Regioselectivity Control in Diels−Alder Reactions of Surfactant 1,3-Dienes with Surfactant Dienophiles

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Abstract: The ability of surfactant aggregate−H_2O interfaces to control the regioselectivity of Diels−Alder reactions has been investigated. Cycloadditions of surfactant 1,3-dienes 2-[[3-(dimethyldodecylsilyl)-1,3-butadien-2-yl]thio]-*N*,*N*,*N*-trimethyl-1-ethanaminium iodide (**1a**) and 6-[[3-(dimethyloctylsilyl)-1,3-butadien-2-yl]thio]-*N*,*N*,*N*-trimethyl-1-hexanaminium iodide (**1b**) with surfactant dienophiles (*E*)-2-[[[2-(dodecoxycarbonyl)-ethenyl]carbonyl]oxy]-*N*,*N*,*N*-trimethyl-1-ethanaminium iodide (**2a**) and (*E*)-6-[[[2-(octoxycarbonyl)ethenyl]carbonyl]oxy]-*N*,*N*,*N*-trimethyl-1-hexanaminium bromide (**2b**) within their aqueous mixed micelles have been performed at 25(35) °C. The cycloaddition of **1a** and **2a** gave a 30:1 ratio of *trans*-1-[(2-trimethylammonio)-ethylthio]-2-(dimethyldodecylsilyl)-4-(dodecoxycarbonyl)-5-[(2-trimethylammonio)ethoxycarbonyl]-1-cyclohexene dihalide (**15a**) and *trans*-1-[(2-trimethylammonio)ethylthio]-2-(dimethyldodecylsilyl)-4-[(2-trimethylammonio)ethoxycarbonyl]-5-(dodecoxycarbonyl)-1-cyclohexene dihalide (**16a**), respectively, and that of **1b** and **2b** a 6.6:1 ratio of *trans*-1-[(6-trimethylammonio)hexylthio]-2-(dimethyloctylsilyl)-4-(octoxycarbonyl)-5-[6-(trimethylammonio)hexoxycarbonyl]-1-cyclohexene dihalide (**15b**) and *trans*-1-[(6-trimethylammonio)-hexylthio]-2-(dimethyloctylsilyl)-4-[6-(trimethylammonio)hexoxycarbonyl]-5-(octoxycarbonyl)-1-cyclohexene dihalide (**16b**), respectively. The excess of **15** over **16** is consistent with the reaction of **1** and **2** within mixed aggregates in their preferred orientations at the aggregate−H_2O interface. The greater regioselectivity obtained in the reaction of **1a** and **2a** is ascribed to the shorter tether between their reactive functional groups and quaternary ammonium headgroups. A monolayer study of **15a** and **16a** was also performed.

Introduction

The Diels−Alder reaction is one of the most important reactions in organic synthesis.[1] Numerous studies of Diels−Alder cycloadditions performed in H_2O and aqueous surfactant-based media have demonstrated that increased rates and stereoselectivities can be expected relative to reactions performed in conventional organic solvents.[2,3] In particular, J. B. F. N. Engberts and co-workers have recently reported a million-fold rate acceleration of a Diels−Alder reaction resulting from combined Lewis acid and micellar catalysis in H_2O,[3a] and enhanced enantioselectivity in a chiral Lewis acid-catalyzed Diels−Alder reaction in H_2O.[3b] On the other hand, there have been only a few studies of the ability of interfacial orientational effects within aqueous surfactant-based media to control the regioselectivity of Diels−Alder reactions.[4,5] In one involving a surfactant 1,3-diene and a neutral nonsurfactant dienophile, orientational effects were not strong enough to overcome the reaction's intrinsically preferred regiochemistry.[4] In another study involving a different surfactant 1,3-diene and surfactant dienophiles, modest regioselectivity was obtained.[5] There have been a few reports of the effect on regiochemistry of performing Diels−Alder reactions in H_2O alone.[6]

Herein we report the results of a study of regioselectivity control in Diels−Alder reactions of surfactant 1,3-dienes **1** with surfactant dienophiles **2**.[7] Within surfactant pairs **1a** and **2a**, and **1b** and **2b**, the substituted 1,3-diene and dienophile groups are separated from the quaternary ammonium headgroups by

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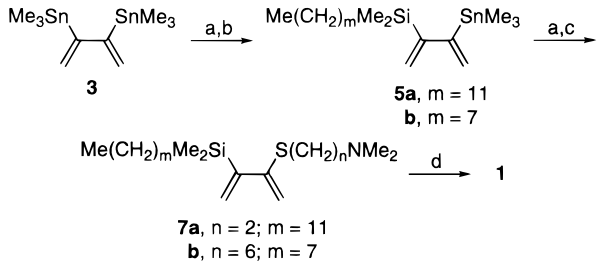
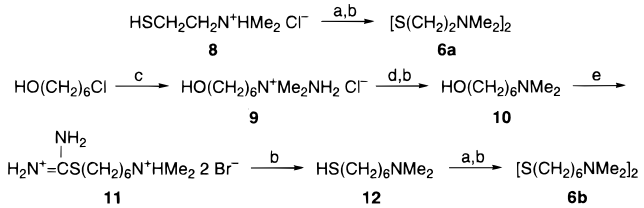
Scheme 1[a]



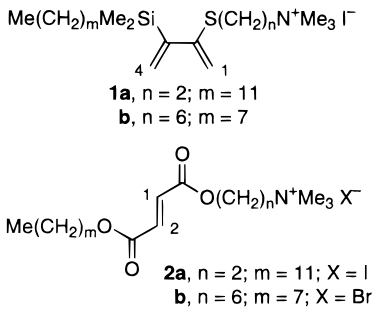
[a] Key: (a) MeLi, THF, −78 °C; (b) **4**; (c) **6**; (d) MeI, THF, 25 °C.

Scheme 2[a]



[a] Key: (a) $NaClO_2$, MeOH−H_2O, 0 °C; (b) NaOH; (c) Me_2NNH_2, 50 °C; (d) $NaNO_2$, 4 M HCl, 0 °C; (e) 48% HBr, H_2NCSNH_2, reflux.

tethers of two and six methylene units, respectively. The total number of carbon atoms in the tether and terminal alkyl chain of each surfactant is 14.



Results and Discussion

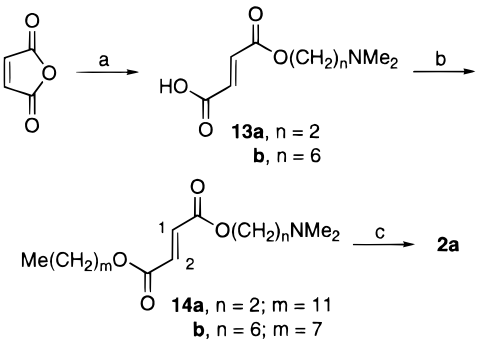
Syntheses. The synthesis of surfactant 1,3-dienes **1** is summarized in Scheme 1. 1,3-Diene **3**[8] was transformed into 1,3-dienes **7** in a one-pot sequence of reactions. The reaction of **3** with MeLi was followed by that of the resultant carbanion with commercially available $Me(CH_2)_mSiMe_2Cl$ (**4a**, $m = 11$; **b**, $m = 7$) to give 1,3-dienes **5**. Then the reaction of **5** with MeLi was followed by that of the resultant carbanion with $[S(CH_2)_nNMe_2]_2$ (**6a**, $n = 2$; **b**, $n = 6$) to give **7**. Quaternization of **7** with MeI gave **1**.

Disulfides **6** used above were prepared as outlined in Scheme 2. Commercially available **8** was converted into **6a**. Quaternary hydrazinium chloride **9**, obtained from the reaction of 6-chloro-1-hexanol with *N*,*N*-dimethylhydrazine, was converted into amino alcohol **10**. The reaction of **10** with hydrobromic acid and thiourea gave isothiuronium salt **11**, which without isolation was hydrolyzed to yield amino thiol **12**. Then **12** was converted into **6b**.

The synthesis of amino diesters **14** and surfactant dienophile **2a** is outlined in Scheme 3; **2b** was prepared previously by another pathway.[5a,b] The reaction of maleic anhydride with $HO(CH_2)_2NMe_2$ or **10** gave half esters **13**, which were then esterified to give **14**. Quaternization of **14a** with MeI gave **2a**.

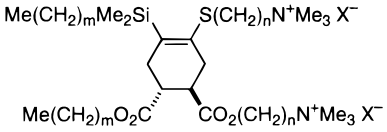
By surface tensiometry (du Noüy ring) the critical micelle concentrations (cmcs) of **1a**, **1b**, **2a**, and **2b** in H_2O at 25 °C are 0.75×10^{-4}, 1.0×10^{-4}, 0.30×10^{-3}, and 4.4×10^{-3} M,[5a,b] respectively. The Krafft temperatures in H_2O of **1a**, **1b**, and **2b** are ≤25 °C, and that of **2a** is ca. 45 °C.

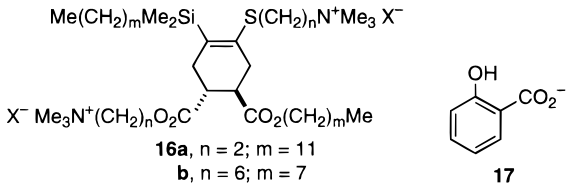
Scheme 3[a]



[a] Key: (a) $HO(CH_2)_2NMe_2$ or **10**, C_6H_5Me, reflux; (b) $Me(CH_2)_mOH$ ($m = 7$ or 11), DCC, DMAP, CH_2Cl_2, 25 °C; (c) MeI, MeCN, 25 °C.

