Regioselectivity of Diels–Alder Reactions of a Surfactant 1,3-Diene with Surfactant Dienophiles†

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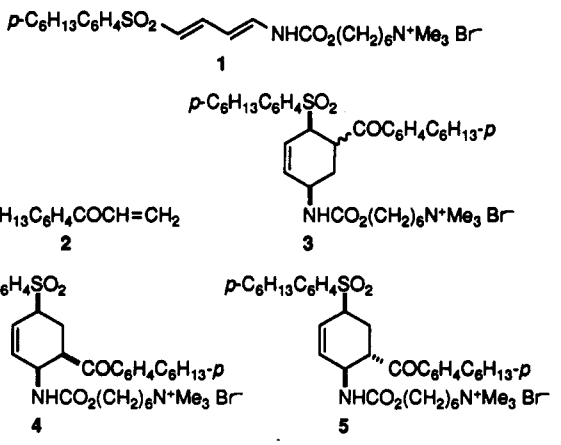
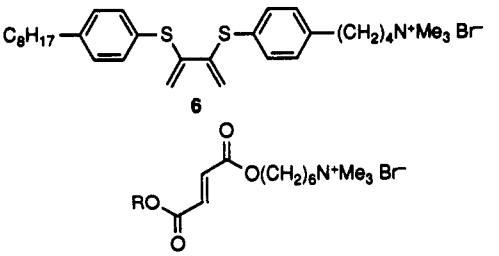
The ability of aqueous surfactant aggregates to control the regiochemistry of Diels–Alder reactions was investigated with surfactant 1,3-diene 4-[*p*-[[3-[(*p*-octylphenyl)thio]-1,3-butadien-2-yl]thio]-phenyl]-*N,N,N*-trimethyl-1-butanaminium bromide (**6**), derived *in situ* by thermal extrusion of SO_2 from 4-[[[1,1-dioxo-4-[(*p*-octylphenyl)thio]-2,5-dihydrothiophen-3-yl]thio]phenyl]-*N,N,N*-trimethyl-1-butanaminium bromide (**8**), and surfactant dienophiles (*E*)-6-[[[2-(alkoxycarbonyl)ethenyl]carbonyl]-oxy]-*N,N,N*-trimethyl-1-hexanaminium bromide (**7**) (**a**, R = Me; **b**, R = Bu; **c**, R = C_8H_{17}). In each case an excess of 1-[[*p*-[(4-trimethylammonio)butyl]phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-(alkoxycarbonyl)-5-[[6-(trimethylammonio)hexoxy]carbonyl]-1-cyclohexene dibromide (**16**) over 1-[[*p*-[(4-trimethylammonio)butyl]phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-[[6-(trimethylammonio)hexoxy]-carbonyl]-5-(alkoxycarbonyl)-1-cyclohexene dibromide (**17**) was obtained, consistent with the reaction of **6** and **7** within a mixed aggregate in their preferred orientations at the aggregate–H_2O interface. The cyclohexene rings of **16** and **17** have different conformational character in chloroform resulting from supramolecular effects within reversed micelles.

The Diels–Alder reaction is one of the most important reactions in organic synthesis.[1] There have been numerous studies of Diels–Alder chemistry performed in H_2O and in aqueous surfactant-based media.[2] The focus of these studies generally has been the dramatic rate and stereoselectivity enhancements observed relative to results obtained in conventional organic solvents. The ability of surfactant-based media to influence the regioselectivity of Diels–Alder reactions has received little attention.[3] In the study reported herein we have addressed the following question: Can the regioselectivity of Diels–Alder reactions be controlled by the alignment of reactants at surfactant aggregate–H_2O interfaces?[4]

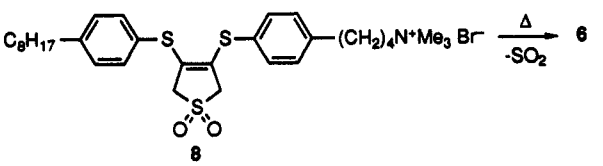
Previously, we reported a study[3] of the Diels–Alder reaction of surfactant 1,3-diene **1** with dienophile **2** in both aqueous and reversed micelles. If **1** and **2** had reacted in their preferred orientations within the surfactant aggregates, cycloadduct **3** would have resulted. In fact, in both micellar media *endo*-**4** and *exo*-**5** were obtained as the major products, which correspond to the theoretically predicted regioisomers.[5] The reaction of a nonsurfactant analogue of **1** with **2** gave exclusively the endo Diels–Alder product of the same regiochemistry. Although the reaction of **1** and **2** gave an indication of the formation of a minor amount of **3**, it is clear that the orientational effects in the aggregates were not strong enough to overcome the reaction's intrinsically preferred regiochemistry.

In the present study we have investigated the ability of aqueous surfactant aggregates to control the regioselectivity of Diels–Alder reactions of surfactant 1,3-diene **6** with dienophiles **7**. Diene **6** was derived *in situ* from surfactant sulfone **8** by thermal extrusion of SO_2 as illustrated. This Diels–Alder system should display no regiochemical bias in the absence of orientational effects since the substituents at carbons 2 and 3 within **6** and those at carbons 1 and 2 within **7** are close to being both electronically and sterically equivalent with respect to the diene and dienophile reaction centers, respectively.





7a, R = Me; **b**, R = Bu; **c**, R = C_8H_{17}



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† Dedicated to the memory of Professor Sara Jane Rhoads (deceased May 1, 1993).

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(1) For reviews, see: (a) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63. (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10.

(2) For examples, see: (a) Blokzijl, W.; Blandamer, M. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1991**, *113*, 4241. (b) Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1991**, *113*, 7430. (c) Braun, R.; Schuster, F.; Sauer, J. *Tetrahedron Lett.* **1986**, *27*, 1285 and references cited therein.

(3) Jaeger, D. A.; Shinozaki, H.; Goodson, P. A. *J. Org. Chem.* **1991**, *56*, 2482.

(4) Some of these results have been communicated (Jaeger, D. A.; Wang, J. *Tetrahedron Lett.* **1992**, *33*, 6415).

(5) Kahn, S. D.; Pau, C. F.; Overman, L. E.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7381.

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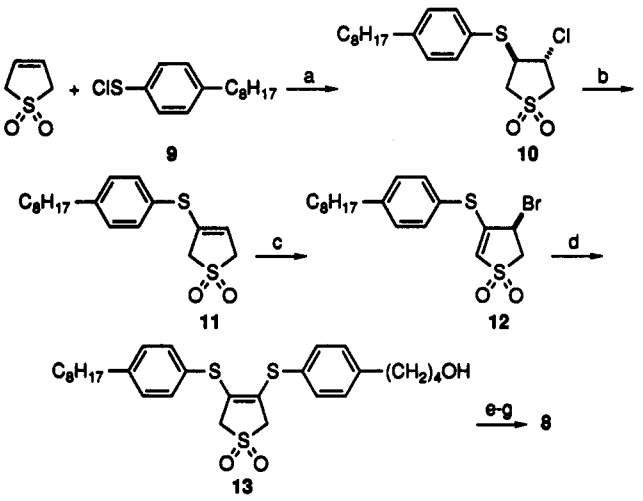
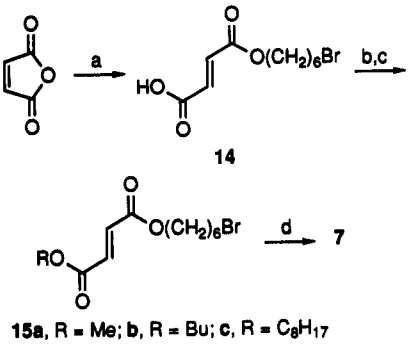
Scheme I[a]



[a]Key: (a) $CHCl_3$; (b) DBU, $CHCl_3$; (c) NBS, MeCN; (d) *p*-$HSC_6H_4(CH_2)_4OH$, NaOH, MeOH; (e) $MeSO_2Cl$, CH_2Cl_2; (f) LiBr, THF; (g) Me_3N, MeOH.

Scheme II[a]



15a, R = Me; **b**, R = Bu; **c**, R = C_8H_{17}

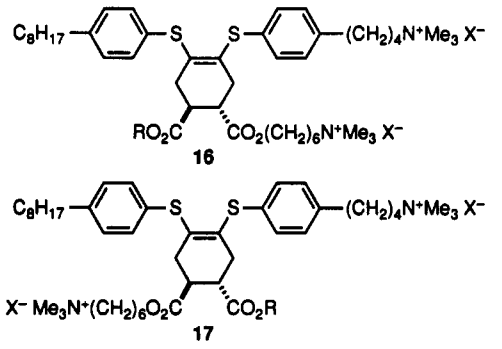
[a]Key: (a) $Br(CH_2)_6OH$, C_6H_5Me; (b) $SOCl_2$; (c) ROH, Et_3N: **a**, R = Me; **b**, R = Bu; **c**, R = C_8H_{17}; (d) Me_3N, MeCN.

Results and Discussion

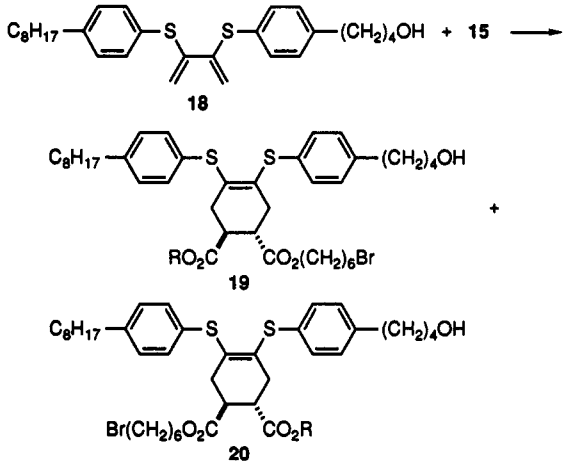
Syntheses. The synthesis of **8** is summarized in Scheme I. The addition of sulfenyl chloride **9** to 2,5-dihydrothiophene 1,1-dioxide gave *trans* chloro sulfone **10**. DBU-catalyzed dehydrochlorination of this material yielded **11**, which was converted into **12** by reaction with *N*-bromosuccinimide (NBS). Displacement of bromide by the conjugate base of the indicated substituted thiophenol gave alcohol **13** after rearrangement. Then **13** was converted into surfactant **8** through the corresponding bromide. The critical micelle concentration (cmc) of **8** in H_2O at 25 °C is 3.7×10^{-5} M.

The synthesis of dienophiles **7** is summarized in Scheme II. The reaction of 6-bromo-1-hexanol with maleic anhydride gave *trans* mono ester **14**. This material was converted into the acid chloride, which gave bromo diesters **15** on reaction with the corresponding alcohols. Then **15** was converted into **7**. Compound **7a** did not display a detectable cmc in H_2O at 25 °C up to 0.11 M. The cmc's of **7b** and **7c** under the same conditions are 5.3×10^{-2} and 4.0×10^{-3} M, respectively.

Diels–Alder Reactions. Reactions of **7** and **8** were performed in a pH 7.0 phosphate buffer with added 4-*tert*-butylcatechol at 100 or 130 °C (sealed tubes). In each case the molar ratio of **7** to **8** was 4:1. Under these conditions **8** is transformed into **6**, which undergoes Diels–Alder reaction with **7** to give regioisomers **16** and **17**. The reaction mixtures, diluted with MeCN, were analyzed by calibrated reversed-phase HPLC to give the **16**/**17** ratios, and then they were worked up to give the **16** + **17** yields, followed by preparative HPLC to afford **16** and **17** with $X^- = ClO_4^-$. The results are summarized in runs 1–16 of Table I.



