

and the addition of the thiolate to the activated form of bicyclomyacin. Definitive information concerning the precise pathway of this transformation and its relevance to the biological process are still lacking. Investigations are currently in progress aimed at addressing both of these questions.

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**Supplementary Material Available:**  $^1\text{H}$  NMR spectra (80, 300 MHz) for bicyclomyacin–sodium methanethiolate adducts **2** and **3** and the proton detected long range heteronuclear multiple quantum chemical shift correlation (HMBC) NMR spectrum and a table of NMR correlations for **4** (6 pages). Ordering information is given on any current masthead page.

## The First Cyclooctatetraene to Which Bond Shifting Is More Accessible Than Ring Inversion<sup>†</sup>

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A vast amount of kinetic and thermodynamic data makes clearly evident the fact that [8] annulenes experience mechanical tub-to-tub ring inversion (RI) more readily than alternation of their double bonds.<sup>1</sup> This has most often,<sup>1,2</sup> though not always,<sup>3</sup> been attributed to the added energy costs associated with a planar-delocalized  $4n$  transition state during the  $\pi$ -bond shifting (BS) process. Only in the case of 1,2,3,4-tetramethylcyclooctatetraene do the values for  $\Delta G_{\text{BS}}^\ddagger$  and  $\Delta G_{\text{RI}}^\ddagger$  become equalized.<sup>4</sup> In this instance, the need to eclipse and buttress a contiguous array of methyl groups external to the annulene core outweighs and levels the customarily distinguishable energy demands imposed intramolecularly.<sup>5</sup> We document herein the first example of a cyclooctatetraene which finds bond shifting to be the most kinetically accessible dynamic process available to it. Particular interest is attached to this finding because of its possible bearing on the

<sup>†</sup> Dedicated to Professor Melvin S. Newman on the occasion of his 80th birthday.

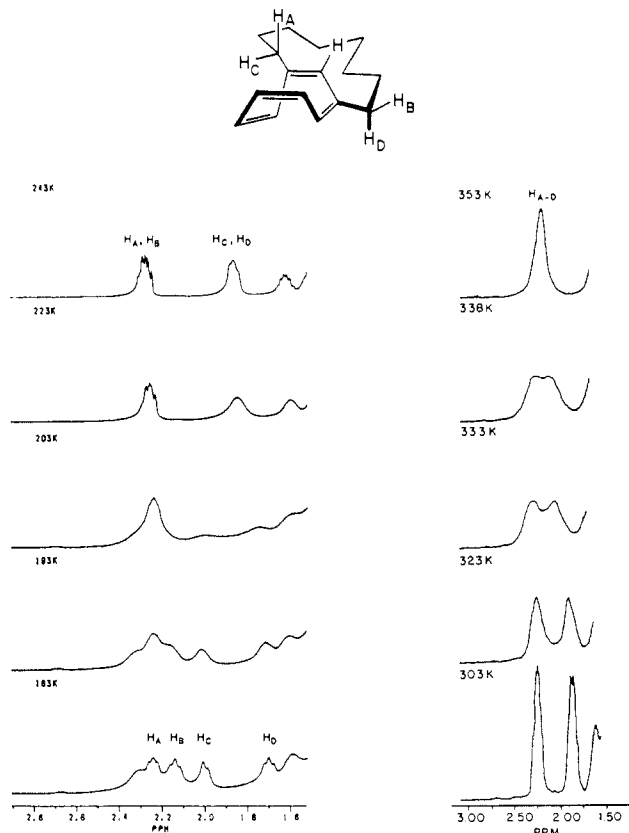
(1) (a) Anet, F. A. L. *J. Am. Chem. Soc.* **1962**, *84*, 671. (b) Anet, F. A. L.; Bourn, A. J. R.; Lin, Y. S. *Ibid.* **1964**, *86*, 3576. (c) Anet, F. A. L.; Bock, L. A. *Ibid.* **1968**, *90*, 7130. (d) Oth, J. F. M. *Pure Appl. Chem.* **1971**, *25*, 573. (e) Paquette, L. A. *Ibid.* **1982**, *54*, 987. (f) Maier, G.; Sayrac, T.; Kalinowski, H.-O.; Askani, R. *Chem. Ber.* **1982**, *115*, 2214. (g) Paquette, L. A.; Wang, T.-Z.; Cottrell, C. E. *J. Am. Chem. Soc.* **1987**, *109*, 3730 and relevant references cited in these papers.

