH	PEG-Sulf. Acid X = SO_3H	PEG-Bromide X = Br	PEG-Ammonium X = $N(CH_3)_3Br$
—C**H**$_2$X	3.724	4.157	3.398	2.715	2.697	3.358	3.476	4.050
—C**H**$_2$CH$_2$X	3.59–3.62	3.683	3.679	Coincident[a]	3.618	4.529	3.816	3.970
(C**H**$_2$—CH$_2$—O)$_n$[b]	3.58–3.62	3.58–3.64	3.65–3.67	3.59–3.74	3.64–3.66	3.65–3.93	3.66–3.68	3.59–3.64
m-Ts-H	—	7.343	—	—	—	—	—	—
o-Ts-H	—	7.796	—	—	—	—	—	—
Ts-CH_3	—	2.446	—	—	—	—	—	—
NH_2	—	—	—	1.257	—	—	—	—
SH	—	—	—	—	1.597	—	—	—
$^+N(CH_3)_3$	—	—	—	—	—	—	—	3.451
OH	2.780	—	—	—	—	—	—	—

[a] This signal is lost in the resonance of bulk polymer signals (3.59–3.74 ppm).
[b] The bulk of this signal always occurs at 3.640 ± 0.02 ppm.

Table III ^{1}H-NMR Chemical Shifts (δ) of Pluronic®F108 and Its Derivatives in $CDCl_3$ at 25°C

Proton	Pluronic®F108 X = OH	Plur.-Tosylate X = OTs	Plur.-Azide X = N_3	Amino-Plur. X = NH_2	Plur.-Thiol X = SH	Plur.-Sulf. Acid X = SO_3H	Plur.-Bromide X = Br	Plur.-Ammonium X = $N(CH_3)_3Br$
—C**H**$_2$X	3.70–3.74	4.159	Coincident[a]	2.739	2.696	Coincident[a]	3.475	4.040
—C**H**$_2$CH$_2$X	3.58–3.64	3.685	Coincident[a]	Coincident[a]	Coincident[a]	4.502	3.814	3.960
(C**H**$_2$—C**H**$_2$—O)$_n$[b]	3.64–3.66	3.58–3.64	3.64–3.85	3.64–3.73	3.64–3.88	3.67–4.15	3.65–3.66	3.55–3.65
O—CH**H**CH(CH$_3$)—O	3.36–3.43	3.37–3.42	3.37–3.42	3.37–3.42	3.37–3.42	3.433	3.38–3.43	3.358
O—C**H**HC**H**(CH$_3$)—O	3.50–3.58	3.50–3.57	3.50–3.57	3.50–3.62	3.50–3.62	3.666	3.50–3.59	3.407
O—CHHCH(C**H**$_3$)—O	1.135; 1.143	1.135; 1.143	1.135; 1.143	1.135; 1.143	1.145; 1.153	1.136	1.136; 1.144	1.141
m-Ts-H	—	7.344	—	—	—	—	—	—
o-Ts-H	—	7.799	—	—	—	—	—	—
Ts-CH$_3$	—	2.450	—	—	—	—	—	—
NH$_2$	—	—	—	1.256	—	—	—	—
SH	—	—	—	—	1.596	—	—	—
$^{+}$N(CH$_3$)$_3$	—	—	—	—	—	—	—	Coincident[a]
OH	2.450	—	—	—	—	—	—	—

[a] This signal is lost in the resonance of bulk polymer signals (3.40–3.70 ppm)
[b] The bulk of this signal always occurs at 3.640 ± 0.02 ppm.

Table IV ^{13}C-NMR Chemical Shifts (δ) of DEG and Its Derivatives in $CDCl_3$ at 25°C