Reactions of **13** and **15** were performed in C_6H_5Me with added 4-*tert*-butylcatechol at 130 °C (sealed tubes) to establish the regioselectivities that would likely result from reactions of **6** and **7** in the absence of orientational effects within surfactant aggregates. Under these conditions **13** is converted into **18**, which undergoes Diels–Alder reaction with **15** to give regioisomers **19** and **20**. The reaction mixtures were worked up and the product mixtures analyzed by reversed-phase HPLC. Base line separation of the regioisomers was obtained only for **19c** and **20c**, with the **19c**/**20c** ratio = 1.0. Partial resolution was obtained for **19a** and **20a** and for **19b** and **20b**, with an estimated regioisomer ratio of 1 in each case. Preparative HPLC gave **19c** and **20c**. The results are summarized in runs 17–22 of Table I.



As noted above, the cmc of **8** in H_2O at 25 °C is 3.7×10^{-5} M. The cmc's at 100 and 130 °C in the pH 7.0 buffer should be somewhat, but not significantly, higher. In general, cmc's do not increase much with temperature.[6] For example, the cmc's of hexadecyltrimethylammonium bromide are 0.955×10^{-3} and 6.12×10^{-3} m at 25 and 130 °C, respectively.[6a] Also, at a given temperature the salts of the buffer will reduce the cmc relative to its value in

(6) (a) Evans, D. F.; Allen, M.; Ninham, B. W.; Fouda, A. *J. Solution Chem.* **1984**, *13*, 87. (b) Jaeger, D. A.; Mohebalian, J.; Rose, P. L. *Langmuir* **1990**, *6*, 547.

Table I. Diels–Alder Reactions

	diene precursor		dienophile						
run	nature	concn, M	nature	concn, M	medium[a,b]	reactn temp, °C	reactn time, h	% yield[c]	regioisomer ratio[d]
1	**8**	0.10	**7a**	0.40	buffer	100	40	41	1.6:1
2	**8**	0.10	**7a**	0.40	buffer	100	40	47	1.7:1
3	**8**	0.10	**7b**	0.40	buffer	100	40	66	2.4:1
4	**8**	0.10	**7b**	0.40	buffer	100	40	67	2.4:1
5	**8**	0.10	**7c**	0.40	buffer	100	40	94	2.9:1
6	**8**	0.10	**7c**	0.40	buffer	100	40	84	3.0:1
7	**8**	0.10	**7a**	0.40	buffer	130	2	57	1.4:1
8	**8**	0.10	**7a**	0.40	buffer	130	2	63	1.4:1
9	**8**	0.10	**7b**	0.40	buffer	130	2	76	1.9:1
10	**8**	0.10	**7b**	0.40	buffer	130	2	85	2.0:1
11	**8**	0.10	**7c**	0.40	buffer	130	2	80	2.6:1
12	**8**	0.10	**7c**	0.40	buffer	130	2	90	2.6:1
13	**8**	0.10	**7c**	0.40	buffer	130	1		2.7:1
14	**8**	0.10	**7c**	0.40	buffer	130	1		2.7:1
15	**8**	0.010	**7c**	0.040	buffer	130	2	94	2.6:1
16	**8**	0.010	**7c**	0.040	buffer	130	2	72	2.8:1
17	**13**	0.10	**15a**	0.41	C_6H_5Me	130	2	41	1:1
18	**13**	0.12	**15a**	0.49	C_6H_5Me	130	2.5	36	1:1
19	**13**	0.20	**15b**	0.81	C_6H_5Me	130	2.5	26	1:1
20	**13**	0.21	**15b**	0.84	C_6H_5Me	130	2.5	28	1:1
21	**13**	0.18	**15c**	0.74	C_6H_5Me	130	2	52	1:1
22	**13**	0.095	**15c**	0.45	C_6H_5Me	130	2.5	49	1:1

[a] Buffer = pH 7.0 phosphate buffer (0.063 M). [b] The reaction mixtures in the buffer and C_6H_5Me contained 0.002–0.02 M and 0.02–0.16 M 4-*tert*-butylcatechol, respectively. [c] **16** + **17** in runs 1–16 or **19** + **20** in runs 17–22. [d] **16**/**17** in runs 1–16 or **19**/**20** in runs 17–22.

H_2O alone.[7] Thus, it is likely that runs 1–14, with 0.10 M **8**, and even runs 15 and 16, with 0.010 M **8**, were performed well above the cmc's of **8** at 100 and 130 °C. Furthermore, the cmc's of **6** at the two temperatures are almost certainly comparable to those of **8**, or perhaps even lower, since **6** does not contain the polar sulfone group. On the basis of the above considerations, it is probable that runs 5, 6, and 11–16 were performed above the cmc's of **7c** at 100 and 130 °C. But the situation is unclear for **7a** (runs 1, 2, 7, and 8) and **7b** (runs 3, 4, 9, and 10), whose cmc's are >0.11 and 5.3×10^{-2} M, respectively, at 25 °C in H_2O as noted above.

The reaction of **6** and **7** gave an excess of **16** over **17** in every case (runs 1–16). The former is indeed the expected regioisomer if **6** and **7** react in their preferred orientations within a mixed micelle, with the quaternary ammonium head groups at the aggregate–H_2O interface and the remainder of each extended into the micelle interior. These orientations for *s-cis*-**6** and **7c** 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.[8] Cycloadduct **17** results from the reaction of misaligned **6** and **7** within the mixed micelles and/or within the bulk aqueous phase. The former could reasonably involve **6** and **7** with their 1,3-diene and polar dienophile units, respectively, looped to the aggregate–H_2O interface. It is known that aromatic groups can associate with quaternary ammonium head groups.[9] The latter involves **6** and **7** in monomeric and/or premicellar forms.[10] The orientational effects in both are expected to be less than within the mixed micelles. The 4-*tert*-butylcatechol in each reaction mixture likely resides at

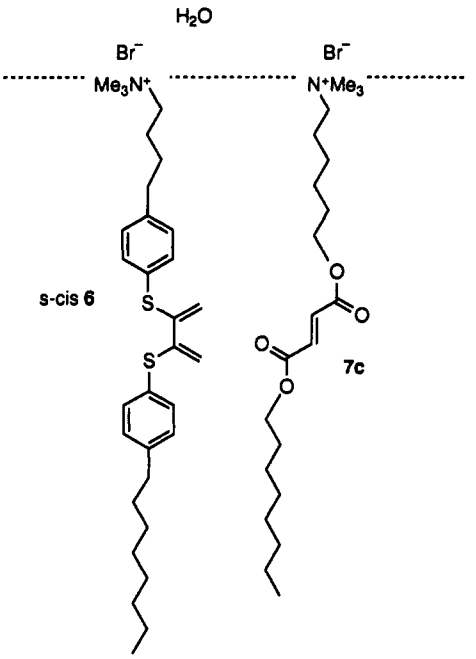


Figure 1. Preferred orientations of *s-cis*-**6** and **7c** at a surfactant aggregate–H_2O interface.

the aggregate–H_2O interface, resulting in an indeterminate effect, if any, on the **16**/**17** ratio.

In runs 1–6 at 100 °C the **16**/**17** ratio and the **16** + **17** yield increased going from **7a** to **7b** to **7c**. The trend in the **16**/**17** ratio results from the increasing lipophilic character of the alkyl substituent and is consistent with (a) an increasing population of the preferred orientation of **7** within the mixed micelles and (b) an increasing fraction of **7** incorporated into the mixed micelles, resulting in a decreasing fraction of the reaction occurring in the bulk aqueous phase. The increasing **16** + **17** yields going from **7a** to **7b** to **7c** are consistent with a greater reaction rate for micellar than for monomeric **6** and **7** in these presumed second-order reactions.[11] The effective concentrations of **6** and **7** within a mixed micelle are greater than those in the bulk aqueous phase.

(7) Heckmann, K.; Schwarz, R.; Strnad, J. *J. Colloid Interface Sci.* **1987**, *120*, 114.
(8) (a) Menger, F. M.; Dulany, M. A.; Carnahan, D. W.; Lee, L. H. *J. Am. Chem. Soc.* **1987**, *109*, 6899. (b) Menger, F. M.; Doll, D. W. *J. Am. Chem. Soc.* **1984**, *106*, 1109 and references cited therein.
(9) For examples, see: Bacaloglu, R.; Bunton, C. A.; Cerichelli, G.; Ortega, F. *J. Phys. Chem.* **1989**, *93*, 1490 and references cited therein.
(10) Bunton, C. A.; Bacaloglu, R. *J. Colloid Interface Sci.* **1987**, *115*, 288.

In runs 7–12 at 130 °C the 16/17 ratio increased going from 7a to 7b to 7c, but the values were less than those in runs 1–6 at 100 °C. The lesser regioselectivity in the former runs probably resulted from decreased populations of the preferred orientations of 6 and 7 within the mixed micelles at the higher temperature. As in runs 1–6, the 16 + 17 yield increased going from 7a to 7b to 7c.

Runs 15 and 16 were made with reagent concentrations 10 times less than those in runs 11 and 12. Nevertheless, the 16/17 ratios were identical and the 16 + 17 yields comparable under the two conditions. These facts are consistent with most of the Diels–Alder reaction occurring within mixed micelles in each run.

As formed, 16 and 17 are no doubt incorporated into the mixed surfactant aggregates of 6–8. Thus, the nature of the aggregates changes during the course of the reaction. Note that the same 16/17 ratio was obtained in runs 13 and 14 as in runs 11 and 12, indicating that the regioisomer ratio does not change with time at 130 °C. Apparently, regiochemical control in these Diels–Alder reactions derives from interfacial effects that are insensitive to aggregate composition. At present it is not known whether the 16/17 ratios are kinetically or thermodynamically controlled.

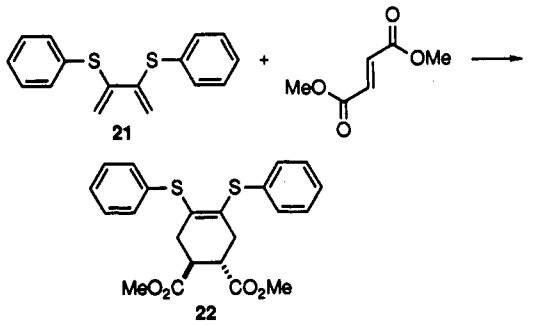
As noted above, the Diels–Alder reactions of nonsurfactant analogues 15 and 18 yielded regioisomers 19 and 20 in equal amounts in runs 17–22. Thus, in the absence of significant reagent aggregation and resultant orientational effects, as in micelles, the Diels–Alder reactions have no regiochemical bias.

Regiochemical control resulting from orientation of substrates within aqueous and reversed micelles has been obtained in several photochemical [2 + 2] and [4 + 4] cycloadditions.[12] However, the anticipated selectivity is not always realized.[13]

Characterization of Diels–Alder Adducts. The structures of 16, 17, 19, and 20 were derived from their ^1H and ^{13}C NMR spectra (20–27 °C, $CDCl_3$) and ^1H NMR homonuclear decoupling experiments. However, the NMR data did not allow the differentiation of 16 and 17 and of 19c and 20c. The assignments illustrated for 16 and 17 are based on arguments made earlier[4] and on the results of a monolayer study of 16c and 17c,[14] and those for 19c and 20c are arbitrary but consistent with their HPLC elution order. Structural assignments involving chemical conversions and/or X-ray diffraction studies were precluded by the small amounts available of 16 and 17 and of 19c and 20c and by their amorphous natures, respectively.

The order of elution from the reversed-phase HPLC column was the same for each pair of 16 and 17 from the reactions of 6 with 7a–c: the major product, assigned to structure 16, eluted second. A definitive assignment of structures 19 and 20 to the regioisomeric cycloadducts from the reactions of 13 with 15a–c could not be made. But for consistency within the series and with the HPLC elution order of 16 and 17, the isomer eluting second from the reversed-phase column was assigned structure 19.