(2) (a) Allinger, N. L. *J. Org. Chem.* **1962**, *27*, 443. (b) Snyder, L. C. *J. Chem. Phys.* **1962**, *66*, 2299. (c) Finder, C. J.; Chung, D.; Allinger, N. L. *Tetrahedron Lett.* **1972**, 4677. (d) Wipff, G.; Wahlgren, U.; Kochanski, E.; Lehn, J. M. *Chem. Phys. Lett.* **1971**, *11*, 350. (e) Allinger, N. L.; Sprague, J. T.; Finder, C. J. *Tetrahedron* **1973**, *29*, 2519.

(3) (a) Dewar, M. J. S.; Harget, A.; Haselbach, E. *J. Am. Chem. Soc.* **1969**, *91*, 7521. (b) Ermer, O.; Klärner, F.-G.; Wette, M. *Ibid.* **1986**, *108*, 4908.

(4) Paquette, L. A.; Gardlik, J. M.; Johnson, L. K.; McCullough, K. J. *J. Am. Chem. Soc.* **1980**, *102*, 5026.

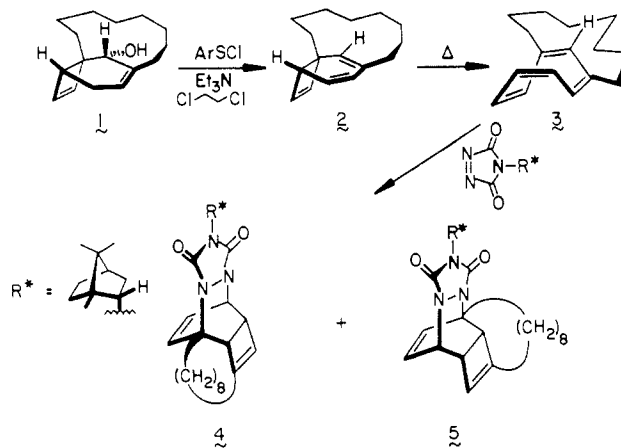
(5) (a) Gardlik, J. M.; Paquette, L. A.; Gleiter, R. *J. Am. Chem. Soc.* **1979**, *101*, 1617. (b) Paquette, L. A.; Gardlik, J. M. *Ibid.* **1980**, *102*, 5033.



**Figure 1.** Variable temperature  $^1\text{H}$  NMR spectra of the allylic protons in **3**: left panel, below room temperature (500 MHz,  $\text{CD}_2\text{Cl}_2$  solution); right panel, above room temperature (300 MHz, toluene- $d_8$  solution).

long-standing mechanistic controversy surrounding the precise reaction profile for BS.

Allylic alcohol **1**<sup>6</sup> is capable of being dehydrated at room temperature with 2,4-dinitrobenzenesulfonyl chloride and triethylamine in 1,2-dichloroethane.<sup>7</sup> The resulting bicyclo-[4.2.0]octatriene (**2**)<sup>8</sup> is more stable than its homologues having longer methylene chains because of the necessity that the interior vinylic proton pass through the loop during disrotatory opening of the cyclohexadiene subunit. The  $t_{1/2}$  for first-order isomerization of **2** to **3** at 30 °C is approximately 90 min.<sup>9</sup>