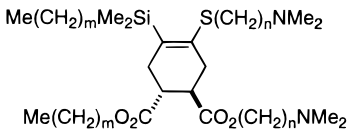
Diels−Alder Reactions. Diels−Alder reactions of **1** with excess **2** in H_2O at 25(35) °C, with added 4-*tert*-butylcatechol, gave cycloadducts **15** and **16**. Several reactions of **1b** and **2b**

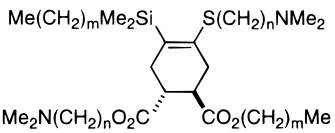




were performed with added salicylate anion (**17**, from sodium salicylate). Each crude product mixture was analyzed by ^1H NMR and/or analytical reversed-phase HPLC, giving the **15**/**16** ratio and the yield of **15** + **16**. Preparative reversed-phase HPLC afforded separated **15b** and **16b**. The results are summarized in runs 1−14 of Table 1.

Diels−Alder reactions of amines **7** and **14**, with added 4-*tert*-butylcatechol, were performed in C_6H_5Me at 75−85 °C to give regioisomeric cycloadducts **18** and **19**. Crude product mixtures





containing **18b** and **19b** were analyzed by analytical reversed-phase HPLC, and MPLC on silica gel of all crude product mixtures afforded **18** and **19**. The results are summarized in runs 15−18 of Table 1. Separately, **18** and **19** were converted

Table 1. Diels-Alder Reactions

run	1,3-diene no.	1,3-diene concn, M	dienophile no.	dienophile concn, M	medium[a]	reactn temp, °C	reactn time, h	yield (%)[b]	regioisom ratio[c−f]
1	**1a**	0.0078	**2a**	0.013	H_2O	25	40	79	*g*
2	**1a**	0.0081	**2a**	0.013	H_2O	25	25	83	26:1
3	**1a**	0.0086	**2a**	0.014	H_2O	25	48	70	36:1
4	**1a**	0.019	**2a**	0.027	H_2O	35	48	98	28:1
5	**1b**	0.021	**2b**	0.082	H_2O	25	21	85	6.7:1
6	**1b**	0.020	**2b**	0.074	H_2O	25	52	95	6.6:1
7	**1b**	0.024	**2b**	0.098	H_2O	25	45		6.6:1
8	**1b**	0.030	**2b**	0.12	H_2O	25	22	85	6.4:1
9	**1b**	0.031	**2b**	0.12	H_2O	25	26	86	6.6:1
10	**1b**	0.038	**2b**	0.15	H_2O	25	45		6.7:1
11	**1b**	0.015	**2b**	0.056	H_2O[h]	25	46	86	14:1
12	**1b**	0.030	**2b**	0.11	H_2O[h]	25	46	85	14:1
13	**1b**	0.030	**2b**	0.11	H_2O[h]	25	46	82	13:1
14	**1b**	0.030	**2b**	0.12	H_2O[h]	25	25	52	12:1
15	**7a**	0.066	**14a**	0.14	C_6H_5Me	75	36	74	1:1.6
16	**7a**	0.066	**14a**	0.15	C_6H_5Me	80	48	84	1:1.3
17	**7b**	0.076	**14b**	0.17	C_6H_5Me	75	24	71	1:1
18	**7b**	0.12	**14b**	0.29	C_6H_5Me	85	24	71	1:1

[a] Reaction mixtures contained 4-*tert*-butylcatechol (10−11 mol % with respect to 1,3-diene in runs 1−10 and 15−18, and 23 mol % in runs 11−14). [b] Determined by ^{1}H NMR analysis of crude mixtures of products and unreacted starting materials: **15a** + **16a** in runs 1−4; **15b** + **16b** in runs 5−14; **18a** + **19a** in runs 15 and 16; **18b** + **19b** in runs 17 and 18. [c] In runs 2−4, **15a**/**16a** ratios determined by HPLC analysis of crude mixtures of products and unreacted starting materials. [d] In runs 5−14, **15b**/**16b** ratios determined by ^{1}H NMR and/or HPLC analysis of crude mixtures of products and unreacted starting materials. [e] In runs 15 and 16, **18a**/**19a** ratios determined from masses of isolated **18a** and **19a**. [f] In runs 17 and 18, **18b**/**19b** ratios determined from masses of isolated **18b** and **19b** and by HPLC analysis of crude mixtures of products and unreacted starting materials. [g] No **16a** was detected by ^{1}H NMR analysis of the crude mixture of products and unreacted starting materials. [h] The reaction mixtures of runs 11−14 contained 0.060, 0.086, 0.12, and 0.13 M sodium salicylate, respectively.

into **15** and **16** (X = I), respectively, by quaternization with MeI in MeCN.

The Diels−Alder reactions of surfactants **1** and **2** were performed under mixed micellar conditions at concentrations well above their respective cmc values. An excess of cycloadduct **15** over **16** was obtained in each run. The former is the expected regioisomer if **1** and **2** react in their preferred aligned orientations within a mixed micelle, with the quaternary ammonium headgroups at the aggregate−H_2O interface and the remainder of each surfactant extended into the mixed micelle interior. These orientations for **1a** and **2a** are represented in Figure 1. For simplicity, a flat interface is illustrated, whereas that of a micelle is curved, and the alkyl chains are shown in fully extended conformations, although they are most likely folded.[9] Approximation of the diene and dienophile units for reaction requires mobility of **1** and/or **2** along their radial axes. Cycloadduct **16** results from the reaction of misaligned **1** and **2** within the mixed micelles and/or within the bulk aqueous phase. The latter involves **1** and **2** in monomeric and/or premicellar forms.[10] The orientational effects in both are expected to be less than those within the mixed micelles. The 4-*tert*-butylcatechol in each reaction mixture likely resides at the aggregate−H_2O interface,[11] resulting in an indeterminate effect, if any, on the **15**/**16** ratio.

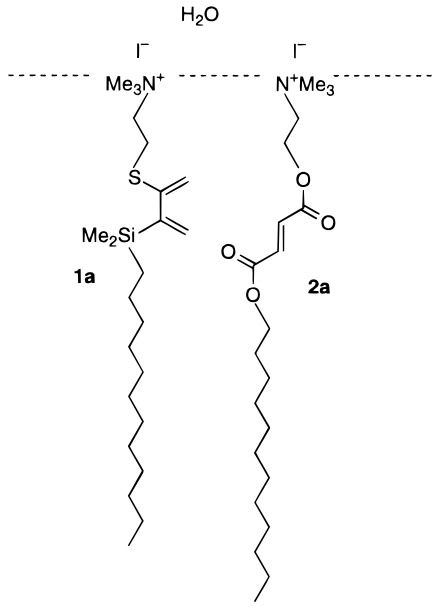


Figure 1. Preferred orientations of **15a** and **16a** at a surfactant aggregate−H_2O interface.

The performance of Diels−Alder reactions under unaggregated conditions in H_2O is impractical given the low cmcs of **1** and **2**. But nevertheless it is interesting to consider the intrinsic regiochemical preferences that would be expected in the cycloadditions of **1** and **2** in the absence of interfacial orientational effects. The proximity of the positively charged headgroup to the substituted dienophile unit renders the ester group at carbon 1 of **2a** more electron withdrawing than the ester group at carbon 2.[12,13] For a 2,3-disubstituted 1,3-diene bearing thio and silyl groups, the former is expected to direct the regioselectivity of its Diels−Alder reactions.[14] The electron-withdrawing inductive effect of $(CH_2)_2N^+Me_3$ within **1a** should not alter this expectation. Overall, the reaction of **1a** and **2a** is predicted[14] to give an excess of cycloadduct **16a** over **15a**. Note that this expectation is indeed opposite to the regiochemical preference obtained in the mixed micellar system under the influence of interfacial orientational effects (runs 1−4). The cycloaddition of **1b** and **2b** should display no regiochemical preference in the absence of interfacial orientational effects, since the substituents at carbons 1 and 2 within **2b**, which contains a tether of six methylene units, are close to being both sterically and electronically equivalent[13] with respect to the dienophile reaction center.

In runs 11−14, containing added **17**, the **15b**/**16b** ratios were higher than those in runs 5−10 without **17**. It is known that the addition of **17** to aqueous solutions of cationic surfactants effects the formation of threadlike micelles.[15] The higher ordering in these systems associated with the transition from spherical to threadlike micelles is apparently accompanied by greater interfacial ordering that leads to greater **15b**/**16b** ratios.

A 1:1.4 ratio of regioisomers **18a** and **19a**, respectively, was obtained in the Diels−Alder reaction of nonsurfactant analogues **7a** and **14a** in C_6H_5Me (runs 15 and 16). The modest excess of **19a** over **18a** is consistent with steric effects but inconsistent with electronic effects. The former involves an unfavorable

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interaction between the large dodecyl-containing substituents within the cycloaddition transition state leading to **18a**, which is unmitigated by hydrophobic association as within mixed micellar **1a** and **2a**. Electronic effects predict[14] an excess of **18a** over **19a** as the result of regiochemical direction by the thio group of **7a** and a greater inductive electron withdrawal by the dodecyl ester group of **14a** relative to its 2-(*N*,*N*-dimethylamino)ethyl ester group.[12,13]

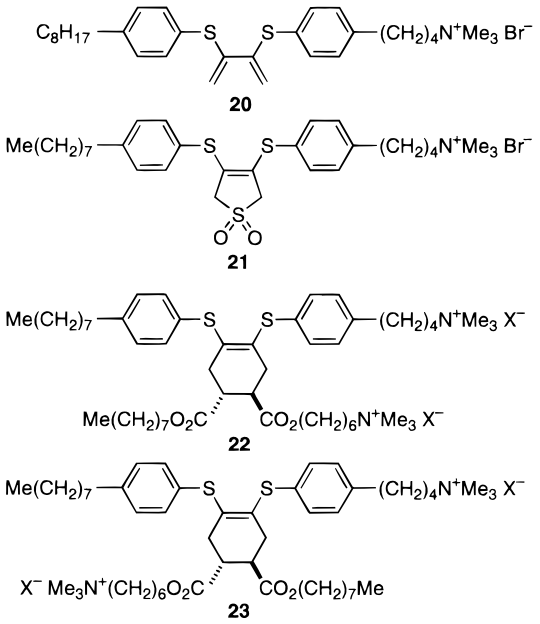
A 1:1 ratio of regioisomers **18b** and **19b**, respectively, was obtained in the Diels−Alder reaction of nonsurfactant analogues **7b** and **14b** in C_6H_5Me (runs 17 and 18), consistent with the expectation that this cycloaddition should display no regiochemical preference since the substituents at carbons 1 and 2 within **14b**, which contains a tether of six methylene units, are close to being both sterically and electronically equivalent[13] with respect to the dienophile reaction center. The 1:1 ratio of **18b** and **19b** is consistent with the likelihood noted above that the cycloaddition of **1b** and **2b** would display no regiochemical preference without interfacial orientational effects.

