situation is not achievable with amphiphiles exposing hydrophobic end groups.

Here we report that amphiphiles having a polar head group such as an α-amino or carboxylic acid and two amide groups along the chain invariably form Z-type multilayers. A list of representative molecules and their behaviors is given in Table I. The remarkably low water contact angles of **1–3**, in spite of their hydrophobic end groups, indicate significant porosity to water. Moreover, groups with high hyperpolarizabilities, such as *p*-nitroaniline or merocyanine **4–6**, covalently attached to the above diamide handles, do not alter their ability to form stable Z-type films, as confirmed by second harmonic generation (SHG) measurements.[24] SHG is a process converting light from wavelength $\lambda = (2\pi c/\omega)$ to $\lambda/2 = (2\pi c/2\omega)$. It proceeds without specific molecular excitation, rather arising from residual noncentrosymmetrical polarizability within small but supermolecular volumes, being thus both highly dependent on and a sensitive probe of molecular packing. The very good N^2 dependence observed with films of compound **4** (see Figure 1) is direct proof of the formation of Z-type films,[25,3a,c] near (optical) equivalence of the layers, and the long term stability of the films since some of these data were reproduced over a year from the deposition date! Mixed multilayers from compounds **4** and **2**, in 1:1 ratio, also exhibited SHG. In this case there was substantial in-plane inhomogeneity indicating clustering and domain formation but nevertheless allowing stable Z-layer production.[27]

The unusual behavior of the diamide amphiphiles can be explained as follows: the amide groups located along the hydrocarbon chains on the periphery of the crystalline domains may bind water via hydrogen bonds, rendering the surface more hydrophilic. Thus, we suggest that the contact angles depend not only on the structure and nature of the terminal group of an amphiphile but also on the extent and character of the voids[19] between the domains at the surface film. This model is supported by grazing angle X-ray diffraction and reflectivity measurements on a floating monolayer of palmitoyl-R-lysine (**7**) at 20 dynes/cm.[28] The monolayer was found to be a two-dimensional powder comprising crystalline domains of approximately 500-Å diameter. The side chains are inclined at an angle of ≈60° to the water surface thus precluding close packing of neighboring domains. Indeed the Fresnel reflectivity data of **7** indicated that the monolayer coverage is 90%, the remaining 10% representing bare patches of water. The role played by the occluded water in determining the mode of deposition is indicated by the following experiments: **7** yields at 20 dynes/cm Z-type multilayers, whereas at 25 dynes/cm or above, it forms a Y-type film, in keeping with tighter packing of the domains. Drying of a deposited monolayer of monoamide **7** for 24 h at 25 °C raised its advancing contact angle and also caused Y-type deposition of the following layer. A similar treatment of a monolayer of diamide **3** did raise the contact angle but not above 90°, and thus the following depositions continued to be Z-type.

In agreement with this model, is the observation that monolayers incorporating ester groups **8** and **9**, known to bind water less firmly than amides, form Y-type films.

In order to test the generality of the present model, we are preparing new amphiphiles with different groups along the hydrocarbon chain, which should affect retention of water, the tilt of the chains, and size of domains.

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Registry No. 1, 113321-78-1; **2**, 113321-79-2; **3**, 113321-80-5; **4**, 113321-81-6; **5**, 113321-84-9; **6**, 113321-82-7; **7**, 59012-43-0; **8**, 113321-83-8; **9**, 83789-61-1.

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(20) In general, the three-phase line movement during monolayer deposition is not accurately described by quasi-static contact angles.[14] However, such angles are easily measured, being of value as indicators of the expected trend. It should also be noted that the water surface tension is lowered by the presence of a floating monolayer. According to Young's equation, for a monolayer surface pressure of 20 dynes/cm the contact angle with the floating monolayer will invariably drop to 0° for any pure water contact angle below ca. 44.5°.

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(24) Slides covered with mono- and multilayers of compounds **4–6** were studied by SHG primarily in the $\theta = 45°$ transmission geometry. Both Nd/YAG and Nd/YLF lasers were used, producing harmonics near 530 nm. Conversion efficiencies were measured relative to a quartz crystal and polarization dependences were investigated.