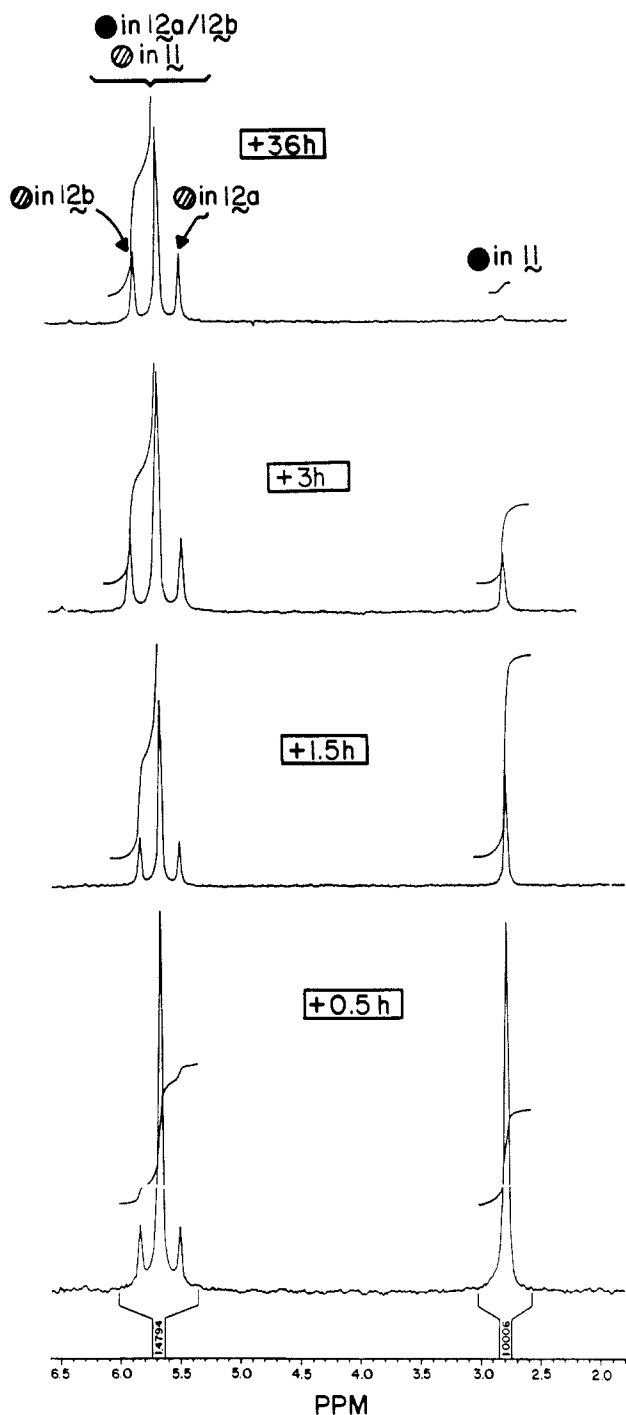
(6) Wang, T.-Z.; Paquette, L. A. *Tetrahedron Lett.* **1988**, *29*, 41.

(7) (a) Reich, H. J.; Wollowitz, S. *J. Am. Chem. Soc.* **1982**, *104*, 7051.

(b) Wang, T.-Z.; Paquette, L. A. *J. Org. Chem.* **1986**, *51*, 5232.

(8) All new compounds reported have been fully characterized by IR,  $^1\text{H}/^{13}\text{C}$  NMR, and high resolution mass spectrometry and/or combustion analysis.

(9) Ring opening of the lower homologue of **2** having a  $(\text{CH}_2)_2$  bridge proceeds yet more slowly and is conveniently amenable to kinetic analysis:  $\Delta H_{35^\circ\text{C}}^\ddagger = 24.4$  kcal/mol,  $\Delta S_{25^\circ\text{C}}^\ddagger = 1.7$  eu,  $\Delta G_{25^\circ\text{C}}^\ddagger = 23.9$  kcal/mol, and  $E_a = 25.0$  kcal/mol.



**Figure 2.** Time-dependent conversion of **11** to **12a** and **12b** (500 MHz  $^2\text{H}$  NMR,  $\text{C}_6\text{H}_6$  solution, room temperature). Note that the areas of the  $\odot$  and  $\bullet$  signals stemming from **11** decrease in intensity at the same rate.

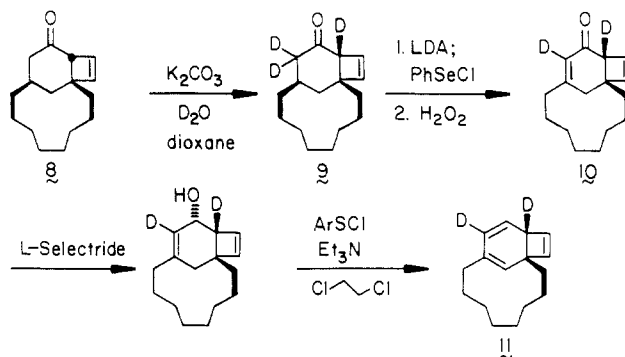
Racemic **3** enters into Diels–Alder reaction with (–)-endo-bornyltriazolinedione<sup>10</sup> when heated together in ethyl acetate solution. Diastereomer separation was achieved by MPLC on silica gel. Oxidative hydrolysis of either urazole **4** or **5** under conditions designed to preclude the use of excessive temperatures<sup>11</sup> invariably returned annulated cyclooctatetraene exhibiting no optical activity. Racemization need therefore be occurring rapidly below 20 °C.