The **15a**/**16a** ratio of 30:1 obtained in the cycloaddition of **1a** and **2a** is substantially greater than the **15b**/**16b** ratio of 6.6:1 obtained from **1b** and **2b**. The greater regioselectivity with the former pair is attributed to the shorter tether between their quaternary ammonium headgroups and 1,3-diene and dienophile groups. The shorter tether provides less opportunity for misalignment of these reactive groups, which can lead to minor regioisomer **16**.

A previous study[5a,b] included the cycloaddition of surfactant dienophile **2b** with surfactant 1,3-diene **20**, which was generated in situ at 100 °C by the thermal extrusion of SO_2 from precursor surfactant **21**. Even though the lengths of the tethers between the quaternary ammonium headgroups and dienophile groups of **1b** and **20** are comparable, the **15b**/**16b** ratio of 6.6:1 obtained from **1b** and **2b** in the present study at 25 °C is more than twice the **22**/**23** ratio of 3.0:1 obtained from **20** and **2b** at 100 °C.[5a,b] The greater regioselectivity obtained with the former pair is attributed at least in part to the expected greater organizational abilities of micelles at low compared to high temperatures. Also, **1b**, unlike **20**, does not contain aromatic groups, which can associate with quaternary ammonium headgroups.[16] It is possible that **20**'s aromatic groups promote looping to the mixed micelle−H_2O interface, where they can interact with quaternary ammonium groups, resulting in misalignment of **20** and **2b**, with resultant formation of minor regioisomer **23**.

As formed, cycloadducts **15** and **16**, which are surfactants themselves, no doubt remain within the mixed micelles of **1** and **2**, thereby changing the detailed nature of the aggregates as the reaction proceeds. But note that about the same **15**/**16** ratio was obtained in run 14 as in runs 11−13, suggesting that the regioisomer ratio does not change appreciably with the extent of reaction. Thus regiochemical control in the cycloadditions derives from interfacial effects that are relatively insensitive to specific aggregate composition, as was the case in the cycloaddition of **2b** and **20** to give **22** and **23**.[5a] It is not known whether the **15**/**16** ratios are kinetically or thermodynamically controlled, although the former is more likely.

Characterization of Diels−Alder Cycloadducts. Surfactant cycloadducts **15** and **16** and nonsurfactant cycloadducts **18** and **19** were characterized by ^1H and ^{13}C NMR spectroscopy and FAB high-resolution mass spectrometry. Cycloadducts **15a** and **16a** were also characterized by ^1H,^1H COSY and ^1H,^1H ROESY NMR spectroscopy in both CD_3OD and $CDCl_3$; spectra are



found in the Supporting Information. The results from these 2D methods provided definitive structural assignments for **15a** and **16a** and, in turn, **18a** and **19a**, since the former were prepared from the latter as noted above.

The trans stereochemistry of cycloadducts **15** and **16** is consistent with the known stereochemical course of Diels−Alder reactions[17] and with the trans stereochemistry established for closely related cycloadducts **22** and **23**.[5a,c] On the basis of analogy to the known half-chair conformation[18] of **22** in $CDCl_3$,[5a,c] it is probable that **15a** also adopts a half-chair conformation with diequatorial ester groups in $CDCl_3$ and CD_3OD as well. Since the signals for the cyclohexene ring hydrogens in the ^1H NMR spectra of **15a** and **16a** in CD_3OD have similar appearances, **16a** should also have a half-chair conformation. The probable half-chair conformations of **15a** and **16a** in CD_3OD with diequatorial ester groups are illustrated in Figure 2.

In the ^1H,^1H ROESY NMR spectrum (400 MHz) of the major diastereomer of the cycloadduct pair **15a**,**16a** in CD_3OD, several pertinent correlations were observed, which correspond to hydrogens on both carbon-1′ and carbon-2′ interacting with two of the following three hydrogen sets: $N_a^+Me_3$, $N_b^+Me_3$, and one of the hydrogens on carbon-1″. The uncertainty derives from overlap of the signal for one of the N^+Me_3 groups with that for a hydrogen on carbon-1″. The assignments for the N^+Me_3 groups of Figure 2 are arbitrary. Regardless of which hydrogen sets are involved with hydrogens on carbon-1′ and carbon-2′, the correlations indicate through-space interactions between the two chains bearing the N^+Me_3 groups.

In the ^1H,^1H ROESY NMR spectrum (400 MHz) of the minor diastereomer of the cycloadduct pair **15a**,**16a** in CD_3OD, several pertinent correlations were observed, which correspond to hydrogens on both carbon-1′ and carbon-2′ interacting with one of the following three hydrogen sets: $N_a^+Me_3$, $N_b^+Me_3$, and one of the hydrogens on carbon-1″. As above, the uncertainty derives from overlap of the signal for one of the N^+Me_3 groups with that for a hydrogen on carbon-1″. These correlations do not require, but do not preclude, through-space interactions between the two chains bearing the N^+Me_3 groups.

(16) For examples, see: Bacaloglu, R.; Bunton, C. A.; Cerichelli, G.; Ortega, F. *J. Phys. Chem.* **1989**, *93*, 1490, and references therein.

(17) (a) Sauer, J. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 16. (b) Telan, L. A.; Firestone, R. A. *Tetrahedron* **1999**, *55*, 14269.

(18) Anet, F. A. L.; Freedberg, D. I.; Storer, J. W.; Houk, K. N. *J. Am. Chem. Soc.* **1992**, *114*, 10969.

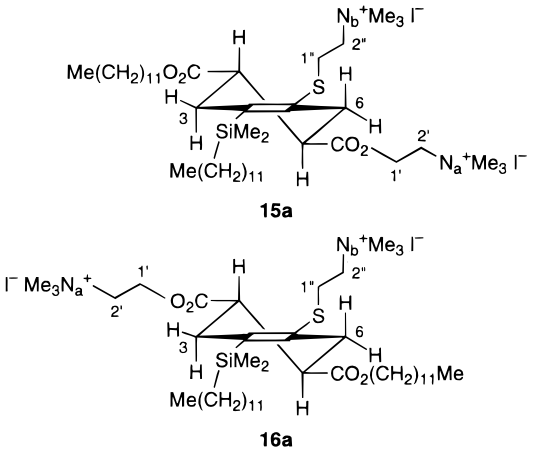


Figure 2. Half-chair conformations of **15a** and **16a** with diequatorial ester groups.

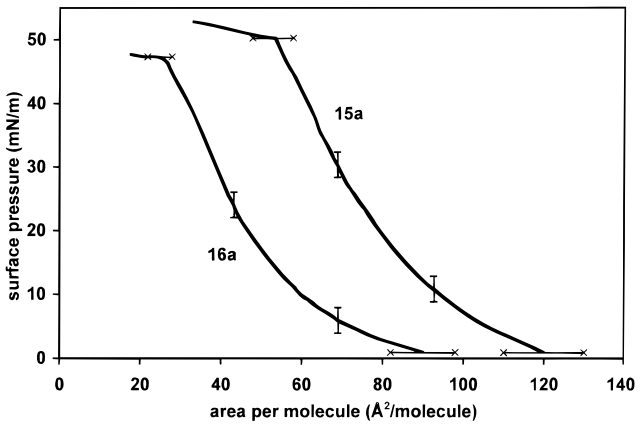


Figure 3. Surface pressure vs molecular area isotherms for the compression of monolayers of **15a** and **16a** on a pH 8.0 buffer (10.0 mM Tris, 1.0 M NaCl) subphase at 23 °C with a compression rate of 3 Å^2/min/molecule. Isotherms are representative of four different experiments; vertical bars correspond to mean ± σ, and horizontal bars to mean ± σ for molecular areas at lift-off and collapse.

The ^{1}H,^{1}H ROESY NMR results obtained in CD_3OD suggest that the major diastereomer is **15a**. An inspection of CPK molecular models indicates that interactions between the two chains bearing the N^+Me_3 groups are much more probable for **15a** than for **16a**, given their relative dispositions on the cyclohexene rings.

In the ^{1}H,^{1}H ROESY NMR spectrum (400 MHz) of the major diastereomer of the **15a**,**16a** pair in $CDCl_3$, a strong correlation was observed which corresponds to one of the hydrogens on carbon-3 interacting with one or both of the dodecyl chains. Only a weak correlation, if any, was observed between one of the hydrogens on carbon-6 or the hydrogen on carbon-4 with one or both of the dodecyl chains. In the^{1}H,^{1}H ROESY NMR spectrum (400 MHz) of the minor diastereomer of the **15a**,**16a** pair in $CDCl_3$, two correlations of comparable intensity were observed, which correspond to one or both of the hydrogens on each of carbon-3 and carbon-6 interacting with one or both of the dodecyl chains.