The *trans* stereochemistry of the cycloadducts is consistent with the known stereochemical course of Diels–Alder reactions.[11] Indeed, the reaction of 21, derived *in situ* by thermal extrusion of SO_2 from 3,4-bis(phenylthio)-2,5-dihydrothiophene 1,1-dioxide,[15] with dimethyl fumarate at 130 °C in C_6H_5Me gave 22, whose *trans* stereochemistry was established by a single-crystal X-ray diffraction study.[16] Homonuclear decoupling experiments and simulations of a portion of the ^1H NMR spectrum of 22 established that in solution (27 °C, $CDCl_3$) its cyclohexene ring is predominantly in the half-chair conformation[17,18] with diequatorial ester groups.[16]



The ^1H and ^{13}C NMR spectra of 19c and 20c are almost identical. The former are illustrated in Figure 2. Homonuclear decoupling experiments and simulation of a portion of the ^1H NMR spectrum of 19c indicated that the cyclohexene rings of 19c and 20c are predominantly in half-chair conformations with *trans* diequatorial ester groups as illustrated for the former in Figure 3a. The ^1H NMR spectra of the 1:1 mixtures of 19a and 20a and of 19b and 20b suggest that the individual components of each pair have identical spectra. Also, the ^1H and ^{13}C NMR spectra indicate that each cyclohexene ring is in the half-chair conformation with diequatorial ester groups.

For both 19c and 20c the methine and methylene protons of the cyclohexene ring comprise an ABWXYZ system with multiplets centered at δ 2.91 and 2.45, respectively. The appearance and chemical shifts of this system are very similar to those of the AA'XX'YY' system of 22.[16] In homonuclear decoupling experiments (400 MHz) with 19c, irradiation of the methylene multiplet at δ 2.34 and 2.51 resulted in collapse of the methine multiplet into a singlet at δ 2.92, indicating that H_4 and H_5 are almost, if not, isochronous. Irradiation of the methine signal resulted in collapse of the methylene multiplet into an apparent AB quartet broadened by long-range coupling: δ 2.34, H_{3a}-(H_{6a}); 2.51, H_{3e}(H_{6e}); J = 16.4 Hz. Thus, H_{3a} and H_{6a} are almost, if not, isochronous, as are H_{3e} and H_{6e}. In a simulation of the ABWXYZ system of 19c, $J_{4,5}$ = 12.7 Hz, which is consistent with a *trans* diaxial, and not a *trans* diequatorial (or a *cis* axial–equatorial), disposition of H_4

(11) Sauer, J. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 16.
(12) (a) Takagi, K.; Suddaby, B. R.; Vadas, S. L.; Backer, C. A.; Whitten, D. G. *J. Am. Chem. Soc.* **1986**, *108*, 7865. (b) Ramesh, V.; Ramamurthy, V. *J. Org. Chem.* **1984**, *49*, 536. (c) Ramnath, N.; Ramamurthy, V. *J. Org. Chem.* **1984**, *49*, 2827. (d) Ramamurthy, V. *Tetrahedron* **1986**, *21*, 5753. (e) Nakamura, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 477. (f) Berenjian, N.; de Mayo, P.; Sturgeon, M.; Sydnes, L. K.; Weedon, A. C. *Can. J. Chem.* **1982**, *60*, 425. (g) Fargues, R.; Maurette, M. T.; Oliveros, E.; Riviere, M.; Lattes, A. *Nouv. J. Chim.* **1979**, *3*, 487. (h) Wolff, T.; Mueller, N. *J. Photochem.* **1983**, *23*, 131. (i) Kato, T.; Nakamura, Y.; Morita, Y. *Chem. Pharm. Bull.* **1983**, *31*, 2552 and references cited therein.
(13) Muthuramu, K.; Ramnath, N.; Ramamurthy, V. *J. Org. Chem.* **1983**, *48*, 1872.
(14) Wang, J. Y.; Wang, J.; Jaeger, D. A.; Uphaus, R. A. To be published.
(15) Chou, T.; Lee, S.; Peng, M.; Sun, D.; Chou, S. P. *J. Org. Chem.* **1988**, *53*, 3027.
(16) Jaeger, D. A.; Wang, J.; Goodson, P. A. *J. Crystallogr. Spectrosc. Res.*, in press.
(17) Anet, F. A. L.; Freedberg, D. I.; Storer, J. W.; Houk, K. N. *J. Am. Chem. Soc.* **1992**, *114*, 10969.
(18) For a review of the conformational analysis of cyclohexenes, see: Anet, F. A. L. In *The Conformational Analysis of Cyclohexenes, Cyclohexadienes, and Related Hydroaromatic Compounds*; Rabideau, P. W., Ed.; VCH Publishers: New York, 1989, Chapter 1.

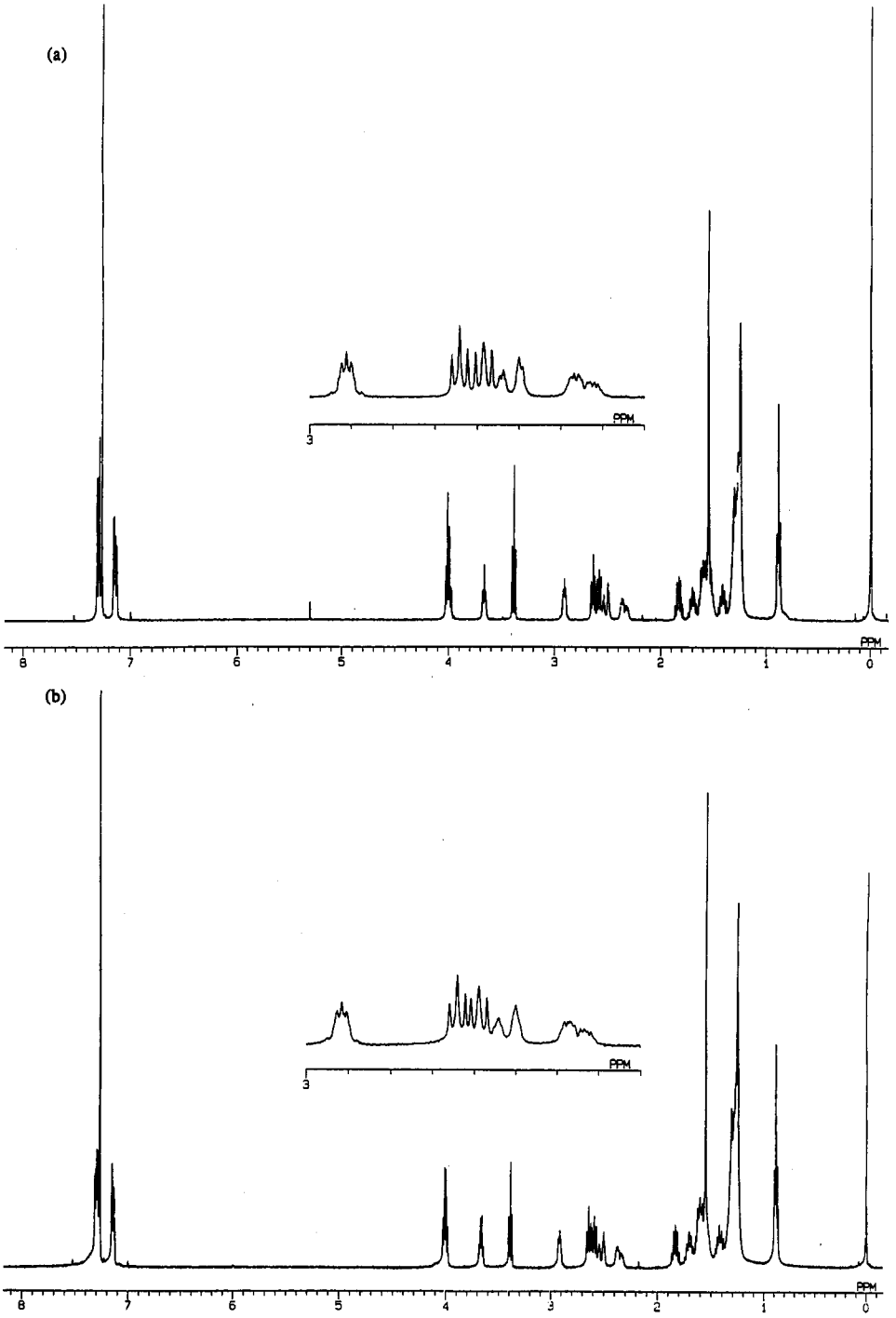


Figure 2. ^1H NMR spectra (400 MHz, $CDCl_3$) of (a) **19c** and (b) **20c** . The singlets at δ 1.55 and 7.27 are due to H_2O and $CHCl_3$, respectively.

and H_5.[19] Also, the chemical shift of H_4 and H_5, compared to those of the analogous protons of **16c** and **17c** as discused below, is indicative of their axial character.

The ^1H and ^{13}C NMR spectra of **16a–c** are very similar, as are those of **17a–c**. However, unlike for **19c** and **20c**, there are significant differences in the spectra of **16** and **17**. The ^1H NMR spectra of **16c** and **17c** are illustrated in Figure 4. Homonuclear decoupling experiments and simulation of a portion of the ^1H NMR spectrum of **16c** indicated that, analogous to **19c/20c**, its cyclohexene ring is predominantly in the half-chair conformation with *trans* diequatorial ester groups as illustrated in Figure 3a.

(19) Aycard, J.-P.; Bodot, H. *Org. Magn. Res.* **1975**, *7*, 226.

As for **19c** and **20c**, the methine and methylene protons of the cyclohexene rings of **16c** and **17c** comprise ABWXYZ systems. For **16c**, multiplets for the methine and methylene protons are centered at δ 2.90 and 2.40, respectively. In homonuclear decoupling experiments (400 MHz) with **16c**, irradiation of the methylene multiplet at δ 2.30 and 2.48 resulted in collapse of the methine multiplet into a singlet at δ 2.90, indicating that H_4 and H_5 are almost, if not, isochronous. Irradiation of the methine signal resulted in collapse of the methylene multiplet into two apparent AB quartets broadened by long-range coupling: δ 2.34, $H_{3a}(H_{6a})$; 2.51, $H_{3e}(H_{6e})$; J = 17.3 Hz, and δ 2.26, $H_{6a}(H_{3a})$; 2.44, $H_{6e}(H_{3e})$; J = 17.3 Hz. Thus H_{3a} and H_{6a}, and H_{3e} and H_{6e} are not isochronous. In a simulation of the

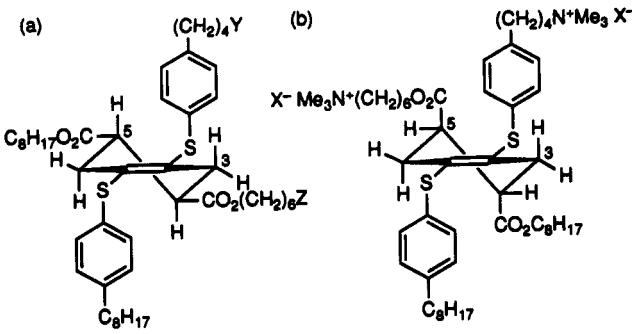


Figure 3. (a) Half-chair conformation of **16c** (Y = Z = N^+Me_3 X^-) and **19c** (Y = OH; Z = Br) with *trans* diequatorial ester groups. (b) Half-chair conformation of **17c** with *trans* diaxial ester groups.

ABWXYZ system, $J_{4,5}$ = 10.4 Hz, which is consistent with a predominant *trans* diaxial disposition of H_4 and H_5.[19] Also, the chemical shift of H_4 and H_5, compared to those of the analogous protons of **17c** and **19c** as discussed below, is indicative of their axial character.