This striking behavior can be attributed to bond shifting, ring inversion, or a combination of the two since both processes en-

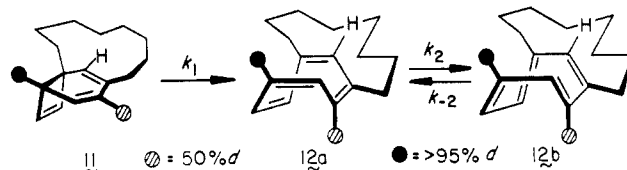
antiomerize the molecule. In this particular instance, ring inversion mandates that the [8]annulene framework be flattened, the  $\Delta G^\ddagger$  for which is recognized to be in excess of 18–20 kcal/mol for a 1,3-dialkyl-substituted cyclooctatetraene.<sup>12</sup> The total activation energy for **3** was therefore expected to be higher since the C-2 hydrogen is also required to be forced through the loop. The latter process is related to that operational in the conformational flipping within [7]metacyclophane (**6**)<sup>13</sup> and *trans*-cyclononene (**7**).<sup>14</sup> In striking contrast to expectation, however, the methylene loop in **8** significantly accelerates bond shifting.

This conclusion was verified spectroscopically. At –90 °C, the four allylic protons ( $\text{H}_A$ – $\text{H}_D$ ) in **3** exhibit distinctively different chemical shifts (Figure 1). A 2-D C–H correlation experiment confirmed that the geminal proton pairs consisted of  $\text{H}_A/\text{H}_C$  and  $\text{H}_B/\text{H}_D$ . Ring inversion in **3** would switch the environment of the geminal protons and effect coalescence between  $\text{H}_A/\text{H}_C$  and  $\text{H}_B/\text{H}_D$ . On the other hand, bond shifting interchanges the environment of the two sets of methylene protons when sufficiently rapid. A gradual increase in temperature provides clear indication for almost immediate onset of  $\text{H}_A/\text{H}_B$  and  $\text{H}_C/\text{H}_D$  coalescence. Only above 50 °C does evidence materialize for exchange between all four methylene protons. Consequently, for tub inversion  $\Delta G^\ddagger$  equals 16.0 kcal/mol at 334 K and for bond isomerization  $\Delta G^\ddagger$  equals 9.3 kcal/mol at 202 K!<sup>15</sup>

To confirm that bond shifting does operate very rapidly, ketone **8** was subjected to base-catalyzed H/D exchange, and **9** was subsequently transformed into **11**.<sup>6</sup> The  $^1\text{H}$  NMR spectrum of



**10** showed that 50% of its vinyl deuterium had been washed out, presumably as a direct result of the enhanced acidity of the  $\alpha$ -proton in the  $\alpha$ -phenylselenenyl precursor. When **11** was subjected to thermal activation as before and the course of its ring opening was monitored by  $^1\text{H}$  decoupled  $^2\text{H}$  NMR (Figure 2), three new absorptions made their appearance simultaneously. The two equally intense peaks at  $\delta$  5.88 and 5.46 are each one-fourth the area of the signal at  $\delta$  5.69. The latter is due to deuterium  $\bullet$  in



both **12a** and **12b** which overlap. The pair of smaller area peaks arise from deuterons  $\odot$ , which happen to be easily distinguished because of the differing nature of the substituent positioned alongside them on the double bond. Accordingly,  $k_1 \ll k_2$  and  $k_{-2}$ .

The amazingly low free energy of activation for bond shift isomerization is without precedent in cyclooctatetraene chemistry

(12) Paquette, L. A.; Hanzawa, Y.; McCullough, K. J.; Tagle, B.; Swenson, W.; Clardy, J. *J. Am. Chem. Soc.* **1981**, *103*, 2262.

(13) Hirano, S.; Hara, H.; Hiyama, T.; Fujita, S.; Nozaki, H. *Tetrahedron* **1975**, *31*, 2219.

(14) Cope, A. C.; Banholzer, K.; Keller, H.; Pawson, B. A.; Whang, J. J.; Winkler, H. J. S. *J. Am. Chem. Soc.* **1965**, *87*, 3644.

(15) These values are accurate only to a fraction of a kcal since they are calculated on the basis of best guesses for  $T_C$  without consideration of the spin coupling associated with two-site exchange.

(10) Gardlik, J. M.; Paquette, L. A. *Tetrahedron Lett.* **1979**, 3597.

(11) Consult, for example: (a) Paquette, L. A.; Gardlik, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 5016. (b) Reference 5b.