The ^{1}H,^{1}H ROESY NMR results obtained in $CDCl_3$ are consistent with the assignment of **15a** as the major cycloadduct. It is reasonable that a hydrogen on carbon-3 of **15a** interacts with one or both dodecyl chains, given the proximity of carbon-3 to the chain-bearing carbons, and that one or both hydrogens on each of carbon-3 and carbon-6 of **16a** interact with an alkyl chain, given the proximity of carbon-3 and carbon-6 to chain-bearing carbons.

The structural assignments for isomers **15b** and **16b** were made by analogy to those for **15a** and **16a**. The assignments for **15** and **16** are also consistent with their HPLC behavior and analogy to closely related systems.[5]

Monolayer Study. Surface pressure vs molecular area isotherms for **15a** and **16a** on a pH 8.0 buffer at 23 °C are illustrated in Figure 3. The two diastereomers gave decidedly different isotherms, with lift-off areas of 120 ± 10 and 90 ± 8 Å^2/molecule for **15a** and **16a**, respectively. At lift-off, molecules at the air−H_2O interface begin to interact with each other, and as compression continues, intermolecular interactions produce measurable surface pressures. For both **15a** and **16a**, the surface pressures increase monotonically after lift-off with decreasing area per molecule, until monolayer film collapse begins at ca. 50 and 47 mN/m, respectively. The limiting molecular areas (just prior to collapse) are ca. 93 and 61 Å^2/molecule for **15a** and **16a**, respectively.

It is interesting to consider the orientations of **15a** and **16a** with respect to the air−H_2O interface at their limiting molecular areas. At the outset, it is reasonable to assume that the hydrophilic quaternary ammonium headgroups are at the interface and the dodecyl chains are extended into the air. Now consider a compact conformation for each of **15a** and **16a** within which the two quaternary ammonium headgroups as well as the two fully extended dodecyl chains are side-by-side along a common axis, separated by the substituted cyclohexene ring.[19] It is unlikely that both **15a** and **16a** are in such a conformation, however, with the quaternary ammonium headgroups at the interface and the remaining structural units extended directly into the air. An inspection of CPK molecular models of these compact conformations clearly indicates that **15a** has a lesser cross sectional area than **16a**, opposite to the actual limiting molecular areas. The discrepancy between expectations based on these conformations and the experimental results may derive from a preference for the interface of one or both of the ester groups of **15a**, but not of **16a**. An ester group has a weak attraction for H_2O within a monolayer, relative to the strong attraction of a quaternary ammonium group.[20]

In summary, the Diels−Alder reaction of **1a** and **2a** gave a 30:1 ratio of cycloadducts **15a** and **16a**, respectively, and that of **1b** and **2b** a 6.6:1 ratio of **15b** and **16b**, respectively. The greater regioselectivity of the former reaction is ascribed to the shorter tether between **1a** and **2a**'s reactive functional groups and quaternary ammonium headgroups. Interfacial and related orientational effects associated with surfactant aggregation can impart substantial regioselectivity to a thermal cycloaddition reaction. In a monolayer study of **15a** and **16b**, the latter occupied less area per molecule at the air−H_2O interface.

Experimental Section

General Procedures and Materials. ^{1}H (400 MHz) and ^{13}C (100.6 MHz) NMR spectra were recorded in $CDCl_3$ unless noted otherwise with Me_4Si or $CHCl_3$ (δ 7.27 relative to Me_4Si) and $CDCl_3$ (center line at δ 77.00 relative to Me_4Si) as internal standards, respectively. ^{1}H and ^{13}C NMR spectra recorded in CD_3OD employed CD_2HOD (center line at δ 3.30 relative to Me_4Si) and CD_3OD (center line at δ 49.00 relative to Me_4Si) as internal standards, respectively. J values are in hertz. High-resolution FAB MS was performed at the Washington University Resource for Biomedical and Bioorganic Mass Spectrometry. GC-MS was performed with a 30 m × 0.25 mm (i.d.) capillary column

(19) See Figures 5a and 6 of ref 5a for analogous conformations of closely related cycloadducts **22** and **23**.

(20) Gaines, G. L., Jr. *Insoluble Monolayers at Liquid−Gas Interfaces*; Interscience: New York, 1966; pp 136−139.

(HP 190915-433) containing HP-5MS (cross-linked 5% Ph Me silicone; film thickness 0.25 μm). Medium-pressure liquid chromatography (MPLC) was performed with a Bæström Separo AB column packed (1.5 cm × 10 cm) with silica gel (EM 9385). Sonication was performed with a Branson 2200 (125 W) ultrasonic cleaner. The cac values, averages of two runs with different samples for each surfactant, were obtained from plots of surface tension (du Noüy ring) vs [surfactant] using a Fisher model 20 tensiometer. Krafft temperatures were determined according to a literature procedure.[21] Analytical and preparative reversed-phase HPLC were performed with evaporative light scattering detection (Sedex 55) on a 25-cm × 4.6-mm (i.d.) 8-μm C8 column (Rainin R0086300C8) and a 25-cm × 21.4-mm (i.d.) 8-μm C8 column (Rainin R0080320C8), respectively. Eluants were prepared with ammonium trifluroacetate and HPLC-grade H_2O, MeOH, MeCN, and CH_2Cl_2. Solvents were distilled and stored under N_2. Tetrahydrofuran (THF) was freshly distilled from benzophenone K ketyl. Pentane and hexanes were distilled from CaH_2 and stored over 4 Å molecular sieves; Et_3N was likewise distilled and stored over KOH. Both CH_2Cl_2 and C_6H_5Me were dried and stored over 4 Å molecular sieves. Extracts were dried over Na_2SO_4. All melting points were taken in open capillary tubes and are uncorrected. Ratios describing the compositions of solvent mixtures represent relative volumes. Elemental analyses were performed by Atlantic Microlab, Norcross, GA.

Bis[2-(*N*,*N*-Dimethylamino)ethyl] Disulfide (6a).[22] A solution of 2.22 g (24.5 mmol) of $NaClO_2$ in 35 mL of H_2O was added dropwise to a stirred solution of 4.56 g (32.2 mmol) of 2-(*N*,*N*-dimethylamino)-ethanethiol hydrochloride (**8**) (Aldrich) in 35 mL of MeOH held at 0−5 °C. After the reaction mixture was stirred at 25 °C for 30 min, it was rotary evaporated, and the residue was basified to pH 11 with aqueous 10% NaOH and extracted with three 60-mL portions of $CHCl_3$. The combined extracts were dried and rotary evaporated to leave 2.74 g (82%) of **6a**: ^{1}H NMR δ 2.79 (m, 4H, 2 CH_2S), 2.59 (m, 4H, 2 CH_2N), 2.26 (s, 12H, 2 $(CH_3)_2N$); ^{13}C NMR δ 58.98, 45.58, 37.15.

2-[2-(*N*,*N*-Dimethylamino)ethylthio]-3-dimethyldodecylsilyl-1,3-butadiene (7a). Into one side of a double round-bottom flask was placed 1.49 g (3.92 mmol) of 2,3-bis(trimethylstannyl)-1,3-butadiene (**3**)[8] in 7.0 mL of THF and into the other side, 0.808 g (3.88 mmol) of **6a** in 3.0 mL of THF. To the diene solution at −78 °C (dry ice−acetone) 3.10 mL (3.94 mmol) of 1.27 M MeLi in Et_2O was added dropwise over 8 min. The resultant yellow solution was stirred at −78 °C for 10 min, followed by the addition of a solution of 1.05 g (3.99 mmol) of chlorododecyldimethylsilane (**4a**) (Aldrich) in 3.0 mL of THF. After the reaction mixture was stirred at −78 °C for 20 min, 3.10 mL (3.94 mmol) of 1.27 M MeLi in Et_2O was added, followed by the addition of the **6a** solution in one portion. After the reaction mixture was stirred at −78 °C for 20 min, it was added to 50 mL of aqueous 1.5 M NaOH and extracted with three 50-mL portions of 1:1 Et_2O−pentane. The combined extracts were dried and rotary evaporated to give an oil that was chromatographed (MPLC) on silica gel with hexanes−EtOAc (100:0 to 20:80) as eluant to yield 0.198 g (13%) of **7a** as an oil: ^{1}H NMR δ 5.92 (d, J = 2.9, 1H, CH), 5.49 (d, J = 2.9, 1H, CH), 5.03 (s, 1H), 4.94 (s, 1H, CH), 2.78 (t, J = 7.5, 2H, CH_2S), 2.57 (m, 2H, CH_2N), 2.30 (s, 6H, $(CH_3)_2N$), 1.20−1.37 (m, 20H, $(CH_2)_{10}$), 0.89 (m, 3H, CH_3), 0.66 (m, 2H, CH_2Si), 0.15 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR δ 150.92, 147.17, 128.65, 108.43, 58.07, 45.27, 33.65, 31.67, 29.76, 29.74, 29.70, 29.65, 29.40, 29.39, 23.87, 22.74, 15.44, 14.17, −2.64. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{22}H_{46}NSSi$ (M + H) 384.3120, found 384.3110.

2-[[3-(Dimethyldodecylsilyl)-1,3-butadien-2-yl]thio]-*N*,*N*,*N*-trimethyl-1-ethanaminium Iodide (1a). A mixture of 0.198 g (0.516 mmol) of **7a**, 0.223 g (1.57 mmol) of MeI, and 15 mL of THF was stirred at 25 °C overnight and rotary evaporated to give 0.248 g (91%) of **1a** as an amorphous solid: ^{1}H NMR δ 5.95 (d, J = 2.6, 1H, CH), 5.55 (d, J = 2.6, 1H, CH), 5.21 (s, 1H, CH), 5.17 (s, 1H, CH), 3.69 (m, 2H, CH_2N), 3.55 (s, 9H, $(CH_3)_3N$), 3.04 (m, 2H, CH_2S), 1.25 (s, 20H, $(CH_2)_{10}$), 0.87 (t, 3H, CH_3), 0.62 (m, 2H, CH_2Si), 0.14 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR δ 150.31, 144.24, 130.00, 114.00, 65.70, 54.07, 33.56, 31.89, 29.59, 29.35, 29.33, 29.67, 29.62, 24.84, 23.77, 22.66, 15.24, 14.11, −2.65. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{23}H_{48}NSSi$ (cation) 398.3277, found 398.3276.