Carbon	DEG X = OH	DEG-Tosylate X = OTs	DEG-Azide X = N_3	Amino-DEG X = NH_2	DEG-Thiol X = SH	DEG-Sulf. Acid[a] X = SO_3H	DEG-Bromide X = Br	DEG-Ammonium X = $N(CH_3)_3Br$
—CH$_2$	61.75	69.23	50.69	41.71	24.22	51.13	30.15	65.63
—C̲H$_2$CH$_2$X	72.59	68.72	70.05	73.47	73.01	66.80	71.27	65.20
—CH$_3$—O—CH$_2$C̲H$_2$	70.32	70.69	70.66	70.26	70.19	69.11	70.46	70.34
CH$_3$—O—C̲H$_3$—X	71.99	71.83	71.99	71.96	71.00	71.18	71.90	71.60
O—CH$_3$	59.00	59.04	59.12	59.06	59.10	57.96	59.09	58.95
o-Ts	—	127.99	—	—	—	—	—	—
m-Ts	—	129.82	—	—	—	—	—	—
p-Ts	—	133.06	—	—	—	—	—	—
ipso-Ts	—	144.79	—	—	—	—	—	—
Ts-CH$_3$	—	21.63	—	—	—	—	—	—
$^{+}$N(CH$_3$)$_3$	—	—	—	—	—	—	—	54.64

[a] DMSO-d_6 was used as solvent.

Table V ^{13}C-NMR Chemical Shifts (δ) of PEG and Its Derivatives in $CDCl_3$ at 25°C

Carbon	PEG X = OH	PEG-Tosylate X = OTs	PEG-Azide X = N_3	Amino-PEG X = NH_2	PEG-Thiol X = SH	PEG-Sulf. Acid X = SO_3H	PEG-Bromide X = Br	PEG-Ammonium X = $N(CH_3)_3Br$
—CH_2—X	61.69	69.26	50.72	40.99	24.27	54.89	30.35	65.62
—CH_2—CH_2—X	72.62	68.68	70.05	72.76	72.89	64.72	71.37	65.28
(CH_2—CH_2—O)$_n$	70.32; 70.53; 70.57[a]; 70.62	70.52; 70.57[a]; 70.61; 70.74	70.60[a]; 70.60; 70.70; 70.73	70.28; 70.38; 70.64; 70.56[a]	70.24; 70.39; 70.42; 70.57[a]	70.26; 70.36; 70.46; 70.58[a]	70.59[a]; 70.67	70.23; 70.47[a]
o-Ts	—	127.97	—	—	—	—	—	—
m-Ts	—	129.82	—	—	—	—	—	—
p-Ts	—	133.07	—	—	—	—	—	—
ipso-Ts	—	144.78	—	—	—	—	—	—
Ts-CH_3	—	21.64	—	—	—	—	—	—
$^+N(CH_3)_3$	—	—	—	—	—	—	—	54.59

[a] Major signal.

To quantify the ^{1}H spectra a pulse angle of 20° was used, together with a long repetition time of 4 s. Up to 2000 transients were accumulated in order to enhance sensitivity for the ^{1}H. Depending on the amount of material available, a repetition time of either 0.82 or 0.41 s was used together with a pulse angle of 45° for the ^{13}C. The ^{13}C multiplicities were determined by means of the Attached Proton Test (APT) technique.[16]

RESULTS AND DISCUSSION

Amine terminated Pluronic®F108, DEG, and PEG were prepared as follows (Scheme 1): the alcohol termini were tosylated,[17] the tosylate substituted with azide,[18,19] and the azide reduced with lithium aluminum hydride.[19–22] Trimethylammonium terminated Pluronic®F108, DEG, and PEG were prepared (Scheme 2) by conversion of the tosylate to the bromide[23,24] and then substitution of the bromide with trimethylamine.[25,26] The sulfonic acid terminated Pluronic®F108, DEG, and PEG were prepared (Scheme 3) by replacing the tosylate with a thiol[27,28] followed by oxidation with oxone.[29]

The ^{1}H-NMR chemical shifts of DEG, PEG, and Pluronic®F108 and their derivatives are summarized in Tables I–III, respectively. Likewise, Tables IV–VI summarize all the ^{13}C-NMR chemical shifts of DEG, PEG, and Pluronic®F108, respectively, and their respective derivatives. Comparing the chemical shifts of all the compounds as the terminal functional groups are progressively modified presents a data base that allows for the unambiguous assignment of all the signals. The closer the nuclei are to the termini where modification occurs, the greater is the effect of the functional groups on the chemical shifts of those nuclei. Some of the signals cannot be assigned because of their coincidence with the bulk polymer signals or their insignificance relative to the magnitude of the polymer bulk signals. The corresponding peaks in the model compounds indicate where those signals occur.