The appearance of the ABWXYZ system of **17c** is distinctly different than that of **16c**. The methylene protons give a sharp multiplet at δ 2.45, as opposed to a broad multiplet for the analogous protons of **16c**, and the methine protons give a multiplet at δ 3.02. If it is assumed[11,16] that the ester groups of **17c** are *trans* as in **16c**, **19c**, and **20c**, the above spectral difference suggests that the cyclohexene rings of **16c** and **17c** have different conformational character. A reasonable alternative to the half-chair conformation with diequatorial ester groups is the inverted half-chair conformation with diaxial ester groups, as illustrated in Figure 3b.[20] The energy difference between the axial and equatorial dispositions of a substituent is typically smaller for the half-chair conformation of cyclohexene than for the chair conformation of cyclohexane.[21] A boat conformation for **17c** is unlikely. For cyclohexene the boat is less stable than the half-chair conformation by 5–7 kcal/mol and represents the transition state for half-chair ring inversion (reversal).[17,18]

Homonuclear decoupling experiments (400 MHz) suggest that the cyclohexene ring of **17c** is in conformational equilibrium between the half-chair with diequatorial ester groups and the inverted half-chair with diaxial ester groups. Irradiation of the methylene multiplet at δ 2.44 resulted in collapse of the methine signal into an AB quartet: δ 3.03, $H_4(H_5)$; 3.04, $H_5(H_4)$, $J_{4,5}$ = 7.3 Hz. This value of $J_{4,5}$ is intermediate between those estimated for the half-chair conformations with diaxial and diequatorial ester groups, 3.0 and 13.2 Hz, respectively, and corresponds to an equilibrium composed of about 60% of the former.[19] Irradiation of the methine signal resulted in collapse of the methylene multiplet into two overlapping apparent AB quartets broadened by long range coupling: δ 2.44, $H_{3a}(H_{6a})$; 2.46, $H_{3e}(H_{6e})$; J = 19.0 Hz, and δ 2.41, $H_{6a}(H_{3a})$; 2.46, $H_{6e}(H_{3e})$; J = 19.0 Hz. In the conformation of **17c** with diaxial ester groups, H_4 and H_5 are diequatorial. Note that the signals for H_4 and H_5 of **17c** (δ 3.03, 3.04) are downfield from those of **16c** (δ 2.90) and **19c** (δ 2.91). Usually, but not always, there is a downfield shift of equatorial relative to axial protons of chair conformations of six-membered rings.[19,22,23]

(20) This and other half-chair conformations may be more or less distorted toward the sofa conformation.[18]
(21) Lambert, J. B.; Marko, D. E. *J. Am. Chem. Soc.* **1985**, *107*, 7978.

Why is the conformational character of **17c** different than that of **16c**, **19c**, and **20c**, even though the ester substituents at carbons 4 and 5 of each compound are close to, if not, sterically equivalent? Surfactants **16c** and **17c** probably form reversed micelles in chloroform.[24] Indeed, the occurrence of different conformations for **16c** and **17c** can be attributed to aggregation effects (vida infra). There are two limiting orientations of the average plane of a half-chair cyclohexene ring with respect to the radial axis of a reversed micelle: parallel and perpendicular. Surfactant **16c** in either orientation with diequatorial ester groups can readily form a reversed micelle as illustrated in Figure 5. The two chains bearing the quaternary ammonium head groups can extend directly into the ionic micelle core, and the two octyl chains can extend directly into chloroform. The parallel is perhaps preferred to the perpendicular orientation since its cross section with respect to the radial axis is less, allowing for tighter surfactant packing within the reversed micelle. Surfactant **17c** in the parallel orientation with diequatorial or diaxial ester groups cannot easily form a reversed micelle. One of the head group chains and one of the octyl chains can extend directly into their preferred microenvironments, but the other two cannot. Both head group chains and both octyl chains of **17c** in the perpendicular orientation, with diaxial or diequatorial ester groups, can extend readily into their preferred microenvironments as illustrated in Figure 6. However, the diaxial half-chair conformation is likely preferred because the extensions of its chains are more direct, and the two head group chains are closer to one another, as are the two octyl chains, resulting in greater intramolecular lipophilic interactions and tighter surfactant packing. Overall, **16c** within a reversed micelle is best represented by Figure 5a, and **17c**, by a combination of Figures 6a and 6b, with an excess of the former.

The ^{13}C NMR data are consistent with the assignments of diequatorial half-chair conformation for **16c** and an equilibrium between diequatorial and diaxial half-chair conformations for **17c**. It is known that α- and β-carbons are deshielded more by an equatorial than by an axial methoxycarbonyl group.[25] The chemical shifts of C_4 and C_5 (α) and of C_3 and C_6 (β) of **16**, **17**, **19c**, and **20c** are given in Table II. The C_3 and C_6 signals of **16** are uniformly downfield from those of **17**. However, the C_4 and C_5 signals of **16** have about the same chemical shifts as those of **17**. The downfield shifts for the α-carbons of **16** resulting from the equatorial ester groups have likely been countered by upfield shifts resulting from their *gauche* relationship.[26] Note that the chemical shifts of C_4 and C_5 and of C_3 and C_6 of **16**, **19c**, and **20c** are about the same, consistent with diequatorial half-chair conformations for all these cycloadducts.

There have been several previous reports of conformational changes due to surfactant aggregation.[8a,27] And in

(22) Jensen, F. R.; Bushweller, C. H. *J. Am. Chem. Soc.* **1969**, *91*, 5774.
(23) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; 2nd ed.; Pergamon Press: New York, 1969; pp 238–241.
(24) Fendler, J. H. *Membrane Mimetic Chemistry*; Wiley-Interscience: New York, 1982; Chapter 3.
(25) Wilson, N. K.; Stothers, J. B. In *Topics in Stereochemistry*; Eliel, E. L., Allinger, N. L., Eds.; Interscience: New York, 1974; Vol. 8, pp 25–30.
(26) For examples of such upfield shifts involving dimethylcyclohexanes, see: Dalling, D. K.; Grant, D. M. *J. Am. Chem. Soc.* **1972**, *94*, 5318.

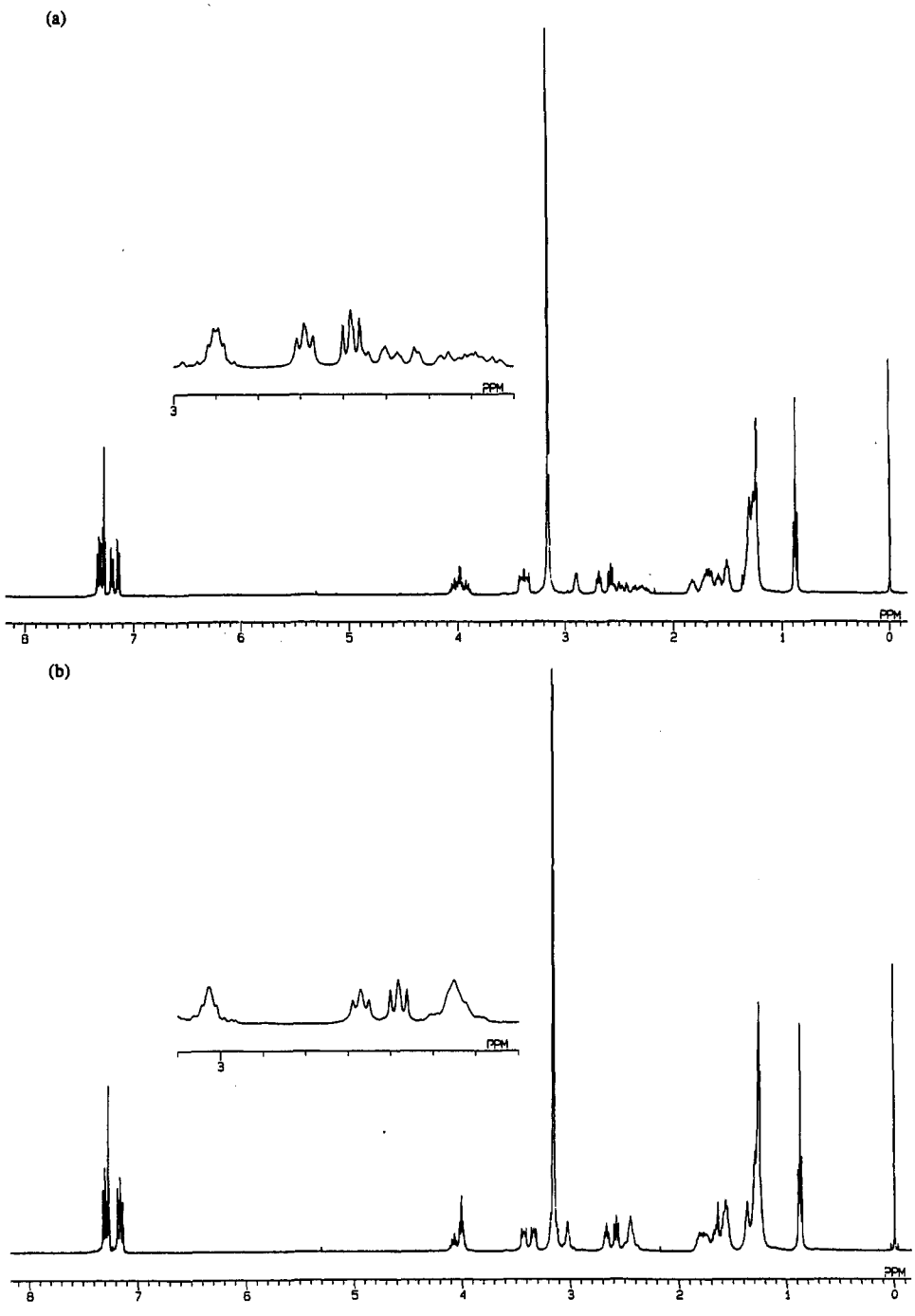


Figure 4. ^1H NMR spectra (400 MHz, $CDCl_3$) of (a) **16c** and (b) **17c**. The singlets at δ 1.55 and 7.27 are due to H_2O and $CHCl_3$, respectively.

particular, these changes represent examples of the ability of hydrophobic effects to alter intrinsic molecular properties.[28]

Summary

We have demonstrated that interfacial and related orientational effects associated with aqueous micelles can impart regioselectivity control in Diels–Alder reactions of **6** and **7**, resulting in an up to 3:1 excess of **16** over **17**. The cyclohexene rings of **16** and **17** have different conformational character in chloroform, most likely due to supramolecular effects within reversed micelles. On the former the ester groups are predominantly diequatorial, whereas on the latter a significant fraction of the ester groups are diaxial.

(27) For examples, see: (a) Menger, F. M.; Vasquez, P. C. *J. Org. Chem.* **1982**, *47*, 5400. (b) Wu, W.-G.; Chi, L.-M. *J. Am. Chem. Soc.* **1991**, *113*, 4683. (c) Ambühl, M.; Bangerter, F.; Luisi, P. L.; Skrabal, P.; Watzke, H. J. *Langmuir* **1993**, *9*, 36 and references cited therein.

(28) For other examples, see: (a) Porter, N. A.; Ok, D.; Huff, J. B.; Adams, C. M.; McPhail, A. T.; Kim, K. *J. Am. Chem. Soc.* **1988**, *110*, 1896. (b) Jaeger, D. A.; Chou, P. K.; Bolikal, D.; Ok, D.; Kim, K. Y.; Huff, J. B.; Yi, E.; Porter, N. A. *J. Am. Chem. Soc.* **1988**, *110*, 5123. (c) Jaeger, D. A.; Mohebalian, J.; Rose, P. L. *Langmuir* **1990**, *6*, 547.