(25) (a) For surface SHG in the dipole approximation $I_{2\omega} \propto |\bar{e}_{2\omega}\cdot\chi_s^{(2)}\cdot\cdot\bar{e}_\omega\hat{e}_\omega|^2$, a square projection of the surface nonlinear susceptibility (a polar third-rank Cartesian tensor). Modelling $\chi_s^{(2)}$ for LB multilayers as a tensorial summation of N layer-contributions, $\chi_s^{(2)}$ depends on the layers' equivalence, registries and orientations. For idealized X- or Z-type films $I_{2\omega} \propto N^2$. Interference between successive layers in idealized Y-type films results in complete cancellation or a residual monolayer contribution when N is even or odd, respectively. SHG thus provides a critical, unambiguous test of type in well behaved films. Rigorous analysis will be presented elsewhere. (b) Heinz, T. F.; Chen, C. K.; Ricard, D.; Shen, Y. R. *Phys. Rev. Lett.* **1982**, *48*, 478.

(26) It should be commented that the scatter of data at $N = 1$ is a consequence of nonlinear constructive interference by SHG at front and back surfaces of the slide. The slides have been wiped with solvent on one side to remove the second surface layer, but, as was proved by observation and analysis of 'Maker fringe' rotation patterns, it seems that the robust first layer was not completely removed by this procedure.

(27) Details of the SHG conversion also indicate that the "nonlinearly polarizable marker" in **4**, *p*-nitroaniline, is oriented on average at a very large tilt angle from the LB film normal.

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Macroring Contraction Methodology. 4. A Novel Route to Steroid A, B, C Rings by the Transannular Diels–Alder Reaction of the 14-Membered (*E*,*E*,*E*)-Macrocyclic Triene

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Received December 14, 1987

Intermolecular reactions on macrocycles can proceed with high stereoselectivity.[1] We recently demonstrated that the transannular [2,3]-Wittig rearrangement of 13-membered diallylic ethers yields germacrane lactones.[2] We wish now to report a novel route to the steroid skeletone (A/B/C/D,cis-anti-trans-anti-trans) via the transannular Diels–Alder reaction of the 14-membered cyclic triene.[3] Intramolecular Diels–Alder reactions are useful synthetic methods, and their regio- and stereoselectivities have been well studied.[4] However, few synthetic studies on transannular

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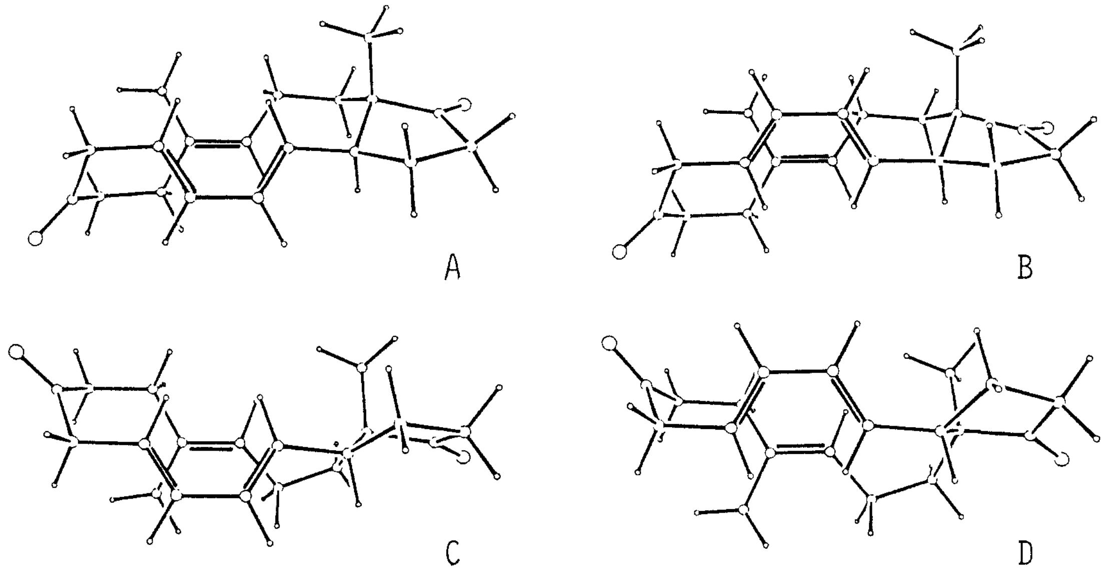
0002-7863/88/1510-2674$01.50/0