Several signals are observed for the bulk of PEG and its derivatives, but one towers above the others in both the ^{1}H- and ^{13}C-NMR spectra (Tables II, V). The strong signal is due to the methylene groups present in the EG repeating unit. The chemical shifts of the nuclei that are close to the termini appear as small signals at the base of the main signal. The same is true for the PEG blocks of Pluronic®F108, which pro-

Table VI ^{13}C-NMR Chemical Shifts (δ) of Pluronic®F108 and Its Derivatives in $CDCl_3$ at 25°C

Carbon	Pluronic®F108 X = OH	Plur.-Tosylate X = OTs	Plur.-Azide X = N_3	Amino-Plur. X = NH_2	Plur.-Thiol X = SH	Plur.-Sulf. Acid X = SO_3H	Plur.-Bromide X = Br	Plur.-Ammonium X = $N(CH_3)_3Br$
—**C**H$_2$—X	61.69	69.28	50.70	41.00	24.28	—	30.35	65.66
—**C**H$_2$—CH$_2$—X	Coincident[a]	68.69	Coincident[a]	Coincident[a]	Coincident[a]	—	71.23	65.30
(**C**H$_2$—**C**H$_2$—O)$_n$	70.57[b]; 70.84	70.58[b]	70.58[b]	70.58[b]	70.58[b]	70.48[b]; 70.78	70.58[b]	70.52[b]
O—**C**HHCH(**C**H$_3$)—O	17.35; 17.46	17.36; 17.48	17.36; 17.48	17.35; 17.48	17.35; 17.48	15.73; 18.59	17.33; 17.45	17.30; 17.40
O—**C**HHCH(CH$_3$)—O	72.93; 73.37	72.85; 72.90;	72.86; 72.90;	72.85; 72.90;	72.85; 72.90;	72.74; 72.95;	72.84; 72.88;	72.84; 72.89;
		72.93; 72.98;	72.95; 72.99;	72.93; 72.98;	72.94; 72.98;	73.34	72.92; 72.97;	72.93; 73.31
		73.38	73.40	73.39	73.38		73.36	
O—CHH**C**H(CH$_3$)—O	75.12; 75.34;	75.12; 75.33;	75.14; 75.34;	75.13; 75.33;	75.14; 75.34;	75.19; 75.38;	75.13; 75.33;	75.12; 75.30;
	75.52	75.37; 75.53	75.37; 75.53	75.37; 75.53	75.38; 75.54	75.54	75.37; 75.52	75.33; 75.48
o-Ts	—	127.97	—	—	—	—	—	—
m-Ts	—	129.81	—	—	—	—	—	—
p-Ts	—	133.07	—	—	—	—	—	—
ipso-Ts	—	144.74	—	—	—	—	—	—
Ts-CH$_3$	—	21.64	—	—	—	—	—	—
$^{+}$N(CH$_3$)$_3$	—	—	—	—	—	—	—	54.66

[a] This signal is lost in the resonance of bulk polymer signals (64–73 ppm)
[b] Major signal.

duce signals with the same chemical shifts as those of the PEG equivalents (Tables III, VI). The PPG block of Pluronic®F108 has several signals for each type of nucleus, especially in the ^{13}C spectra. This may be ascribed to the localized relative tacticity of the methyl substituents on the polymer backbone.

Tables VII and VIII provide a comparative study of the ^{1}H- and ^{13}C-NMR chemical shifts, respectively, of the first ethylene node of DEG, PEG, and Pluronic®F108 and all of their derivatives. The av erage chemical shift, as determined from the available data, is shown. In the last columns of Tables VII and VIII the deviation in chemical shift for a given nucleus from the average chemical shift of an equivalent nucleus in the center of PEG is given [δ 3.640 for protons (Table II) and δ 70.58 for ^{13}C (Table V)]. This comparison allows for the accurate empirical assignment of the ^{1}H- and ^{13}C-NMR signals of the terminal functional groups of Pluronic®F108 and its derivatives, as well as the terminal ethylene nodes bearing these functional groups. It was thus possible to confidently characterize the chemistry of Pluronic®F108.