6-(*N*,*N*-Dimethylamino)-1-hexanol (10).[23] A modified literature procedure[24] was followed. A mixture of 11.4 g (83.7 mmol) of 6-chloro-1-hexanol (Aldrich) and 6.07 g (101 mmol) of *N*,*N*-dimethylhydrazine was held at 50 °C overnight, and the resultant waxlike solid was washed with Et_2O to give **9** that was used without further purification: ^{1}H NMR (CD_3OD) δ 3.57 (t, J = 6.4, 2H, CH_2O), 3.48 (m, 2H, CH_2N), 3.30 (s, 9H, $(CH_3)_3N$), 1.85 (m, 2H, CH_2CH$_2$N), 1.56 (m, 2H, CH_2CH$_2$O), 1.42 (m, 4H, CH_2CH_2). A solution of 17.4 g (0.252 mol) of $NaNO_2$ in 60 mL of H_2O was added dropwise to a solution of the above **9** in 60 mL of aqueous 4 M HCl held at 0−5 °C. After the resultant mixture was stirred at 5−10 °C for 1 h and then at 25 °C for 1 h, it was basified to pH 13.5 with 3 M NaOH and extracted three times with 80-mL portions of $CHCl_3$. The combined extracts were dried and rotary evaporated to leave a residue that was distilled (Kugelrohr) to give 8.78 g (72%) of **10** as an oil: ^{1}H NMR δ 3.64 (t, J = 6.6, 2H, CH_2O), 2.27 (t, J = 7.5, 2H, CH_2N), 2.22 (s, 6H, $(CH_3)_2N$), 1.58 (m, 2H, CH_2), 1.48 (m, 2H, CH_2), 1.36 (m, 4H, $(CH_2)_2$); ^{13}C NMR δ 62.73, 59.88, 45.63, 32.90, 27.73, 27.31, 25.83.

6-(*N*,*N*-Dimethylamino)-1-hexanethiol (12).[25] A modified literature procedure[26] was followed. A mixture of 4.85 g (33.4 mmol) of **10**, 3.12 g (41.0 mmol) of thiourea, and 11.4 mL (0.101 mol) of 48% hydrobromic acid was refluxed for 3.5 days to give **11**, which was not isolated. After 4.05 g (0.101 mol) of NaOH was added to the reaction mixture at 25 °C, it was refluxed for an additional 1.5 h. The organic phase was separated while the reaction mixture was still hot, and the aqueous phase was diluted with 45 mL of H_2O, basified to pH 13 with aqueous 3 M NaOH, and extracted with three 50-mL portions of $CHCl_3$. The combined organic phases were dried and rotary evaporated, and the residue was distilled (Kugelrohr) to give 4.20 g (78%) of **12** as an oil: ^{1}H NMR δ 2.53 (q, J = 7.4, 2H, CH_2S), 2.28 (t, J = 7.5, 2H, CH_2N), 2.23 (s, 6H, $(CH_3)_2N$), 1.63 (p, J = 7.3, 2H, $CH_2CH_2CH_2S$), 1.25−1.51 (m, 7H, $(CH_2)_3$, SH). GC MS *m*/*z* 161 (M), 128, 58.

Bis[6-(*N*,*N*-dimethylamino)hexyl] Disulfide (6b). A modified literature procedure[27] was followed. A solution of 4.21 g (26.1 mmol) of **12** in 40 mL of MeOH was added dropwise to a stirred solution of 1.79 g (19.8 mmol) of $NaClO_2$ in 60 mL of H_2O held at 0−5 °C. After the reaction mixture was stirred at 25 °C for 30 min, it was rotary evaporated, and the residue was diluted with 40 mL of H_2O, basified to pH 13 with 3 M NaOH, and extracted with three 60-mL portions of $CHCl_3$. The combined extracts were dried and rotary evaporated to leave 4.19 g (100%) of **6b** as an oil that was used without further purification: ^{1}H NMR δ 2.68 (t, J = 7.4, 4H, 2 CH_2S), 2.38 (t, J = 7.5, 4H, 2 CH_2N), 2.23 (s, 12H, 2 $(CH_3)_2N$), 1.69 (p, J = 7.4, 4H, 2 $CH_2CH_2CH_2S$), 1.48 (p, J = 7.4, Hz, 4H, 2 $CH_2CH_2CH_2N$), 1.25−1.45 (m, 8H, 2 $(CH_2)_2$); ^{13}C NMR δ 59.99, 45.71, 39.26, 29.35, 28.69, 27.83, 27.30. GC MS *m*/*z* 160, 128, 58.

2-[6-(*N*,*N*-Dimethylamino)hexylthio]-3-dimethyloctylsilyl-1,3-butadiene (7b). Into one side of a double round-bottom flask was placed 1.10 g (2.90 mmol) of **3** in 20.0 mL of THF and into the other side 0.605 g (2.90 mmol) of chlorodimethyloctylsilane (**4b**) (United Chemical Technologies) in 5.0 mL of THF. To the diene solution at −78 °C was added 2.20 mL (3.06 mmol) of 1.39 M MeLi in Et_2O dropwise over 4 min. After the resultant bright yellow solution was stirred at −78 °C for 20 min, it was transferred in one portion to the silane solution at −78 °C. The resultant colorless mixture was stirred for 40 min at −78 °C, followed by the dropwise addition over 10 min of 2.40 mL (3.34 mmol) of 1.39 M MeLi in Et_2O. The yellow solution, held at −78 °C, was stirred for 10 min, followed by the addition of 0.995 g (3.11 mmol) of **6b** in 5.0 mL of THF. The resultant colorless solution was stirred at −78 °C for 10 min and then poured into a mixture

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of 50 mL of aqueous 1.5 M NaOH and 100 mL of Et_2O. The organic layer was extracted with 1.5 M NaOH, dried, and rotary evaporated. The residue was chromatographed (MPLC) on silica gel with CH_2Cl_2−MeOH (100:0 to 80:20) as eluant to give 0.546 g (49%) of **7b** as a yellow oil: ^{1}H NMR δ 5.91 (d, J = 2.9, 1H, CH), 5.47 (d, J = 2.9, 1H, CH), 5.00 (s, 1H, CH), 4.84 (s, 1H, CH), 2.64 (t, J = 7.4, 2H, CH_2S), 2.29 (m, 2H, CH_2N), 2.26 (s, 6H, $(CH_3)_2N$), 1.64 (p, J = 7.4, 2H, CH_2CH$_2$S), 1.21−1.54 (m, 18H, $(CH_2)_6$, $(CH_2)_3$), 0.89 (t, J = 6.9, 3H, CH_3), 0.66 (m, 2H, CH_2Si), 0.14 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR δ 151.37, 148.00, 128.49, 107.60, 59.90, 45.54, 33.82, 32.16, 32.10, 29.51, 29.49, 29.19, 28.55, 27.61, 27.27, 24.05, 22.90, 15.64, 14.35, −2.45. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{22}H_{46}NSSi$ (M + H) 384.3120, found 384.3134.

6-[[3-(Dimethyloctylsilyl)-1,3-butadien-2-yl]thio]-*N,N,N*-trimethyl-1-hexanaminium Iodide (1b). A mixture 0.520 g (1.35 mmol) of **7b**, 0.57 g (4.0 mmol) of MeI, and 20 mL of THF was stirred at 25 °C overnight and rotary evaporated. The residue was chromatographed (MPLC) on silica gel with CH_2Cl_2−MeOH (100:0 to 88:12) as eluant to give 0.423 g (59%) of **1b** as an amorphous solid: ^{1}H NMR δ 5.90 (d, J = 2.9, 1H, CH), 5.47 (d, J = 2.9, 1H, CH), 5.01 (s, 1H, CH), 4.85 (s, 1H, CH), 3.62 (m, 2H, CH_2N), 3.47 (s, 9H, $(CH_3)_3N$), 2.64 (t, J = 7.1, 2H, CH_2S), 1.79 (m, 2H, CH_2CH$_2$N), 1.64 (p, J = 7.2, 2H, CH_2CH$_2$S), 1.40−1.55 (m, 4H, $(CH_2)_2$), 1.20−1.33 (m, 12H, $(CH_2)_6$), 0.88 (t, 3H, CH_3), 0.65 (m, 2H, CH_2Si), 0.14 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR δ 151.21, 147.59, 128.59, 108.10, 67.32, 53.97, 33.80, 32.14, 31.78, 29.50, 29.47, 28.64, 28.26, 25.67, 24.02, 23.31, 22.89, 15.60, 14.36, −2.44. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{23}H_{48}NSSi$ (cation) 398.3277, found 398.3282.