Experimental Section

General Procedures and Materials. ^1H (270 and 400 MHz) and ^{13}C (67.9 and 100.6 MHz) NMR spectra were recorded in $CDCl_3$ with Me_4Si or $CHCl_3$ (δ 7.26) as internal standard for the former and $CDCl_3$ (δ 77.00) for the latter. *J* values are in hertz. High-resolution mass spectra were obtained at the Midwest

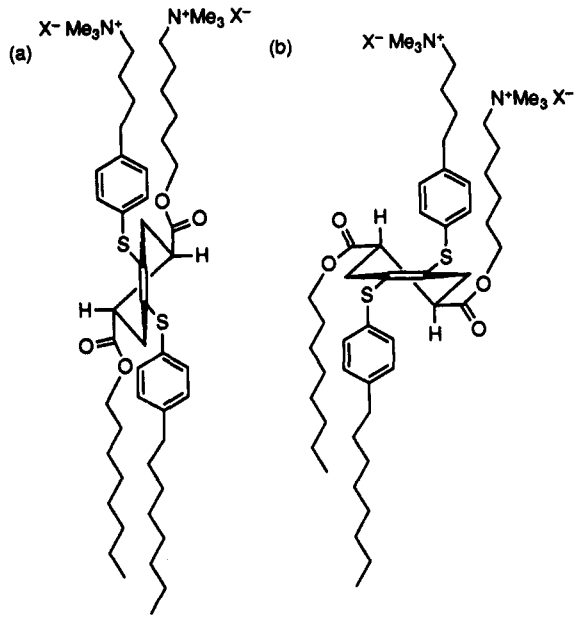


Figure 5. Orientations within a reversed micelle of **16c** with the cyclohexene ring in a half-chair conformation with diequatorial ester groups. Average plane of the cyclohexene ring (a) parallel and (b) perpendicular to the radial axis of the micelle.

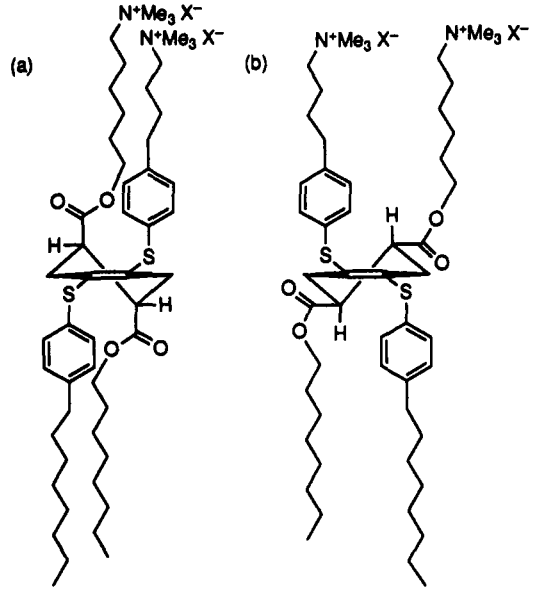


Figure 6. Orientations within a reversed micelle of **17c** with the cyclohexene ring in a half-chair conformation perpendicular to the radial axis of the micelle with (a) diaxial and (b) diequatorial ester groups.

Center for Mass Spectrometry with partial support by the National Science Foundation, Biology Division (Grant No. DIR 9017262). TLC analyses of surfactants and nonsurfactants were performed on 0.25-mm aluminum oxide (Merck 5731-3) and 0.25-mm silica gel plates (Merck 5714-3). Solutions were dried with $MgSO_4$ or Na_2SO_4, and all melting points were taken with open capillary tubes and are uncorrected. The cmc's were obtained from plots of surface tension (du Noüy ring) *vs* the log of surfactant concentration using a Fisher Model 20 tensiometer. The pH 7.0 buffer was prepared by adding 29.1 mL of 0.10 M NaOH to 50.0 mL of 0.10 M KH_2PO_4. HPLC-grade THF was distilled from $LiAlH_4$, and anhydrous Et_2O from Na. Reversed-phase HPLC was performed with UV (254 nm) detection on 8-μm C18 columns: analytical, 25 cm × 4.6 mm (i.d.) with a 1.5 cm × 4.6 mm (i.d.) guard column (Rainin 83-201-C and 83-201-G, respectively); preparative, 25 cm × 21.4 mm (i.d.) with a 5.0 cm × 21.4 mm (i.d.) guard column (83-221-C and 83-221-G). Eluants were prepared with $NaClO_4 \cdot H_2O$ and HPLC-grade H_2O and MeCN. Flash chromatography was performed with silica gel (Merck 9385, 60 Å, 230-400 mesh) and neutral aluminum oxide (J. T. Baker 0537). Column chromatography was performed with silica gel (J. T. Baker 3405) and neutral aluminum oxide. Unless noted otherwise, the ratios describing the compositions of solvent mixtures represent relative volumes. Elemental analyses were performed by Atlantic Microlab, Atlanta, GA.

Table II. ^{13}C NMR Chemical Shifts[a,b]

compd	C_4	C_5	C_3	C_6
16a	41.83	41.98	33.31	33.51
17a	41.90	42.02	32.65	33.18
16b	41.92	41.92	33.38	33.51
17b	41.79	41.88	32.31	32.96
16c	41.88	41.88	33.33	33.48
17c	41.68	41.77	32.10	32.82
19c	42.13	42.13	33.63	33.70
20c	42.14	42.14	33.64	33.64

[a] From spectra recorded in $CDCl_3$ with $CDCl_3$ (δ 77.00) as internal standard. [b] Assignments of the signals for the indicated carbons are based on comparisons of the spectra of **16**, **17**, **19c**, and **20c** with those of **8**, **11**, **13**, **22**, and 3-[(*p*-octylphenyl)thio]-4-[[*p*-(4-bromobutyl)phenyl]thio]-2,5-dihydrothiophene 1,1-dioxide. Since the signals for C_4 and C_5 and for C_3 and C_6 cannot be distinguished, the assignments within each pair are arbitrary.

***trans*-3-Chloro-4-[(*p*-octylphenyl)thio]tetrahydrothiophene 1,1-Dioxide (10).** Modified literature procedures were used.[29] *p*-$C_8H_{17}C_6H_4SCl$ (**9**) was prepared[3] from *p*-$C_8H_{17}C_6H_4SH$[30] and used without purification. A solution of 3.6 g (31 mmol) of 2,5-dihydrothiophene 1,1-dioxide (Aldrich) in 100 mL of $CHCl_3$ was added to 8.7 g (34 mmol) of *p*-$C_8H_{17}C_6H_4SCl$ under N_2 at 25 °C. The reaction mixture was stirred at 25 °C for 3 days, during which time it changed from red to light yellow, and then it was rotary evaporated. The resultant 9.16 g of solid was recrystallized from 1:10 Et_2O-hexane (0 °C) to give 6.84 g (59%) of **10** as white crystals: mp 57-58 °C; ^1H NMR (270 MHz) δ 7.31 (AA'BB', 4), 4.34 (m, 1), 3.91 (m, 2), 3.70 (m, 1), 3.41 (m, 1), 3.16 (m, 1), 2.62 (t, 2, J = 7.8), 1.62 (m, 2), 1.27 and 1.31 (2 s, 10), 0.88 (t, 3); ^{13}C NMR (67.9 MHz) δ 134.77, 129.94, 126.09, 58.73, 55.73, 55.24, 51.52, 35.64, 31.84, 31.20, 29.40, 29.29, 29.20, 22.64, 14.09. Anal. Calcd for $C_{18}H_{27}ClS_2O_2$: C, 57.66; H, 7.26. Found: C, 57.76; H, 7.28.

3-[(*p*-Octylphenyl)thio]-2,5-dihydrothiophene 1,1-Dioxide (11). To a solution of 6.2 g (17 mmol) of **10** in 100 mL of $CHCl_3$ under N_2 at -40 °C was added 3.41 g (22.4 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) during 15 min. The reaction mixture was stirred at -40 °C for 1 h and then warmed to -15 °C during 2 h, followed by the addition of 100 mL of 10% hydrochloric acid. The organic layer was dried and rotary evaporated to give 5.39 g (94%) of crude product that was flash chromatographed two times on 20- × 5.0-cm columns of silica gel packed in hexane with 1:4 EtOAc-hexane as eluant to give 4.10 g of **11** as an oil: ^1H NMR (270 MHz) δ 7.28 (AA'BB', 4), 5.67 (m, 1), 3.85 (m, 2), 3.72 (m, 2), 2.61 (t, 2, J = 7.9), 1.60 (m, 2), 1.29 (m, 10), 0.88 (t, 3); ^{13}C NMR (67.9 MHz) δ 144.65, 133.76, 133.33, 129.78, 125.66, 118.10, 57.88, 57.54, 35.56, 31.79, 31.18, 29.35, 29.20, 29.15, 22.59, 14.05. Anal. Calcd for $C_{18}H_{28}S_2O_2$: C, 63.86; H, 7.74. Found: C, 63.95; H, 7.75.

3-[(*p*-Octylphenyl)thio]-4-bromo-4,5-dihydrothiophene 1,1-Dioxide (12). By a literature procedure[15] 5.0 g (15 mmol) of **11** gave 6.26 g of a 4:1 mixture of **12** and 3-[(*p*-octylphenyl)thio]-4-bromo-2,5-dihydrothiophene 1,1-dioxide. This material was flash chromatographed on a 25- × 5.0-cm column of silica gel packed in hexane with 1:4 EtOAc-hexane as eluant to give 3.21 g (51%) of **12** as an oil: ^1H NMR (270 MHz) δ 7.38 (AA'BB', 4), 5.85 (s, 1), 5.11 (m, 1), 3.99 (m, 1), 3.77 (m, 1), 2.65 (t, 2, J = 7.9), 1.62 (m, 2), 1.27 (m, 10), 0.88 (t, 3); ^{13}C NMR (67.9 MHz) δ 158.00, 146.49, 135.04, 130.44, 124.21, 122.50, 59.86, 38.83, 35.69, 31.81, 31.14, 29.35, 29.20, 29.15, 22.61, 14.07. Anal. Calcd for $C_{18}H_{25}BrS_2O_2$: C, 51.79; H, 6.03. Found: C, 51.63; H, 6.08.

(29) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208.
(30) Neubert, M. E.; Laskos, S. J., Jr.; Griffith, R. F.; Stahl, M. E.; Maurer, L. *J. Mol. Cryst. Liq. Cryst.* **1979**, *54*, 221.

3-[(*p*-Octylphenyl)thio]-4-[[*p*-(4-hydroxybutyl)phenyl]thio]-2,5-dihydrothiophene 1,1-Dioxide (13). A solution of 0.79 g (1.9 mmol) of **12** in 10 mL of MeOH was added dropwise during 20 min to a solution of 0.23 g (4.3 mmol) of NaOMe and 0.70 g (3.8 mmol) of 4-(*p*-mercaptophenyl)-1-butanol in 10 mL of MeOH under N_2 at 25 °C. The reaction mixture was stirred for 72 h, and 80 mL of H_2O was added, followed by extraction with three 50-mL portions of Et_2O. The combined extracts were dried and rotary evaporated to leave a residue that was flash chromatographed on a 20- × 2.0-cm column of silica gel packed in hexane with 1:2 EtOAc–hexane as eluant to give 0.88 g (89%) of **13** as an oil that solidified at 5 °C: mp 39–40 °C; ^{1}H NMR (270 MHz) δ 7.16–7.41 (m, 8), 3.75 (s, 4), 3.67 (t, 2, J = 6.3), 2.58–2.71 (m, 4), 1.55–1.78 (m, 7), 1.31 (m, 10), 0.88 (t, 3); ^{13}C NMR (67.9 MHz) δ 144.38, 143.67, 132.99, 132.90, 129.72, 128.52, 127.69, 127.39, 126.99, 62.57, 60.27, 35.56, 35.22, 32.17, 31.81, 31.22, 29.36, 29.22, 29.17, 27.32, 22.61, 14.07. Anal. Calcd for $C_{28}H_{38}S_3O_3$: C, 64.83; H, 7.38. Found: C, 64.86; H, 7.43.