^{1}H-NMR proved to be especially useful in ascertaining the success of the tosylation reaction (Scheme 1) on Pluronic®F108. The tosylate-bearing methylene group is shifted downfield from underneath the bulk signal to δ 4.16 (Table III). However, this causes a problem in determining the success of the reaction because any unconverted hydroxyl termini are not visible for quantitative comparison. The problem was circumvented by adding a drop of trichloroacetyl isocyanate[30,31] to the NMR tube. This reagent instantaneously binds to the unreacted hydroxyl groups (Scheme 4), forming an imidic carbamoate that shifts the methylene signal of the primary hydroxyl group downfield to δ 4.42 where it can be integrated and compared to the corresponding tosylate methylene signal at δ 4.16. A typical conversion in the tosylation of Pluronic®F108 with a 50-fold excess of tosyl chloride is 89%. The successful tosylation of Pluronic®F108 is also indicated by the presence of the aromatic and benzylic signals in the ^{1}H- and ^{13}C-NMR spectra.

Displacement of the tosylate with azide was manifested by the absence of the tosylate signals and the shift of the α-carbon signal to a higher field at δ 50.70 (Table VI). The analogous proton signal could not be observed due to overlap with polymer signals. The success of the reduction of the azide was confirmed by the presence of broad

Table VII Comparative Study of ^{1}H-NMR Chemical Shifts of Terminal Ethylene Nodes of DEG, PEG, and Pluronic®F108 and Their Derivatives

—X		DEG	PEG	Pluronic®F108	Average	Increment[a]
—OH	α	3.736	3.724	3.720	3.727	+0.09
	β	3.615	3.603	3.610	3.609	−0.03
—OTs	α	4.172	4.157	4.159	4.163	+0.52
	β	3.690	3.683	3.685	3.686	+0.05
—N_3	α	3.408	3.398	—	3.403	−0.24
	β	3.673	3.679	—	3.676	+0.04
—NH_2	α	2.895	2.715	2.739	2.783	−0.86
	β	3.519	—	—	3.519	−0.12
—SH	α	2.713	2.697	2.696	2.702	−0.94
	β	3.623	3.618	—	3.621	−0.02
—SO_3H	α	2.739[b]	3.358	—	3.358	−0.28
	β	3.621[b]	4.529	4.502	4.529	+0.89
—Br	α	3.482	3.476	3.475	3.478	−0.16
	β	3.815	3.816	3.814	3.815	+0.18
—$N(CH_3)_3^+$	α	4.001	4.050	4.040	4.030	+0.39
	β	3.980	3.970	3.960	3.970	+0.33

[a] Increment relative to PEG backbone signals (δ 3.640).
[b] Recorded in DMSO-d_6 and not incorporated into the calculations.

Table VIII Comparative Study of ^{13}C-NMR Chemical Shifts of Terminal Ethylene Nodes of DEG, PEG, and Pluronic®F108 and Their Derivatives

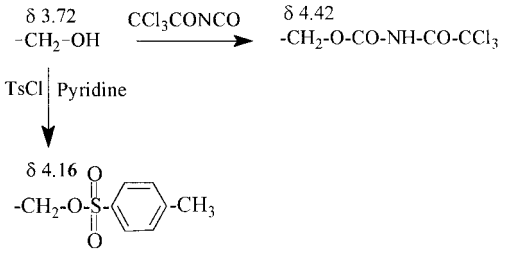
—X		DEG	PEG	Pluronic®F108	Average	Increment[a]
—OH	α	61.75	61.69	61.69	61.71	−8.9
	β	72.59	72.62	—	72.61	+2.0
—OTs[b]	α	69.23	69.26	69.28	69.26	−1.3
	β	68.72	68.68	68.69	68.70	−1.9
—N_3	α	50.69	50.72	50.70	50.70	−19.9
	β	70.05	70.05	—	70.05	−0.5
—NH_2	α	41.71	40.99	41.00	41.23	−29.4
	β	73.47	72.76	—	73.12	+2.5
—SH	α	24.22	24.27	24.28	24.26	−46.3
	β	73.01	72.89	—	72.95	+2.4
—SO_3H	α	51.13[c]	54.89	—	54.89	−15.7
	β	66.80[c]	64.72	—	64.72	−5.9
—Br	α	30.15	30.35	30.35	30.28	−40.3
	β	71.27	71.37	71.23	71.29	+0.7
—$N(CH_3)_3^+$	α	65.63	65.62	65.66	65.64	−4.9
	β	65.20	65.28	65.30	65.26	−5.3

[a] Increment relative to PEG backbone signals (δ 70.85).
[b] The α and β assignments are interchangeable.
[c] Recorded in DMSO-d_6 and not incorporated into the calculations.