2-(*N,N*-Dimethylamino)ethyl Hydrogen Fumarate (13a). To a stirred mixture of 3.98 g (40.6 mmol) of maleic anhydride and 10 mL of C_6H_5Me at 25 °C was added 3.51 g (39.4 mmol) of 2-(*N,N*-dimethylamino)ethanol (Aldrich) dropwise over 15 min. The resultant dark purple reaction mixture was refluxed for 3.5 h and rotary evaporated. A slurry of the residue and 40 mL of CH_2Cl_2 was filtered, and the filtrate was rotary evaporated to leave a solid that was recrystallized from MeOH to give 3.60 g (47%) of **13a**: mp 90→130 °C; ^{1}H NMR (CD_3OD) δ 6.90 (d, J = 15.7, 1H, CH_a=CH$_b$), 6.52 (d, J = 15.7, 1H, CH$_a$=CH_b), 4.51 (m, 2H, CH_2O), 3.42 (m, 2H, CH_2N), 2.89 (s, 6H, $(CH_3)_2N$); ^{13}C NMR (CD_3OD) δ 172.74, 167.31, 143.34, 129.14, 59.35, 57.00, 43.38. Anal. Calcd for $C_8H_{13}NO_4\cdot H_2O$: C, 46.82; H, 7.37. Found: C, 46.63; H, 7.22.

2-(*N,N*-Dimethylamino)ethyl Dodecyl Fumarate (14a). A literature esterification procedure[28] was followed. A mixture of 1.24 g (6.62 mmol) of **13a**, 1.23 g (6.60 mmol) of 1-dodecanol, 1.50 g (7.27 mmol) of *N,N*′-dicyclohexylcarbodiimide (DCC), 88.7 mg (0.726 mmol) of 4-(*N,N*-dimethylamno)pyridine (DMAP), and 33 mL of CH_2Cl_2 was stirred under N_2 for 18 h and then filtered and rotary evaporated. The resultant oil was chromatographed (MPLC) on silica gel with hexanes−EtOAc−Et_3N (100:0:0 to 60:30:10) as eluant to give 1.24 g (53%) of **14a** as an oil: ^{1}H NMR δ 6.89 (AB, J = 15.8, 2H, CH=CH), 4.32 (t, J = 5.7, 2H, CH_2O), 4.19 (t, J = 6.7, 2H, CH_2O), 2.65 (t, J = 5.6, 2H, CH_2N), 2.32 (s, 6H, $(CH_3)_2N$), 1.68 (p, J = 7.0, 2H, CH_2CH$_2$O), 1.27 (m, 18H, $(CH_2)_9$), 0.89 (t, 3H, CH_3); ^{13}C NMR δ 165.27, 165.18, 134.17, 133.51, 65.71, 63.23, 57.83, 45.90, 32.10, 29.82, 29.75, 29.69, 29.53, 29.41, 28.69, 26.06, 22.88, 14.31. FAB HRMS (3-nitrobenzyl alcohol−glycerol−trifluoroacetic acid matrix) calcd for $C_{20}H_{38}NO_4$ (M + H) 356.2801, found 356.2810.

(*E*)-2-[[[2-(Dodecoxycarbonyl)ethenyl]carbonyl]oxy]-*N,N,N*-trimethyl-1-ethanaminium Iodide (2a). A mixture of 0.652 g (1.83 mmol) of **14a**, 0.798 g (5.62 mmol) of MeI, and 10 mL of MeCN was stirred under N_2 at 25 °C overnight and rotary evaporated. The residue was recrystallized from Et_2O-MeCN to give 0.640 g (70%) of **2a**: mp 147−149 °C (dec); ^{1}H NMR) δ 6.87 (AB, J = 15.8, 1H, CH=CH), 4.76 (m, 2H, OCH_2CH$_2$N), 4.28 (m, 2H, CH_2N), 4.20 (t, J = 6.8, 2H, CH_2O), 3.59 (s, 9H, $(CH_3)_3N$), 1.68 (p, J = 7.0, 2H, CH_2CH$_2$O), 1.26 (m, 18H, $(CH_2)_9$), 0.88 (t, 3H, CH_3); ^{13}C NMR δ 164.74, 164.19, 135.83, 131.85, 66.09, 65.14, 59.00, 55.06, 32.10, 29.83, 29.78, 29.71, 29.54, 29.43, 28.66, 26.03, 22.88, 14.33. FAB HRMS (3-nitrobenzyl alcohol−glycerol−trifluoroacetic acid matrix) calcd for $C_{21}H_{40}NO_4$ (cation) 370.2957, found 370.2962.

6-(*N,N*-Dimethylamino)hexyl Hydrogen Fumarate (13b). To a stirred mixture of 2.82 g (28.8 mmol) of maleic anhydride and 25 mL of C_6H_5Me at 25 °C was added dropwise during 10 min 4.35 g (30.0 mmol) of **10**. Then the reaction mixture was refluxed for 6 h and rotary evaporated, and the resultant oil was chromatographed (MPLC) on silica gel with CH_2Cl_2−MeOH−Et_3N (100:0:0 to 0:92:8) to yield 2.23 g (32%) of **13b**: mp 82−87 °C; ^{1}H NMR δ 6.95 (d, J = 15.7, 1H, CH_a=CH$_b$), 6.62 (d, J = 15.7, 1H, CH$_a$=CH_b), 4.17 (t, J = 5.9, 2H, CH_2O), 2.83 (m, 2H, CH_2N), 2.69 (s, 6H, $(CH_3)_2N$), 1.70 (m, 2H, CH_2), 1.64 (m, 2H, CH_2), 1.44 (m, 2H, CH_2), 1.34 (m, 2H, CH_2); ^{13}C NMR δ 171.55, 166.87, 141.32, 128.82, 64.27, 57.93, 42.80, 28.83, 26.91, 26.15, 25.12. Anal. Calcd for $C_{12}H_{21}NO_4\cdot 0.5H_2O$: C, 57.12; H, 8.79. Found: C, 57.37; H, 8.69.

6-(*N,N*-Dimethylamino)hexyl Octyl Fumarate (14b). A mixture of 1.75 g (7.19 mmol) of **13b**, 1.63 g (7.90 mmol) of DCC, 98.9 mg (0.810 mmol) of DMAP, 0.936 g (7.19 mmol) of 1-octanol, and 35 mL of CH_2Cl_2 was stirred under N_2 for 24 h and then filtered and rotary evaporated. The resultant oil was chromatographed (MPLC) on silica gel with hexanes−EtOAc−Et_3N (100:0:0 to 60:15:25) to yield 1.17 g (46%) of **14b** as an oil: ^{1}H NMR δ 6.82 (AB, J = 18.0, 2H, CH=CH), 4.19 (t, J = 6.8, 4H, 2 CH_2O), 2.29 (t, J = 7.5, 2H, CH_2N), 2.25 (s, 6H, $(CH_3)_2N$), 1.68 (m, 4H, 2 CH_2), 1.49 (p, J = 7.3, 2H, CH_2CH_2-CH_2), 1.21−1.44 (m, 14H, $(CH_2)_2$, $(CH_2)_5$), 0.88 (t, 3H, CH_3); ^{13}C NMR δ 165.32, 133.88, 133.78, 65.75, 65.59, 59.85, 45.59, 31.97, 29.37, 28.70, 28.68, 27.66, 27.25, 26.07, 22.84, 14.30. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{20}H_{38}NO_4$ (M + H) 356.2801, found 356.2773.

Diels−Alder Reactions. All Diels−Alder reactions were performed under N_2, and the results are summarized in Table 1. In each run, the total yield of cycloadducts was determined by ^{1}H NMR analysis of the crude mixture of products and unreacted starting materials, and the ratio of regioisomeric cycloadducts was determined, as described below, by one or more or the following methods: ^{1}H NMR analysis; HPLC analysis; masses of isolated regioisomers. The **15b**/**16b** ratios in some runs and the **18b**/**19b** ratios in others were obtained by both HPLC analysis and either ^{1}H NMR analysis or the masses of isolated regioisomers, respectively. Since the same regioisomer ratio was obtained in each instance by both methods, the relative response ratio for the **15b**,**16b** and **18b**,**19b** pairs in their HPLC analyses is 1:1. It is reasonably assumed that the relative response ratio in HPLC analysis of the **15a**,**16a** pair is also 1:1.

(a) 1a and 2a. The procedure for run 3 is as follows, and those for other runs were analogous. A mixture of 20.6 mg (0.0414 mmol) of **2a** and 3.0 mL of H_2O was sonicated at 45 °C for ca. 5 min to give a clear solution, followed by the addition of 0.45 mg (0.0027 mmol) of 4-*tert*-butylcatechol and 13.6 mg (0.0259 mmol) of **1a**. The resultant mixture was sonicated at 45 °C for 3 min and stirred at 25 °C for 48 h. Then the reaction mixture was diluted with MeCN and rotary evaporated at ca. 45 °C to leave an amorphous solid, which was analyzed by ^{1}H NMR (400 MHz, $CDCl_3$) and analytical HPLC (eluant = 0.020 M ammonium trifluroacetate in 85.5:9.5:5 MeCN−CH_2Cl_2−MeOH; flow rate = 1.0 mL/min; retention times = 3.5 min for **2a**, 4.2 min for **16a**, 4.7 min for **1a**, and 5.7 min for **15a**). The results are given in runs 1−4 of Table 1.

(b) 1b and 2b. The procedure for run 5 is as follows, and those for other runs were analogous. A mixture of 33.1 mg (0.0630 mmol) of **1b** and 3.0 mL of H_2O was sonicated at 25 °C for ca. 15 min to give a cloudy solution, followed by the addition of 122 mg (0.245 mmol) of **2b** and 1.0 mg (0.0060 mmol) of 4-*tert*-butylcatechol. The resultant mixture was stirred at 25 °C for 21 h, becoming clear by the end of this time. Then the reaction mixture was diluted with MeCN and rotary evaporated at ca. 45 °C to leave an amorphous solid, which was analyzed by ^{1}H NMR (400 MHz, $CDCl_3$) and analytical HPLC (eluant = 0.020 M ammonium trifluroacetate in 90:10 MeCN−H_2O; flow rate = 1.0 mL/min; retention times = 6.2 min for **16b** and 8.4 min for **15b**). Preparative HPLC afforded separated **15b** and **16b** (eluant = same as for analytical HPLC; flow rate = 20.0 mL/min; retention times = 7.8 min for **16b** and 8.8 min for **15b**). The results are given in runs 5−10 of Table 1. Controls demonstrated that any Diels−Alder reaction

(28) (a) Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, *19*, 4475. (b) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522.

of **1b** and **2b** during workup did not affect the **15b**/**16b** ratio and the yield of **15b** + **16b**.