3-[(*p*-Octylphenyl)thio]-4-[[*p*-(4-bromobutyl)phenyl]thio]-2,5-dihydrothiophene 1,1-Dioxide. A literature procedure[31] was used to convert 0.629 g (1.21 mmol) of **13** into 0.710 g of crude product. This material was flash chromatographed on a 20- × 2.0-cm column of silica gel packed in hexane with 1:4 EtOAc–hexane as eluant to give 0.633 g (90%) of the title compound as an oil: ^{1}H NMR (270 MHz) δ 7.17–7.42 (m, 8), 3.76 (s, 4), 3.44 (t, 2, J = 6.6), 2.57–2.71 (m, 4), 1.54–1.97 (m, 6), 1.30 (m, 10), 0.88 (t, 3); ^{13}C NMR (67.9 MHz) δ 144.46, 143.07, 133.08, 132.90, 129.76, 129.70, 129.00, 127.75, 127.42, 126.99, 60.31, 35.58, 34.58, 33.37, 32.10, 31.84, 31.23, 29.56, 29.40, 29.26, 29.18, 22.63, 14.07. Anal. Calcd for $C_{28}H_{37}BrS_3O_2$: C, 57.82; H, 6.41. Found: C, 57.87; H, 6.43.

4-[*p*-[[1,1-Dioxo-4-[(*p*-octylphenyl)thio]-2,5-dihydrothiophene-3-yl]thio]phenyl]-*N,N,N*-trimethyl-1-butanaminium Bromide (8). A mixture of 18.9 mg (0.0325 mmol) of 3-[(*p*-octylphenyl)thio]-4-[[*p*-(4-bromobutyl)phenyl]thio]-2,5-dihydrothiophene 1,1-dioxide and 2.0 mL (8.5 mmol) of 25% (w/v) Me_3N–MeOH was stirred at 25 °C under N_2 for 16 h. Rotary evaporation left 20.2 mg (97%) of **8** as an oil: ^{1}H NMR (400 MHz) δ 7.17–7.41 (m, 8), 3.70–3.79 (m, 6), 3.44 (s, 9), 2.72 (t, 2, J = 7.3), 2.61 (t, 2, J = 7.8), 1.55–1.87 (m, 6), 1.30 (m, 10), 0.88 (t, 3); ^{13}C NMR (100.6 MHz) δ 144.48, 142.19, 133.09, 132.80, 129.80, 129.73, 129.52, 128.03, 126.87, 126.82, 66.33, 60.23, 60.18, 53.43, 35.54, 34.61, 31.77, 31.18, 29.33, 29.22, 29.14, 27.51, 22.57, 22.54, 14.04. Anal. Calcd for $C_{31}H_{46}BrNS_3O_2 \cdot H_2O$: C, 56.52; H, 7.34. Found: C, 56.30; H, 6.94. FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{31}H_{46}NS_3O_2$ (cation) 560.2691, found 560.2683. The base peak in the FAB mass spectrum was at m/z = 496, which corresponds to the cation of **6**, formed by the loss of SO_2 from the cation of **8**. The cmc of **8** in H_2O at 25 °C is (3.7 ± 0.2) × 10^{-5} M.

6-Bromohexyl Hydrogen Fumarate (14). A mixture of 5.0 g (28 mmol) of 6-bromo-1-hexanol[32] and 2.7 g (28 mmol) of maleic anhydride in 10 mL of C_6H_5Me was refluxed under N_2 for 12 h and rotary evaporated. Then 10 mL of aqueous 5% $NaHCO_3$ was added to the residue, and the mixture was extracted with two 15-mL portions of Et_2O. The resultant aqueous solution was acidified with 10% sulfuric acid and extracted with three 20-mL portions of $CHCl_3$. The combined extracts were washed with 10 mL of H_2O, dried, and rotary evaporated to give 6.41 g (82%) of a mixture of **14** and its (*Z*) isomer as a solid (4.8:1 ratio, respectively, by ^{1}H NMR analysis). The mixture was recrystallized from 1:8 CCl_4–hexane (25 °C) to give pure **14**: mp 55–56 °C; ^{1}H NMR (270 MHz) δ 10.33 (br s, 1), 6.90 (AB, δ_A = 6.86, δ_B = 6.95, 2, J = 15.8), 4.23 (t, 2, J = 6.3), 3.41 (t, 2, J = 6.9), 1.88 (m, 2), 1.72 (m, 2), 1.46 (m, 4); ^{13}C NMR (67.9 MHz) δ 170.03, 164.67, 135.74, 132.61, 65.45, 33.64, 32.51, 28.29, 27.71, 25.07; IR 3072 (m), 2934 (m), 2849 (m), 1713 (s), 1683 (s), 1632 (s), 1462 (m), 1430 (m), 1315 (s), 1282 (m), 1266 (m), 1176 (s), 990 cm^{-1} (s). Anal. Calcd for $C_{10}H_{15}BrO_4$: C, 43.03; H, 5.42. Found: C, 43.12; H, 5.46.

Methyl 6-Bromohexyl Fumarate (15a). A mixture of 1.0 g (3.6 mmol) of **14** and 0.852 g (7.16 mmol) of $SOCl_2$ was stirred at 25 °C for 12 h and then rotary evaporated to give crude 6-bromohexyl fumaryl chloride. To a solution of this material in 5.0 mL of C_6H_6 at 25 °C were added separately 0.115 g (3.59 mmol) of MeOH and 0.211 g (3.58 mmol) of Et_3N during 13 and 15 min, respectively. Then the reaction mixture was stirred for 2 h, diluted with 50 mL of H_2O, and extracted with three 30-mL portions of Et_2O. The combined extracts were dried and rotary evaporated, and the residue was chromatographed on a 16- × 3.0-cm column of silica gel packed in hexane with 1:10 Et_2O–hexane as eluant to afford 0.820 g (78%) of **15a** as an oil: ^{1}H NMR (270 MHz) δ 6.86 (s, 2), 4.21 (t, 2, J = 6.6), 3.82 (s, 3), 3.42 (t, 2, J = 6.7), 1.88 (m, 2), 1.71 (m, 2), 1.46 (m, 4); ^{13}C NMR (67.9 MHz) δ 165.35, 164.90, 133.75, 133.15, 65.16, 52.26, 33.59, 32.49, 28.29, 27.68, 25.05. Anal. Calcd for $C_{11}H_{17}BrO_4$: C, 45.07; H, 5.85. Found: C, 45.12; H, 5.81.

Butyl 6-Bromohexyl Fumarate (15b). With the procedure used for the preparation of **15a**, 1.0 g (3.6 mmol) of **14**, 0.852 g (7.16 mmol) of $SOCl_2$, 0.265 g (3.58 mmol) of 1-butanol, and 0.211 g (3.58 mmol) of Et_3N gave 0.863 g (72%) of **15b** as an oil: ^{1}H NMR (270 MHz) δ 6.85 (s, 2), 4.21 (t, 4, J = 6.6), 3.42 (t, 2, J = 6.9), 1.88 (m, 2), 1.71 (m, 4), 1.45 (m, 6), 0.95 (t, 3); ^{13}C NMR (67.9 MHz) δ 164.85, 133.57, 133.32, 65.03, 33.48, 32.42, 30.37, 28.20, 27.59, 24.96, 18.94, 13.53. Anal. Calcd for $C_{14}H_{23}BrO_4$: C, 50.16; H, 6.92. Found: C, 50.23; H, 6.93.

Octyl 6-Bromohexyl Fumarate (15c). With the procedure used for the preparation of **15a**, 1.0 g (3.6 mmol) of **14**, 0.852 g (7.16 mmol) of $SOCl_2$, 0.466 g (3.58 mmol) of 1-octanol, and 0.211 g (3.58 mmol) of Et_3N gave 1.14 g (81%) of **15c** as an oil: ^{1}H NMR (400 MHz) δ 6.85 (s, 2), 4.21 (t, 2, J = 6.6), 4.19 (t, 2, J = 6.6), 3.41 (t, 2, J = 6.6), 1.88 (m, 2), 1.70 (m, 4), 1.19–1.53 (m, 14), 0.88 (t, 3); ^{13}C NMR (100.6 MHz) δ 165.06, 133.75, 133.45, 65.54, 65.18, 33.62, 32.54, 31.75, 29.14, 28.48, 28.33, 27.74, 25.85, 25.10, 22.61, 14.07. Anal. Calcd for $C_{18}H_{31}BrO_4$: C, 55.24; H, 7.98. Found: C, 55.30; H, 7.98.

(*E*)-6-[[[2-(Methoxycarbonyl)ethenyl]carbonyl]oxy]-*N,N,N*-trimethyl-1-hexanaminium Bromide (7a). A mixture of 1.10 g (3.75 mmol) of **15a** and 15 mL of a 0.6 M solution of Me_3N (9 mmol) in MeCN was stirred under N_2 at 25 °C for 6 days and rotary evaporated to give 1.31 g (99%) of crude **7a** that was flash chromatographed on a 20- × 2-cm column of neutral aluminum oxide packed in MeCN with 20:1 MeCN–MeOH as eluant. The resultant material was recrystallized from Me_2CO (25 °C) to give **7a**: mp 65–67 °C; ^{1}H NMR (270 MHz) δ 6.84 (s, 2), 4.20 (t, 2, J = 6.6), 3.82 (s, 3), 3.70 (m, 2), 3.48 (s, 9), 1.82 (m, 2), 1.72 (m, 2), 1.48 (m, 4); ^{13}C NMR (67.9 MHz) δ 165.07, 164.62, 133.39, 132.97, 66.24, 64.73, 53.10, 52.06, 27.93, 25.45, 25.20, 22.77. Anal. Calcd for $C_{14}H_{26}BrNO_4$: C, 47.73; H, 7.44. Found: C, 47.63; H, 7.48. No cmc was detected for **7a** in H_2O at 25 °C up to 0.11 M.

(*E*)-6-[[[2-(Butoxycarbonyl)ethenyl]carbonyl]oxy]-*N,N,N*-trimethyl-1-hexanaminium Bromide (7b). A mixture of 1.0 g (3.0 mmol) of **15b** and 15 mL of a 0.6 M solution of Me_3N (9 mmol) in MeCN was stirred under N_2 at 25 °C for 6 days and rotary evaporated to give 1.18 g (100%) of crude product. With the procedure for **7a** this material was chromatographed and recrystallized to give **7b**: mp 58 → 78 °C; ^{1}H NMR (270 MHz) δ 6.84 (s, 2), 4.21 (t, 2, J = 6.6), 4.20 (t, 2, J = 6.6), 3.66 (m, 2), 3.49 (s, 9), 1.81 (m, 2), 1.70 (m, 4), 1.35–1.53 (m, 6), 0.95 (t, 3); ^{13}C NMR (100.6 MHz) δ 164.95, 133.77, 133.28, 66.59, 65.19, 64.85, 53.33, 30.42, 28.17, 25.68, 25.44, 23.00, 19.00, 13.59. Anal. Calcd for $C_{17}H_{32}BrNO_4 \cdot H_2O$: C, 49.52; H, 8.31. Found: C, 49.48; H, 8.12. The cmc of **7b** in H_2O at 25 °C is (5.3 ± 1.2) × 10^{-2} M.

(*E*)-6-[[[2-(Octoxycarbonyl)ethenyl]carbonyl]oxy]-*N,N,N*-trimethyl-1-hexanaminium Bromide (7c). A mixture of 0.377 g (0.963 mmol) of **15c** and 12 mL of a 0.6 M solution of Me_3N (7 mmol) in MeCN was stirred under N_2 at 25 °C for 2 days and rotary evaporated to give 0.433 g (100%) of crude product. With the procedure for **7a** this material was chromatographed and recrystallized to give **7c**: mp 138 → 162 °C; ^{1}H NMR (400 MHz) δ 6.84 (s, 2), 4.19 (t, 4, J = 6.8), 3.68 (m, 2), 3.48 (s, 9), 1.81 (m, 2), 1.70 (m, 4), 1.48 (m, 4), 1.29 (m, 10), 0.88 (t, 3); ^{13}C NMR (100.6 MHz) δ 164.84, 133.64, 133.16, 66.39, 65.39, 64.77, 53.19, 31.55, 28.94, 28.28, 28.05, 25.64, 25.57, 25.30, 22.88, 22.42, 13.90. Anal. Calcd for $C_{21}H_{40}BrNO_4 \cdot H_2O$: C, 53.84; H, 9.04. Found: C, 54.18; H, 9.08. The cmc of **7c** in H_2O at 25 °C is (4.0 ± 0.5) × 10^{-3} M.