Table I. Steric Energy (kcal/mol) of the Four Possible MM2 (STO-3G) Transition Structures



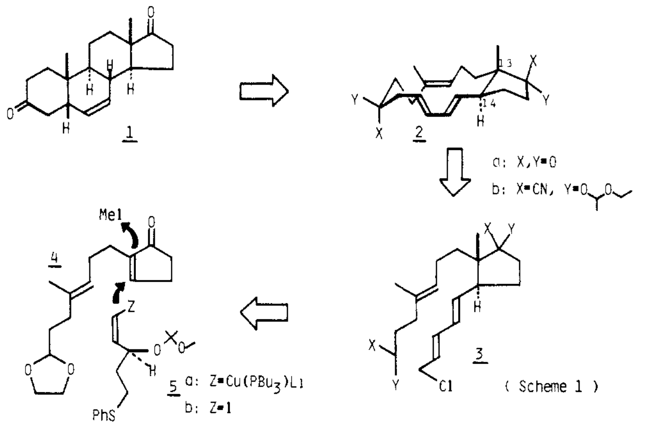
	ΔSE^a	ratio	stretching	bending	torsion	van der Waals
A	0.0	98	0.0	0.0	0.0	0.0
B	3.3	2	0.1	1.9	0.4	0.9
C	6.4	0	0.2	2.3	1.0	2.9
D	7.3	0	0.2	3.1	0.9	3.1

^{a}SE = steric energy (kcal/mol).

Diels–Alder reactions of macrocycles have been reported.[5,6]

The ab initio quantum mechanical calculations are used to obtain quantitative informations about the geometry and energetics of the transition state. This method, however, cannot be applicable directly to complex molecules because of enormous computer time required for calculations. Molecular mechanics calculations also have been proven useful in predictions[1b] (or analyses) of the stereoselectivity in macrocyclic reactions. As described below, MM2 transition structure models[7] based on ab initio calculations (see Table I) suggest that the trans stereochemistry between C(13)-methyl and C(14)-hydrogen in **2a** can control the conformation of the 14-membered ring and provide a highly stereoselective Diels–Alder reaction. Thus, in our synthetic plan (Scheme I) the triene **2a** is the key intermediate, and its 14-membered skeletone is constructed by the intramolecular alkylation[8] of the cyanohydrin **3b**. The trans relative stereochemistry between C(13) and C(14) and all functional groups required to construct **3b** are introduced by the Michael addition[9] of the cuprate **5a** to the enone **4** and subsequent β-methylation[10] of the resulting enolate.

Scheme I



To calculate the MM2 transition structures in the Diels–Alder reaction of **2a**, Houk's synchronous STO-3G transition structure[11a] of the butadiene–ethylene reaction was used as the partial geometry of the reactive diene and dienophile in the macrocycle. Connecting saturated carbon chains were substituted for appropriate hydrogens,[11b] the macroring was constructed by using the MMRS program,[12] and resulting conformations were optimized by using normal MM2 parameters[13] (Table I). Although two lower transition structures A and B have the chair–boat–chair conformations, the structure B is 3.3 Kcal/mol higher in steric energy. Much of this destabilization arises from the van der Waals and the bending energy functions (Table I). A Boltzmann distribution between A and B leads to an expected product ratio of 98:2 (A/B cis:trans).

Preparations of the enone **4** by our method[14] and the iodide **5b** are available in the Supplementary Material. The one-pot conjugate addition–enolate methylation using **4**, *cis*-vinylcopper phosphine complex **5a**, and iodomethane was carried out as previously described.[9] Treatment of the enone **4** (1.9 mmol) with

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(5) (a) Dauben, W. G.; Michno, D. M.; Olsen, E. G. *J. Org. Chem.* **1981**, *46*, 687.

(6) Recent study on the transannular Diels–Alder reaction of macrocycles is illustrated by Deslongchamps et al. (Baettig, K.; Dallaire, C.; Pitteloud, R.; Deslongchamps, P. *Tetrahedron Lett.* **1987**, *28*, 5249, 5253, 5255).

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(12) Our new version (Fukazawa, Y.; Usui, S.; Uchio, Y.; Shiobara, Y.; Kodama, M. *Tetrahedron Lett.* **1986**, *27*, 1825) corresponding to the Still's RING MAKER program: Still, W. C. In *Current Trends in Organic Synthesis*; Nozaki, H., Ed.; Pergamon Press: 1983; pp 223–246 (see ref 1a).