(c) 1b and 2b with Sodium Salicylate. The procedure for run 13 is as follows, and those for other runs were analogous. A mixture of 10.9 mg (0.0207 mmol) of **1b** and 0.70 mL of H_2O was sonicated at 25 °C for ca. 15 min to give a cloudy solution, followed by the addition of 35.6 mg (0.0790 mmol) of **2b** and 0.78 mg (0.0047 mmol) of 4-*tert*-butylcatechol. After the resultant cloudy mixture was stirred at 25 °C for ca. 5 min, it became clear. Then 13.5 mg (0.0843 mmol) of sodium salicylate (Aldrich) was added to give a clear solution with greater viscosity that was stirred at 25 °C for 46 h. The reaction mixture was diluted with MeCN and rotary evaporated at ca. 45 °C to leave an amorphous solid, which was analyzed by ^{1}H NMR (400 MHz, $CDCl_3$) and analytical HPLC (eluant = 0.020 M ammonium trifluroacetate in MeCN−H_2O (80/20 to 95/5 during 20 min); flow rate = 1.0 mL/min; retention times = 6.6 min for **2b**, 18.8 min for **16b**, 19.8 min for **1b**, and 22.8 min for **15b**). The results are given in runs 11−14 of Table 1.

(d) 7a and 14a. The results for **7a** and **14a** are given in runs 15 and 16 of Table 1. The following procedure is for run 16, and that for run 15 was analogous. A solution of 54.0 mg (0.141 mmol) of **7a**, 114 mg (0.321 mmol) of **14a**, and 2.27 mg (0.0137 mmol) of 4-*tert*-butylcatechol in 2.15 mL of C_6H_5Me was stirred at 80 °C for 48 h. The reaction mixture was rotary evaporated to leave a heavy oil, which was chromatographed (MPLC) on silica gel with hexanes−EtOAc−Et_3N (100:0:0 to 70:28:2) as eluant to give 49.2 mg (47%) of *trans*-1-[2-(*N*,*N*-dimethylamino)ethylthio]-2-(dimethyldodecylsilyl)-4-[2-(*N*,*N*-dimethylamino)ethoxycarbonyl]-5-(dodecoxycarbonyl)-1-cyclohexene (**19a**) as a yellow oil, followed by 38.4 mg (37%) of *trans*-1-[2-(*N*,*N*-dimethylamino)ethylthio]-2-(dimethyldodecylsilyl)-4-(dodecoxycarbonyl)-5-[2-(*N*,*N*-dimethylamino)ethoxycarbonyl]-1-cyclohexene (**18a**) as an amorphous solid. For **18a**: ^{1}H NMR δ 4.28 (t, J = 5.6, 2H, $CH_2CH_2CH_2O$), 4.08 (m, 2H, OCH_2CH_2N), 2.18−2.98 (m containing s at 2.41, 24H, SCH_2CH_2N, OCH_2CH_2N, 2 $(CH_3)_2N$, 2 CH_2, 2 CH), 1.61 (m, 2H, $CH_2CH_2CH_2O$), 1.25 (m, 38H, $(CH_2)_9$, $(CH_2)_{10}$), 0.88 (t, 6H, 2 CH_3), 0.73 (m, 2H, CH_2Si), 0.17 (s, 3H, $(CH_3)_aSi(CH_3)_b$), 0.16 (s, 3H, $(CH_3)_aSi(CH_3)_b$); ^{13}C NMR δ 174.81, 174.26, 139.62, 138.05, 65.19, 62.03, 58.93, 57.47, 45.46, 44.94, 42.09, 41.67, 33.96, 33.93, 32.14, 29.97, 29.89, 29.85, 29.82, 29.79, 29.66, 29.58, 29.49, 28.81, 26.09, 24.26, 22.91, 16.49, 14.35, −1.34, −1.42. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{42}H_{83}N_2O_4SSi$ (M + H) 739.5843, found 739.5838. For **19a**: ^{1}H NMR δ 4.26 (t, J = 5.7, 2H, $CH_2CH_2CH_2O$), 4.08 (m, 2H, OCH_2CH_2N), 2.88−2.97 (m, 1H), 2.76−2.84 (m, 3H), 2.63−2.74 (m, 3H), 2.48−2.62 (m, 3H), 2.18−2.47 (m containing 2 s at 2.35 and 2.36, 14H total including 2 $(CH_3)_2N$), 1.60 (m, 2H, $CH_2CH_2CH_2O$), 1.25 (m, 38H, $(CH_2)_9$, $(CH_2)_{10}$), 0.88 (t, 6H, 2 CH_3), 0.73 (m, 2H, CH_2Si), 0.16 (s, 3H, $(CH_3)_aSi(CH_3)_b$), 0.15 (s, 3H, $(CH_3)_aSi(CH_3)_b$); ^{13}C NMR δ 174.94, 174.25, 139.55, 138.26, 65.28, 62.31, 59.09, 57.64, 45.61, 45.11, 42.18, 41.57, 33.95, 33.87, 32.12, 29.95, 29.87, 29.84, 29.76, 29.64, 29.56, 29.48, 28.93, 28.79, 26.08, 24.25, 22.90, 16.49, 14.33, −1.34, −1.44. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{42}H_{83}N_2O_4SSi$ (M + H) 739.5843, found 739.5839.

(e) 7b and 14b. The results for **7b** and **14b** are given in runs 17 and 18 of Table 1. The following procedure is for run 18, and that for run 17 was analogous. A solution of 66.5 mg (0.173 mmol) of **7b**, 152 mg (0.428 mmol) of **14b**, and 3.14 mg (0.0189 mmol) of 4-*tert*-butylcatechol in 1.5 mL of C_6H_5Me was stirred at 85 °C for 24 h. The reaction mixture was rotary evaporated to leave a heavy oil, which was analyzed by analytical HPLC (eluant = 0.020 M ammonium trifluroacetate in MeCN; flow rate = 1.0 mL/min; retention times = 6.0 min for **19b** and 7.7 min for **18b**) and then chromatographed (MPLC) on silica gel with hexanes−EtOAc−Et_3N (100:0:0 to 60:20:20) as eluant to give 46 mg (36%) of *trans*-1-[6-(*N*,*N*-dimethylamino)-hexylthio]-2-(dimethyloctylsilyl)-4-[6-(*N*,*N*-dimethylamino)hexoxycarbonyl]-5-(octoxycarbonyl)-1-cyclohexene (**19b**) as a heavy oil, followed by 43 mg (34%) of *trans*-1-[6-(*N*,*N*-dimethylamino)hexylthio]-2-(dimethyloctylsilyl)-4-(octoxycarbonyl)-5-[2-(*N*,*N*-dimethylamino)hexoxycarbonyl]-1-cyclohexene (**18b**) as a heavy oil. For **18b**: ^{1}H NMR δ 4.02−4.14 (m, 4H, 2 CH_2O), 2.83−2.92 (m, 1H), 2.21−2.79 (m containing s at 2.25, 23H total including 2 $(CH_3)_2NCH_2$), 1.41−1.69 (m, 10H, CH_2CH_2S, 2 CH_2CH_2O, 2 CH_2CH_2N), 1.27 (m, 30H, 2 $(CH_2)_2$, $(CH_2)_5$, $(CH_2)_6$), 0.89 (t, 6H, 2 CH_3), 0.73 (m, 2H, CH_2Si), 0.16 (s, 3H, $(CH_3)_aSi(CH_3)_b$), 0.15 (s, 3H, $(CH_3)_aSi(CH_3)_b$); ^{13}C NMR δ 175.06, 174.56, 139.35, 138.30, 65.06, 65.04, 59.98, 59.96, 45.69, 42.42, 41.94, 34.47, 34.19, 33.92, 32.17, 32.14, 32.01, 30.00, 29.92, 29.59, 29.55, 29.43, 29.27, 28.81, 28.78, 27.82, 27.33, 26.09, 26.06, 24.27, 22.91, 22.86, 16.49, 14.35, 14.31, −1.35, −1.43. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{42}H_{83}N_2O_4SSi$ (M + H) 739.5843, found 739.5834. For **19b**: ^{1}H NMR δ 4.02−4.14 (m, 4H, 2 CH_2O), 2.83−2.92 (m, 1H), 2.20−2.79 (m containing s at 2.25, 23H total including 2 $(CH_3)_2NCH_2$), 1.41−1.68 (m, 10H, CH_2CH_2S, 2 CH_2CH_2O, 2 CH_2CH_2N), 1.28 (m, 30H, 2 $(CH_2)_2$, $(CH_2)_5$, $(CH_2)_6$), 0.89 (t, 6H, 2 CH_3), 0.74 (m, 2H, CH_2Si), 0.16 (s, 3H, $(CH_3)_aSi(CH_3)_b$), 0.15 (s, 3H, $(CH_3)_aSi(CH_3)_b$); ^{13}C NMR δ 175.07, 174.54, 139.38, 138.23, 65.14, 64.95, 59.97, 45.68, 42.42, 41.92, 34.43, 34.19, 33.92, 32.17, 32.12, 32.01, 30.02, 29.92, 29.58, 29.55, 29.43, 29.27, 28.80, 27.83, 27.33, 26.08, 24.27, 22.90, 22.86, 16.49, 14.35, 14.31, −1.34, −1.43. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{42}H_{83}N_2O_4SSi$ (M + H) 739.5843, found 739.5837.