(even the parent hydrocarbon has  $\Delta G^\ddagger = 12$  kcal/mol at 202 K). Thus, the  $(CH_2)_8$  loop dramatically accelerates bond shifting. The barrier to ring inversion is also somewhat lower than normal, despite the need to force a vinyl proton through the methylene bridge. This reversal of the normal dynamic properties of [8]-annulenes may open the way for analysis of how bond shifting actually occurs.

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### Correlations between Wettability and Structure in Monolayers of Alkanethiols Adsorbed on Gold<sup>1</sup>

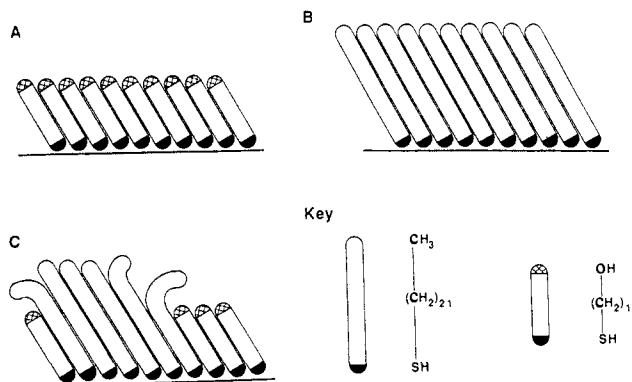
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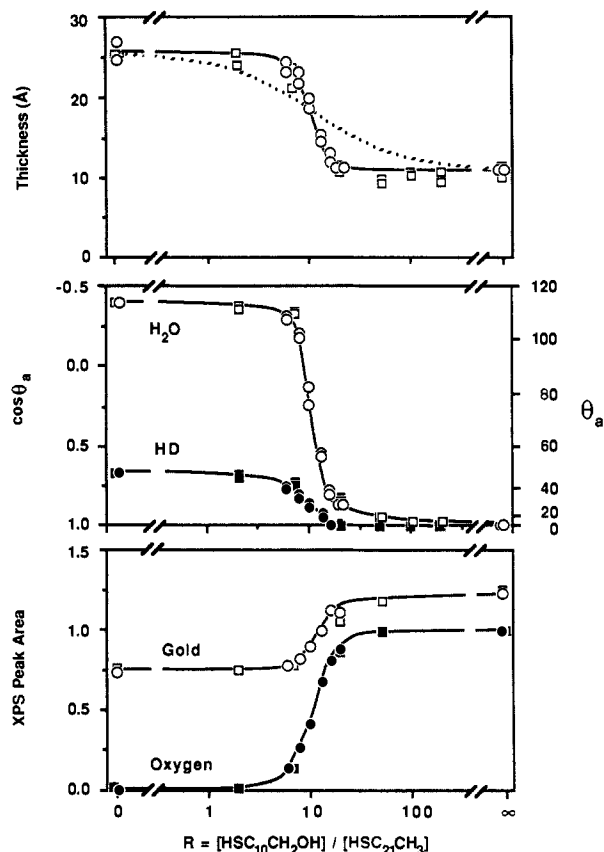
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Long-chain thiols ( $HS(CH_2)_nX$ ) adsorb from solution onto gold surfaces and form well-packed, ordered, oriented monolayers.<sup>3,4</sup> The sulfur coordinates strongly to the gold, the polymethylene chains are all-trans and tilted  $\sim 20$ – $30^\circ$  from the normal to the surface,<sup>4,5</sup> and the tail group, X, is the predominant group exposed at the monolayer/liquid or monolayer/air interface.<sup>6</sup> Co-adsorption of two or more thiols differing in tail group or chain length provides a flexible system for varying the chemistry and structure of the surface in a controlled and predetermined way.<sup>7</sup> In this paper we use monolayers comprising a mixture of  $HS(CH_2)_{11}OH$  (represented as  $HSC_{10}CH_2OH$  to emphasize the two important variables: chain length and tail group) and  $HS(CH_2)_{21}CH_3$  ( $HSC_{21}CH_3$ ) on gold to demonstrate a relationship between the microscopic structure of the surface and the wettability of the monolayer (Figure 1). This work is part of a program of physical-organic chemistry designed to relate atomic-level structure of a surface to macroscopic physical properties such as wetting and adhesion.<sup>8</sup>

Monolayers were formed by immersing gold-mirror substrates (prepared by evaporation of gold onto chromium-primed, polished silicon wafers) in solutions of the thiols in degassed ethanol for 12 h<sup>9</sup> at room temperature.<sup>6</sup> The composition of the monolayer was controlled by varying the ratio  $R = [HSC_{10}CH_2OH]/[HSC_{21}CH_3]$  in solution, with the total concentration of thiols held constant at 1 mM. We used two independent techniques, optical ellipsometry and X-ray photoelectron spectroscopy (XPS), to measure the composition of the monolayer. Since the two thiols differ in chain length, the relative thickness obtained from el-



**Figure 1.** Schematic illustrations of monolayer structures: pure  $HS(CH_2)_{11}OH$  (A); pure  $HS(CH_2)_{21}CH_3$  (B); monolayer containing a mixture of the two thiols (C).