(31) McMurry, J. E.; Erion, M. D. *J. Am. Chem. Soc.* **1985**, *107*, 2712.
(32) Jayasuriya, H.; Bosak, S.; Regen, S. *J. Am. Chem. Soc.* **1990**, *112*, 5844.

4-(*p*-Mercaptophenyl)-1-butanol. In standard fashion 4-(*p*-aminophenyl)butanoic acid (Aldrich) was reduced to crude alcohol with $LiAlH_4$ in THF. This material was purified by flash chromatography on a 20- × 2-cm column of silica gel packed in Et_2O with Et_2O as eluant to give 4-(*p*-aminophenyl)-1-butanol (95%): mp 73–74 °C (lit.[33] mp 71–72 °C). A stirred mixture of 1.5 g (9.1 mmol) of this alcohol, 2.4 mL of concentrated hydrochloric acid, and 3.5 mL of H_2O was cooled to 0 °C, and a solution of 0.75 g (11 mmol) of $NaNO_2$ in 6.0 mL of H_2O was added slowly so that the reaction mixture remained below 4 °C. Then the resultant ice-cold diazonium salt solution was added dropwise during 40 min to a solution of 5.6 g (35 mmol) of potassium ethyl xanthate[34] in 10 mL of H_2O at 40–50 °C. The reaction mixture was stirred at 40–50 °C for an additional 30 min, refluxed for 1 h, diluted with 40 mL of H_2O, and extracted with three 30-mL portions of Et_2O. The combined extracts were washed with 30 mL of aqueous 10% NaOH and two 30-mL portions of H_2O and then dried and rotary evaporated to give 2.27 g (92%) of *O*-ethyl *S*-[*p*-(4-hydroxybutyl)phenyl] xanthate as a red-brown oil, which was used without further purification.

In standard fashion 2.27 g (8.40 mmol) of the above xanthate was reduced with 1.28 g (33.7 mmol) of $LiAlH_4$ in Et_2O to give 1.2 g (78%) of the title compound as a red-brown oil, which was used without purification: ^1H NMR (270 MHz) δ 7.12 (AA′BB′, 4), 3.64 (t, 2, *J* = 6.3), 3.39 (s, 1), 2.59 (t, 2, *J* = 7.0), 1.63 (m, 4), 1.48 (br s, 1); ^{13}C NMR (67.9 MHz) δ 140.88, 140.01, 129.83, 129.18, 62.75, 35.02, 32.19, 27.46.

Diels–Alder Reactions. Regioisomer ratios were obtained by HPLC analysis with UV detection at 254 nm. Since **16c** and **17c** have identical UV spectra (MeCN, λ_{max} = 257 nm, $\epsilon_{max} = 2.00 \times 10^4$, $\epsilon_{254} = 1.90 \times 10^4$), their relative response ratio is 1:1. Given the structural similarities of all the regioisomer pairs, it is reasonably assumed that the relative response ratio for each other pair is also 1:1.

(a) 13 and 15a. A solution of 16.1 mg (0.0310 mmol) of **13**, 36.3 mg (0.124 mmol) of **15a**, 5.2 mg of 4-*tert*-butylcatechol, and 0.30 mL of C_6H_5Me, sealed in a 1-mL ampule with a micro stirring bar, was stirred at 130 °C for 2 h. The reaction mixture was then rotary evaporated and the residue flash chromatographed on a 6- × 0.5-cm column of silica gel packed in hexane with 1:1 EtOAc–hexane as eluant to give 9.4 mg (41%) of a mixture of 1-[[*p*-(4-hydroxybutyl)phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-(methoxycarbonyl)-5-[(6-bromohexoxy)carbonyl]-1-cyclohexene (**19a**) and 1-[[*p*-(4-hydroxybutyl)phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-[(6-bromohexoxy)carbonyl]-5-(methoxycarbonyl)-1-cyclohexene (**20a**) as an oil. By HPLC analysis (eluant = 93:7 MeCN–H_2O; flow rate =1.5 mL/min), the **19a**:**20a** ratio was 1:1 (retention times = 40.3 and 38.2 min, respectively). For the mixture: ^1H NMR (270 MHz) δ 7.10–7.38 (m, 8), 4.02 (t, 2, *J* = 6.4), 3.66 (t, 2, *J* = 6.3), 3.62 (s, 3), 3.39 (t, 2, *J* = 6.8), 2.92 (m, 2), 2.61 (m, 4), 2.46 (m, 4), 1.20–1.90 (m, 25), 0.88 (t, 3); ^{13}C NMR (100.6 MHz) δ 173.95, 173.43, 142.77, 142.69, 142.05, 141.98, 132.21, 132.16, 132.00, 131.98, 131.79, 131.26, 130.69, 129.94, 129.87, 129.50, 129.45, 129.23, 64.73, 64.71, 62.76, 52.03, 42.20, 42.04, 35.59, 35.25, 33.61, 32.54, 32.27, 31.87, 31.33, 29.44, 29.32, 29.23, 28.28, 27.69, 27.36, 24.95, 22.65, 14.08; FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{39}H_{55}{}^{79}BrS_2O_5$ 746.2675, found 746.2649.

(b) 13 and 15b. A solution of 21.1 mg (0.0407 mmol) of **13**, 54.4 mg (0.162 mmol) of **15b**, 4.2 mg of 4-*tert*-butylcatechol, and 0.20 mL of C_6H_5Me, sealed in a 1-mL ampule with a micro stirring bar, was stirred at 130 °C for 2 h. The reaction mixture was then rotary evaporated and the residue flash chromatographed as above with 1:4 EtOAc–hexane as eluant to give 8.0 mg (26%) of a mixture of 1-[[*p*-(4-hydroxybutyl)phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-(butoxycarbonyl)-5-[(6-bromohexoxy)carbonyl]-1-cyclohexene (**19b**) and 1-[[*p*-(4-hydroxybutyl)phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-[(6-bromohexoxy)carbonyl]-5-(butoxycarbonyl)-1-cyclohexene (**20b**) as an oil. By HPLC analysis (eluant = 96:4 MeCN–H_2O; flow rate = 1.5 mL/min), the **19b**:**20b** ratio was 1:1 (retention times = 48.0 and 46.2 min, respectively). For the mixture: ^1H NMR (270 MHz) δ 7.10–7.36 (m, 8), 4.01 (t, 4, *J* = 6.6 Hz), 3.66 (q, 2, *J* = 5.9), 3.39 (t, 2, *J* = 6.8), 2.91 (m, 2), 2.61 (m, 4), 2.44 (m, 4), 1.20–1.90 (m, 29), 0.88 (m, 6); ^{13}C NMR (100.6 MHz) δ 173.53, 173.48, 142.82, 142.08, 141.94, 132.35, 132.27, 131.99, 131.91, 131.37, 130.99, 130.31, 129.98, 129.81, 129.54, 129.34, 129.21, 64.71, 62.76, 42.14, 35.60, 35.25, 33.75, 33.62, 32.55, 32.28, 31.88, 31.35, 30.47, 29.45, 29.33, 29.24, 28.28, 27.71, 27.40, 24.97, 22.67, 18.99, 14.10, 13.66; FAB HRMS (3-nitrobenzyl alcohol/Na_2CO_3 matrix) calcd for $C_{42}H_{61}{}^{79}BrS_2O_5$ 788.3144, found 788.3137.

(b) 13 and 15c. A solution of 9.7 mg (0.019 mmol) of **13**, 35.0 mg (0.0895 mmol) of **15c**, 3.1 mg of 4-*tert*-butylcatechol, and 0.20 mL of C_6H_5Me, sealed in a 1-mL ampule with a micro stirring bar, was stirred at 130 °C for 2 h. The reaction mixture was then rotary evaporated and the residue flash chromatographed as above with 1:4 EtOAc–hexane as eluant to give 7.8 mg (49%) of a mixture of 1-[[*p*-(4-hydroxybutyl)phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-(octoxycarbonyl)-5-[(6-bromohexoxy)carbonyl]-1-cyclohexene (**19c**) and 1-[[*p*-(4-hydroxybutyl)phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-[(6-bromohexoxy)carbonyl]-5-(octoxycarbonyl)-1-cyclohexene (**20c**) as an oil. By HPLC analysis (eluant = 99:1 MeCN–H_2O; flow rate = 1.5 mL/min), the **19c**:**20c** ratio was 1:1 (retention times = 58.3 and 52.9 min, respectively). The mixture was separated by preparative HPLC (eluant as above; flow rate = 22.4 mL/min; retention times = 76.2 and 69.0 min, respectively) and the eluate collected for each isomer was concentrated by rotary evaporation, lyophilized, and extracted with $CHCl_3$. The residue after rotary evaporation was flash chromatographed as above with 1:4 EtOAc–hexane as eluant to give **19c**(**20c**). For **19c**: ^1H NMR (400 MHz) δ 7.11–7.34 (m, 8), 4.01 (m, 4), 3.67 (t, 2, *J* = 6.4), 3.39 (t, 2, *J* = 6.8), 2.91 (m, 2), 2.64 (t, 2, *J* = 7.5), 2.59 (t, 2, *J* = 7.7), 2.45 (m, 4), 1.21–1.89 (m, 37), 0.88 (m, 6); ^{13}C NMR (67.9 MHz) δ 173.50, 173.44, 142.75, 141.96, 132.20, 131.98, 131.78, 130.67, 129.42, 129.21, 65.02, 64.70, 62.75, 42.13, 35.60, 35.25, 33.70, 33.63, 32.54, 32.28, 31.87, 31.78, 31.33, 29.44, 29.34, 29.24, 29.15, 28.46, 28.29, 27.70, 27.40, 25.74, 24.96, 22.65, 14.09; FAB HRMS (3-nitrobenzyl alcohol/Na_2CO_3 matrix) calcd for $C_{46}H_{69}{}^{79}BrS_2O_5$ 844.3770, found 844.3734. For **20c**: ^1H NMR (400 MHz) δ 7.11–7.35 (m, 8), 4.01 (m, 4), 3.66 (q, 2, *J* = 6.0), 3.39 (t, 2, *J* = 6.8), 2.91 (m, 2), 2.64 (t, 2, *J* = 7.6), 2.59 (t, 2, *J* = 7.6), 2.44 (m, 4), 1.21–1.90 (m, 37), 0.88 (t, 6); ^{13}C NMR (67.9 MHz) δ 173.48, 142.70, 141.99, 132.09, 131.38, 131.11, 129.90, 129.51, 129.20, 65.05, 64.67, 62.75, 42.14, 35.60, 35.26, 33.64, 32.54, 32.28, 31.88, 31.77, 31.34, 29.45, 29.33, 29.24, 29.15, 28.47, 28.29, 27.69, 27.37, 25.75, 24.96, 22.66, 14.09; FAB HRMS (3-nitrobenzyl alcohol/Na_2CO_3 matrix) calcd for $C_{46}H_{69}{}^{79}BrS_2O_5$ 844.3770, found 844.3732.