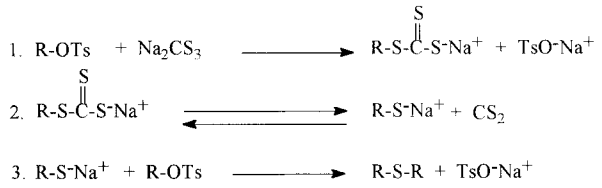
singlets of the α-methylene and amine protons observed at δ 2.74 and δ 1.26 respectively (Table III). In the ^{13}C-NMR spectrum of the amine, the α-carbon signal was observed at δ 41.00. At this stage the percentage of conversion of Pluronic®F108 to amino-pluronic was not ascertained. However, the NMR spectra did not indicate significant amounts of tosylate or azide or any other compound as impurities, although it is difficult to ascertain the presence of other compounds, especially if the diagnostic signals coincide with the polymer bulk signals.

Bromide displacement of tosylate in the preparation of pluronic bromide was confirmed by the absence of tosylate and benzylic methyl signals and the presence of an α-methylene proton signals at δ 3.48 and an α-carbon signal at δ 30.35. The success of the displacement of bromide with trimethylamine was apparent from the downfield shift observed for the α-methylene protons from δ 3.48 to 4.04. The quaternary ammonium protons could not be observed because of overlap with polymer signals. However, in the ^{13}C-NMR spectrum the α-carbon shifted downfield from δ 30.35 to 65.66 and the quaternary ammonium methyl signal was observed at δ 54.66.

The formation of sulfides and disulfides was encountered as by-products in the preparation of thiols from tosylates. The presence of the sulfide was of greater concern than the presence of disulfide because the oxidation of sulfides generally yields sulfoxides[32] or sulfones while the oxidation of disulfides should also yield sulfonic acids.[33,34] During the characterization of pluronic-thiol we found that the β-methylene proton and carbon signals were both lost under the bulk polymer signals in the respective spectra. The ^{13}C-NMR peaks observed at δ 38.30 and 29.99 were assigned to the sulfur-bearing carbon atom of dipluronic-sulfide and dipluronic-disulfide, respectively. The corresponding proton shifts were δ 2.90 for dipluronic-disulfide and δ 2.650–2.740 for the sulfide. The latter overlaps with the corresponding signal of the mercaptan on its downfield side. Signals with very similar shifts were observed for the corresponding minor products of DEG- and PEG-mercaptan. Disulfide formation was reduced by adding excess CS_2, displacing the dissociation equilibrium (Scheme 5) in favor of sodium alkyltrithiocarbonate in the synthesis of thiols.



Scheme 4 Trichloroacetylisocyanate reacts with the unreacted hydroxyl groups after the tosylation of Pluronic®F108. The chemical shifts of the functional-bearing methylene groups are shown.



Scheme 5 The formation of sulfides in the synthesis of thiols from tosylates.

Characterization of the ^{1}H-NMR spectrum of the product of oxone oxidation of pluronic-mercaptan, which was aided by the chemical shifts of DEG- and PEG-sulfonic acid, indicated a very small signal at δ 4.502 that may be assigned to the β-methylene protons of pluronic-sulfonic acid. The α signals could not be observed because of a coincidence with bulk polymer signals (3.36–3.43 ppm). The ^{13}C-NMR signal of the α- and β-carbon of pluronic-sulfonic acid expected at δ 54.89 and 64.72, respectively, according to the corresponding signals of PEG-sulfonic acid, could not be identified in the noise. A prominent signal was the α-methylene signal of Pluronic®F108 at δ 61.69 in the ^{13}C spectra of the oxidation product. The corresponding α-carbon signal was not present in the spectra of pluronic-mercaptan, thus indicating an oxidative hydrolysis process. This is probably due to too great an excess of oxone used in the oxidation process. Thus, the oxidation was not successful as was achieved with the DEG and PEG equivalents. This problem may be remedied by use of smaller amounts of the oxidizing agent. A far better approach to introduce sulfonic acid end groups would be to use propane sultone as an alkylating reagent.[35,36] We avoided this approach in this study because of the extreme toxicity of propane sultone.[37,38] However, careful application of this compound should be rewarding.

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