**Figure 2.** Monolayers formed by the adsorption of mixtures of  $HS(CH_2)_{11}OH$  and  $HS(CH_2)_{21}CH_3$  onto gold from solution. The abscissa represents the ratio;  $R = [HS(CH_2)_{11}OH]/[HS(CH_2)_{21}CH_3]$  in solution. Squares and circles represent data from two separate experiments. Upper figure: ellipsometric thickness. The solid curve is a fit to the data. The dotted curve represents the theoretical thicknesses for  $K_{eq} = 11$  (see text for definition). Middle figure: advancing contact angles of water (open symbols) and hexadecane (HD) (solid symbols) obtained by the sessile drop technique. Lower figure: areas of the Au ( $4f_{7/2}$ ) (open symbols) and O ( $1s$ ) peaks (solid symbols) obtained by XPS. The vertical scale is arbitrary. Data were collected on a SSX-100 X-ray photoelectron spectrometer (Surface Science Instruments) with a monochromatized Al-K $\alpha$  source, 100 eV pass energy, and 1-mm X-ray spot. The peaks were fitted with a symmetrical 90% Gaussian/10% Lorentzian profile.

lipsometry and from the peak area of gold<sup>10</sup> in XPS reflects this composition. Similarly, the difference in tail groups allows us to calculate the surface concentration of  $HSC_{10}CH_2OH$  from the peak area of oxygen. The advancing contact angles ( $\theta_a$ ) of water

(10) The intensity of the photoelectron peak decreases exponentially with the thickness of the monolayer due to inelastic scattering of the photoelectrons (Briggs, D.; Seah, M. P. *Practical Surface Analysis*; Wiley: Chichester, 1983).

(1) Supported in part by the Office of Naval Research and the Defense Advanced Research Projects Agency. XPS spectra were obtained with facilities obtained through the DARPA/URI and maintained in the Harvard University Materials Research Laboratory.

(2) IBM Pre-Doctoral Fellow in Physical Chemistry 1985–1986.

(3) Nuzzo, R. G.; Allara, D. L. *J. Am. Chem. Soc.* **1983**, *105*, 4481–4483. Strong, L.; Whitesides, G. M. *Langmuir*, in press.

(4) Porter, M. D.; Bright, T. B.; Allara, D. L.; Chidsey, C. E. D. *J. Am. Chem. Soc.* **1987**, *109*, 3559–3568.

(5) Nuzzo, R. G.; Dubois, L. H.; Allara, D. L., unpublished results.

(6) Bain, C. D.; Troughton, E. B.; Tao, Y.-T.; Evall, J.; Whitesides, G. M.; Nuzzo, R. G. *J. Am. Chem. Soc.*, submitted for publication.

(7) Bain, C. D.; Whitesides, G. M. *Science (Washington, D.C.)* **1988**, *240*, 62–63.

(8) Troughton, E. B.; Bain, C. D.; Whitesides, G. M.; Nuzzo, R. G.; Allara, D. L.; Porter, M. D. *Langmuir* **1988**, *4*, 365–385. Holmes-Farley, S. R.; Reamey, R. H.; McCarthy, T. J.; Deutch, J.; Whitesides, G. M. *Langmuir* **1985**, *1*, 725–40. Holmes-Farley, S. R.; Whitesides, G. M. *Langmuir* **1986**, *2*, 266–281. Holmes-Farley, S. R.; Whitesides, G. M. *Langmuir* **1987**, *3*, 62–75. Holmes-Farley, S. R.; Reamey, R. H.; Nuzzo, R. G.; McCarthy, T. J.; Whitesides, G. M. *Langmuir* **1987**, *3*, 799–815. Holmes-Farley, S. R.; Bain, C. D.; Whitesides, G. M. *Langmuir*, in press.

(9) For pure thiols, initial monolayer formation is very rapid ( $\sim$  few seconds) with limiting properties reached after a few hours.