(c) 8 and 7a. A mixture of 11.0 mg (0.0172 mmol) of **8**, 24.2 mg (0.0687 mmol) of **7a**, 0.6 mg of 4-*tert*-butylcatechol, and 0.17 mL of the pH 7.0 phosphate buffer, sealed in a 1-mL ampule with a micro stirring bar, was stirred at 130 °C for 2 h. Then it was diluted with 0.17 mL of MeCN and by HPLC analysis (eluant = 0.50 M $NaClO_4 \cdot H_2O$ in 92:8 MeCN–H_2O; flow rate = 1.0 mL/min) contained **7a** (retention time = 3.5 min), **8** (15.7 min), 1-[[*p*-[4-(trimethylammonio)butyl]phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-(methoxycarbonyl)-5-[[6-(trimethylammonio)hexoxy]carbonyl]-1-cyclohexene bisperchlorate (**16a**) (12.6 min), and 1-[[*p*-[4-(trimethylammonio)butyl]phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-[[6-(trimethylammonio)hexoxy]carbonyl]-5-(methoxycarbonyl)-1-cyclohexene bisperchlorate (**17a**) (10.4 min). Chromatography of the diluted reaction mixture on a 7-cm × 0.5-cm column of neutral aluminum oxide packed in hexane with 1:10 MeOH–MeCN as eluant gave 10.0 mg (63%) of a mixture of **16a** and **17a** that was separated by preparative HPLC (eluant as above; flow rate = 15.7 mL/min; retention times = 10.4 and 8.7 min, respectively). The eluate collected for each isomer was concentrated, lyophilized, and extracted with CH_2Cl_2. The combined extracts were rotary evaporated and chromatographed as above to give **16a** (**17a**). For **16a**: ^1H NMR (270 MHz) δ 7.11–7.38 (m, 8), 3.88–4.11 (m, 2), 3.60 (s, 3), 3.40 (m, 4), 3.16 (s, 18), 2.90 (m, 2), 2.69 (t, 2, *J* = 7.1), 2.58 (t, 2, *J* = 7.8), 2.36 (m, 4), 1.21–1.91 (m, 24), 0.88 (t, 3); ^{13}C NMR (67.9 MHz) δ 174.00, 173.35, 142.70, 141.35, 132.96, 131.95, 131.73, 129.90, 129.72, 129.40, 129.33, 66.67, 66.56, 64.51, 53.19, 52.06, 41.98, 41.83, 35.58, 34.54, 33.51, 33.31, 31.86, 31.32, 29.67, 29.44, 29.33, 29.24, 27.87, 27.62, 25.32, 24.84, 22.64, 22.50, 14.11; FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{45}H_{72}ClN_2S_2O_8$ (dication·ClO_4^-) 867.4418, found 867.4404. A peak in the FAB mass spectrum was observed

(33) Oki, M.; Iwamura, H. *Bull. Chem. Soc. Jpn.* **1959**, *32*, 1135.
(34) Jensen, K. K.; Mikkelsen, V. H. *Arch. Pharm. Chemi.* **1941**, *48*, 665.

at m/z = 384, which corresponds to the dication. For **17a**: ^{1}H NMR (400 MHz) δ 7.13-7.37 (m, 8), 3.94–4.16 (m, 2), 3.62 (s, 3), 3.48 (m, 2), 3.37 (m, 2), 3.17 (s, 9), 3.16 (s, 9), 2.98 (m, 2), 2.69 (t, 2, J = 6.4), 2.59 (t, 2, J = 7.8), 2.44 (m, 4), 1.22–1.87 (m, 24), 0.88 (t, 3); ^{13}C NMR (100.6 MHz) δ 173.92, 172.99, 143.00, 140.60, 133.59, 132.54, 131.73, 130.79, 129.42, 129.33, 129.04, 66.70, 66.51, 64.55, 53.30, 53.16, 52.32, 42.02, 41.90, 35.62, 34.50, 33.18, 32.65, 31.88, 31.33, 29.46, 29.35, 29.25, 28.07, 27.58, 25.35, 25.14, 22.67, 22.47, 14.12; FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{45}H_{72}ClN_2S_2O_8$ (dication·ClO_4^-) 867.4418, found 867.4414.

(e) 8 and 7b. A mixture of 10.8 mg (0.0169 mmol) of **8**, 26.6 mg (0.0675 mmol) of **7b**, 0.5 mg of 4-*tert*-butylcatechol, and 0.17 mL of the pH 7.0 phosphate buffer, sealed in a 1-mL ampule with a micro stirring bar, was stirred at 130 °C for 2 h. Then it was diluted with 0.17 mL of MeCN and by HPLC analysis (eluant = 0.30 M $NaClO_4$·H_2O in 95:5 MeCN–H_2O; flow rate = 1.0 mL/min) contained **7b** (2.8 min), **8** (7.3 min), 1-[[*p*-[4-(trimethylammonio)butyl]phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-(butoxycarbonyl)-5-[[6-(trimethylammonio)hexoxy]carbonyl]-1-cyclohexene bisperchlorate (**16b**) (9.0 min), and 1-[[*p*-[4-(trimethylammonio)butyl]phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-[[6-(trimethylammonio)hexoxy]carbonyl]-5-(butoxycarbonyl)-1-cyclohexene bisperchlorate (**17b**) (6.3 min). Chromatography of the diluted reaction mixture as above gave 13.9 mg (85%) of a mixture of **16b** and **17b** that was separated by preparative HPLC (eluant = 0.50 M $NaClO_4$·H_2O in 92:8 MeCN–H_2O; flow rate = 15.7 mL/min; retention times = 20.0 and 13.6 min, respectively). The eluate collected for each isomer was concentrated, lyophilized, and extracted with $CHCl_3$. The combined extracts were rotary evaporated and chromatographed as above to give **16b** (**17b**). For **16b**: ^{1}H NMR (400 MHz) δ 7.11–7.38 (m, 8), 3.88–4.10 (m, 4), 3.43 (m, 4), 3.19 (s, 9), 3.18 (s, 9), 2.90 (m, 2), 2.70 (t, 2, J = 7.3), 2.59 (t, 2, J = 8.1), 2.40 (m, 4), 1.21–1.89 (m, 28), 0.88 (m, 6); ^{13}C NMR (100.6 MHz) δ 173.50, 173.43, 142.82, 141.18, 132.17, 132.09, 130.89, 130.56, 130.09, 129.37, 129.28, 66.68, 66.58, 64.72, 64.43, 53.23, 41.92, 35.61, 34.55, 33.51, 33.38, 31.87, 31.35, 30.45, 29.70, 29.45, 29.35, 29.24, 27.89, 27.63, 25.33, 24.88, 22.66, 22.52, 18.98, 14.10, 13.67; FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{48}H_{78}ClN_2S_2O_8$ (dication·ClO_4^-) 909.4888, found 909.4876. A peak in the FAB mass spectrum was observed at m/z = 405, which corresponds to the dication. For **17b**: ^{1}H NMR (400 MHz) δ 7.13–7.35 (m, 8), 3.96–4.14 (m, 4), 3.46 (m, 2), 3.35 (m, 2), 3.17 (s, 9), 3.16 (s, 9), 3.00 (m, 2), 2.68 (t, 2, J = 7.8), 2.59 (t, 2, J = 7.6), 2.44 (m, 4), 1.22–1.78 (m, 28), 0.88 (m, 6); ^{13}C NMR (100.6 MHz) δ 173.35, 172.91, 143.01, 140.64, 133.92, 132.59, 131.45, 130.87, 129.39, 129.30, 129.01, 128.80, 66.65, 66.48, 65.00, 64.60, 53.27, 53.11, 41.88, 41.79, 35.62, 34.51, 32.96, 32.31, 31.88, 31.33, 30.48, 29.46, 29.36, 29.24, 28.06, 27.67, 25.35, 25.15, 22.67, 22.62, 22.54, 19.07, 14.11, 13.72; FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{48}H_{78}ClN_2S_2O_8$ (dication·ClO_4^-) 909.4888, found 909.4902.

(e) 8 and 7c. A mixture of 10.6 mg (0.0165 mmol) of **8**, 30.0 mg (0.0666 mmol) of **7c**, 0.5 mg of 4-*tert*-butylcatechol, and 0.17 mL of the pH 7.0 phosphate buffer, sealed in a 1-mL ampule with a micro stirring bar, was stirred at 130 °C for 2 h. Then it was diluted with 0.17 mL of MeCN and by HPLC analysis (eluant = 0.30 M $NaClO_4$·H_2O in 95:5 MeCN–H_2O; flow rate = 1.5 mL/min) contained **7c** (2.7 min), **8** (4.9 min), 1-[[*p*-[4-(trimethylammonio)butyl]phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-(octoxycarbonyl)-5-[[6-(trimethylammonio)hexoxy]carbonyl]-1-cyclohexene bisperchlorate (**16c**) (13.9 min), and 1-[[*p*-[4-(trimethylammonio)butyl]phenyl]thio]-2-[(*p*-octylphenyl)thio]-4-[[6-(trimethylammonio)hexoxy]carbonyl]-5-(octoxycarbonyl)-1-cyclohexene bisperchlorate (**17c**) (8.3 min). Chromatography of the diluted reaction mixture as above gave 15.3 mg (90%) of a mixture of **16c** and **17c** that was separated by preparative HPLC (eluant as above; flow rate = 15.7 mL/min; retention times = 28.7 and 17.0 min, respectively). The eluate collected for each isomer was concentrated, lyophilized, and extracted with $CHCl_3$. The combined extracts were rotary evaporated and chromatographed as above to give **16c** (**17c**). For **16c**: ^{1}H NMR (400 MHz) δ 7.11–7.37 (m, 8), 3.89–4.19 (m, 4), 3.39 (m, 4), 3.16 (s, 18), 2.90 (m, 2), 2.69 (t, 2, J = 7.7), 2.58 (t, 2, J = 7.7), 2.40 (m, 4), 1.20–1.89 (m, 36), 0.88 (m, 6); ^{13}C NMR (67.9 MHz) δ 173.51, 173.40, 142.74, 141.25, 132.79, 131.94, 131.25, 130.27, 130.03, 129.36, 129.27, 66.69, 66.57, 65.03, 64.42, 53.21, 41.88, 35.61, 34.54, 33.48, 33.33, 31.88, 31.77, 31.36, 29.69, 29.44, 29.36, 29.25, 29.14, 28.43, 27.90, 27.64, 25.73, 25.35, 24.88, 22.66, 22.52, 14.11; FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{52}H_{86}ClN_2S_2O_8$ (dication·ClO_4^-) 965.5514, found 965.5490. A peak in the FAB mass spectrum was observed at m/z = 433, which corresponds to the dication. For **17c**: ^{1}H NMR (400 MHz) δ 7.12–7.36 (m, 8), 3.97–4.13 (m, 4), 3.46 (m, 2), 3.35 (m, 2), 3.17 (s, 9), 3.15 (s, 9), 3.02 (m, 2), 2.68 (t, 2, J = 7.6), 2.59 (t, 2, J = 7.8), 2.45 (m, 4), 1.20–1.88 (m, 36), 0.88 (m, 6); ^{13}C NMR (100.6 MHz) δ 173.29, 172.86, 143.02, 140.57, 134.33, 132.67, 131.23, 130.97, 129.40, 129.28, 128.98, 128.45, 66.66, 66.49, 65.33, 64.63, 53.25, 53.11, 41.77, 41.68, 35.62, 34.49, 32.82, 32.10, 31.88, 31.78, 31.33, 29.69, 29.46, 29.37, 29.25, 29.21, 29.16, 28.50, 28.07, 27.67, 25.87, 25.37, 25.18, 22.64, 22.53, 14.11; FAB HRMS (3-nitrobenzyl alcohol matrix) calcd for $C_{52}H_{86}ClN_2S_2O_8$ (dication·ClO_4^-) 965.5514, found 965.5496. A peak in the FAB mass spectrum was observed at m/z = 433, which corresponds to the dication.

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Supplementary Material Available: ^{1}H NMR homonuclear decoupling for **16c**, **17c**, and **19c**, ^{1}H NMR simulations for **16c** and **19c**, including tables of chemical shifts and coupling constants, ^{1}H NMR spectra of **8**, **16a**, **17a**, **16b**, **17b**, 1:1 mixture of **19a** and **20a**, 1:1 mixture of **19b** and **20b**, and 4-(*p*-mercaptophenyl)-1-butanol, and ^{1}H NMR data with peak assignments (21 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.