***trans*-1-[(2-Trimethylammonio)ethylthio]-2-(dimethyldodecylsilyl)-4-(dodecoxycarbonyl)-5-[(2-trimethylammonio)ethoxycarbonyl]-1-cyclohexene Diiodide (15a).** A mixture of 38.3 mg (0.0518 mmol) of **18a**, 72.5 mg (0.511 mmol) of MeI, and 2.0 mL of MeCN was stirred at 25 °C under N_2 overnight and then rotary evaporated to leave 52.3 mg (99%) of **15a** as an amorphous solid: ^{1}H NMR δ 4.69 (m, 2H, OCH_2CH_2N), 4.28 (m, 2H, OCH_2CH_2N), 4.06 (m, 2H, $CH_2CH_2CH_2O$), 3.70 (m, 2H, SCH_2CH_2N), 3.57 (s, 18H, 2 $(CH_3)_3N$), 3.24 (m, 2H, SCH_2CH_2N), 3.06 (m, 1H), 2.89 (m, 2H), 2.71 (m, 1H), 2.60 (m, 1H), 2.23 (m, 1H), 1.61 (m, 2H, $CH_2CH_2CH_2O$), 1.26 (m, 38H, $(CH_2)_9$, $(CH_2)_{10}$), 0.89 (t, 6H, 2 CH_3), 0.71 (m, 2H, CH_2Si), 0.19 (s, 3H, $(CH_3)_aSi(CH_3)_b$), 0.18 (s, 3H, $(CH_3)_aSi(CH_3)_b$); ^{13}C NMR δ 174.78, 173.52, 141.38, 136.34, 66.43, 65.25, 65.12, 58.47, 54.96, 54.25, 41.72, 41.37, 34.78, 34.07, 33.91, 32.04, 29.90, 29.81, 29.77, 29.61, 29.49, 29.43, 28.72, 26.03, 25.04, 24.14, 22.81, 16.45, 14.26, −1.31, −1.43. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{44}H_{88}N_2O_4SSiI$ (monocation·I^-) 895.5280, found 895.5257.

***trans*-1-[(2-Trimethylammonio)ethylthio]-2-(dimethyldodecylsilyl)-4-[(2-trimethylammonio)ethoxycarbonyl]-5-(dodecoxycarbonyl)-1-cyclohexene Diiodide (16a).** From **19a**, the same procedure as for **15a** gave (98%) **16a** as an amorphous solid: ^{1}H NMR δ 4.81 (m, 1H, $OCH_aH_bCH_2N$), 4.41 (m, 1H, $OCH_aH_bCH_2N$), 3.98−4.14 (m, 4H, OCH_2CH_2N, $CH_2CH_2CH_2O$), 3.81 (m, 1H, $SCH_2CH_aH_bN$), 3.51−3.63 (2 s at 3.55 and 3.59, overlapping with m, 19H, 2 $(CH_3)_3N$, $SCH_2CH_aH_bN$), 3.10−3.36 (m, 3H), 3.00 (m, 1H), 2.70 (m, 2H), 2.51 (m, 1H), 2.39 (m, 1H), 1.63 (m, 2H, $CH_2CH_2CH_2O$), 1.26 (m, 38H, $(CH_2)_9$, $(CH_2)_{10}$), 0.88 (t, 6H, 2 CH_3), 0.69 (m, 2H, CH_2Si), 0.19 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR δ 174.37, 173.80, 143.32, 134.85, 66.44, 65.81, 65.46, 58.09, 55.31, 54.09, 41.59, 40.80, 33.98, 33.58, 33.38, 32.15, 29.98, 29.95, 29.91, 29.82, 29.67, 29.59, 28.80, 26.16, 24.16, 24.03, 22.92, 16.71, 14.37, −1.10, −1.17. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{44}H_{88}N_2O_4SSiI$ (monocation·I^-) 895.5280, found 895.5286.

***trans*-1-[(6-Trimethylammonio)hexylthio]-2-(dimethyloctylsilyl)-4-(octoxycarbonyl)-5-[(6-trimethylammonio)hexoxycarbonyl]-1-cyclohexene Diiodide (15b).** A mixture of 15.0 mg (0.0203 mmol) of **18b**, 17.7 mg (0.125 mmol) of MeI, and 0.80 mL of MeCN was stirred at 25 °C under N_2 overnight. The residue after rotary evaporation was purified by TLC (0.25-mm aluminum oxide; EM 5731-3) with 60:38:2 MeCN−CH_2Cl_2−MeOH as eluant to give 12.3 mg (59%) of **15b** as an amorphous solid: ^{1}H NMR δ 4.00−4.24 (m, 4H, 2 CH_2O), 3.69−3.80 (m, 4H, 2 CH_2N), 3.46 (s, 18H, 2 $(CH_3)_3N$), 2.87−2.94 (m, 1H), 2.18−2.79 (m, 7H), 1.76−1.89 (m, 4H, 2 CH_2CH_2N), 1.20−1.72 (m, 36H, 2 $(CH_2)_3$, $(CH_2)_6$), 0.89 (t, 6H, 2 CH_3), 0.72 (m, 2H, CH_2Si), 0.17 (s, 3H, $(CH_3)_aSi(CH_3)_b$), 0.16 (s, 3H, $(CH_3)_aSi(CH_3)_b$); ^{13}C NMR δ 175.09, 174.52, 139.23, 138.40, 66.90, 65.09, 64.61, 54.00, 42.22, 41.74, 34.28, 33.94, 33.88, 32.14, 31.97, 31.88, 29.93, 29.54, 29.50, 29.39, 28.76, 28.70, 28.40, 26.05, 25.69, 25.42, 24.21, 23.26, 23.13, 22.87, 22.83, 14.35, 14.30, −1.39, −1.45. FAB HRMS (3-nitrobenzyl alcohol-glycerol-trifluoroacetic acid matrix) calcd for $C_{44}H_{88}N_2O_4SSiI$ (monocation·I^-) 895.5280, found 895.5255.

***trans*-1-[(6-Trimethylammonio)hexylthio]-2-(dimethyloctylsilyl)-4-[(6-trimethylammonio)hexoxycarbonyl]-5-(octoxycarbonyl)-1-cy-**

clohexene Diiodide (16b). From **19b**, the same procedure as for **15b** gave (52%) **16b** as an amorphous solid: ^{1}H NMR δ 4.14−4.25 (m, 1H, CH_aH$_b$O), 3.99−4.09 (m, 3H, CH$_a$$H_bO, CH_2$O), 3.71−3.80 (m, 2H, CH$_2$N), 3.63−3.71 (m, 2H, CH$_2$N), 3.49 (s, 9H, (CH$_3$)$_3$N), 3.47 (s, 9H, (CH$_3$)$_3$N), 2.89−2.98 (m, 1H), 2.75−2.82 (1H), 2.28−2.66 (m, 6H), 1.75−1.90 (m, 4H, 2 CH_2CH$_2$N), 1.20−1.70 (m, 36H, 2 (CH$_2$)$_3$, (CH$_2$)$_6$), 0.89 (t, 3H, CH$_3$), 0.88 (t, 3H, CH$_3$), 0.74 (m, 2H, CH$_2$Si), 0.19 (s, 3H, (CH_3)$_a$Si(CH$_3$)$_b$), 0.18 (s, 3H, (CH$_3$)$_a$Si(CH_3)$_b$); ^{13}C NMR δ 174.71, 174.68, 139.06, 138.49, 66.94, 65.39, 64.55, 53.95, 53.93, 42.35, 41.84, 33.99, 33.88, 33.53, 32.14, 31.97, 31.36, 29.98, 29.53, 29.50, 29.42, 29.37, 28.74, 28.36, 26.09, 25.76, 25.58, 25.46, 24.18, 23.31, 23.00, 22.87, 22.84, 14.36, 14.33, −1.33, −1.44. FAB HRMS (3-nitrobenzyl alcohol−glycerol−trifluoroacetic acid matrix) calcd for $C_{44}H_{88}N_2O_4SSiI$ (monocation·I$^-$) 895.5280, found 895.5277.

^{1}H,^{1}H ROESY NMR Spectroscopy. Experiments were performed on a 400 MHz Bruker Avance DRX-400 instrument at 18 °C with degassed (N_2) CD_3OD and $CDCl_3$ solutions of **15a** and **16a.** In the ROESY pulse sequence the relaxation delay was 2.000 s, and the spin-lock duration was 250.000 ms.

Monolayer Study. A Langmuir trough with a computer-controlled ribbon barrier (Labcon, Darlington, UK) was used.[29] The freshly cleaned trough was filled with a pH 8.0 buffer (10 mM Tris, 1.0 M NaCl), chosen to maximize the insolubility of the monomolecular films. After equilibration of the subphase for 30 min at 23 °C, a $CHCl_3$ solution of **15a** or **16a** was deposited at the air/buffer interface to an initial area of 125 or 95 Å^2/molecule, respectively. Following a 15-min interval for solvent evaporation, the monolayers were compressed at 3 Å^2/molecule/min. Monolayers for which compression was stopped between lift-off and collapse maintained constant surface pressures within 2.5 mN/m for 15 min, confirming their insolubility. Other details of the monolayer protocol have been described previously.[29] The results are given in Figure 3.

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Supporting Information Available: ^{1}H (400 MHz) and ^{13}C NMR (100.6 MHz) spectra of **1**, **2a**, **6**, **7**, **10**, **14**−**16**, **18**, and **19**; ^{1}H NMR (400 MHz) spectra of **9** and **12**; ^{1}H,^{1}H COSY NMR (440 MHz) and ^{1}H,^{1}H ROESY NMR (400 MHz) spectra of **15a** and **16a** in CD_3OD and $CDCl_3$. This information is available free of charge via the Internet at http://pubs.acs.org.

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