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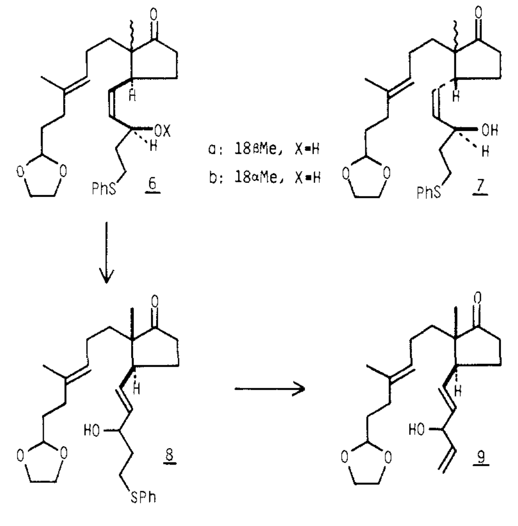
Scheme II



5a (3.8 mmol), prepared by applying Noyori's procedure,[15] in ether at −70 °C for 1.5 h, followed by addition of an excess hexamethylphosphoramide at −40 °C, methylation of the resulting enolate with an excess MeI at −30 °C, and hydrolysis of the 1-methoxyisopropyl group (0.1 N HCl/THF) afforded a readily separable mixture of ketones **6a**,**b**:**7a**,**b** (94:6)[16] in 64% overall yield. The HPLC analysis of a mixture of **6a** and **6b** revealed two peaks in an 80:20 ratio.[16] The assignment of the major isomer to **6a** is based on our previous results.[9,10] Transformation of **6a** to the dienyl chloride **3b** required three operations: (1) isomerization of the (*Z*)- to the (*E*)-olefin, (2) generation of the (*E*,*E*)-dienyl chloride, and (3) cyanohydrin ether formations. The (*Z*)-olefin in **6a** was isomerized to the (*E*)-olefin by the double [2,3]-sigmatropic rearrangements[17] (p-TolSCl/Et_3N, $P(OMe)_3$/MeOH) to give the alcohol **8** in 85% overall yield. Acetylation of **8** (Ac_2O/pyridine), oxidative elimination of the terminal phenyl sulfide ($NaIO_4$, 160 °C/xylene–pyridine), and methanolysis of the acetyl group (K_2CO_3/MeOH) gave **9** in 61% overall yield. The allylic chlorination of **9** ($SOCl_2$/CH_2Cl_2–pyridine at −70 °C, 83% yield), hydrolysis of the acetal (3 N HCl/THF, 73% yield), and protected cyanohydrin formations of the resulting keto aldehyde **3a** under our standard conditions[8a] gave **3b** in 90% yield (Scheme II).

Cyclization of **3b** with $LiN(TMS)_2$ in dioxane at 80 °C gave the macrocyclic product **2b** in 75% yield.[18] Acid treatment of **2b**, followed by base treatment of the resulting cyanohydrin gave the diketone **2a**[19] in 65% overall yield from **3b**. The Diels–Alder reaction of **2a** (in xylene at 180 °C, a catalytic amount of methylene blue) was completed within 1 h to give the tetracyclic diketone **1**[19] in 84% yield. None of the diastereomer of **1** could be detected by HPLC and NMR analyses. The ^1H NMR spectral data of the synthetic (±)-**1** were identical with those previously reported.[20] The predictions of stereoselectivity based on calculations are in quantitative agreement with the experimental trends.

This type of stereocontrol might have predictable value in organic synthesis because easy formations of the tricycles take place under mild condition and even with a less reactive dienophile. Moreover, the ab initio MM2 transition structure models are useful in designing the synthetic key intermediate providing high stereoselectivity.

Supplementary Material Available: Preparation of **4**, III, **5b**, and **3b**, experimental and spectral data for IV, VIII, IXa, IXb, III, XI, XIIa, XV, **6a**, **9**, **3a**, **3b**, and **2a**, MM2 calculations, the processes of one-pot conjugate addition–enolate methylation, the cyclization of **3b**, the Diels–Alder reaction of **2a**, and spectral data for **1** and **4** (22 pages). Ordering information is given on any current masthead page.

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(16) TLC: **6a**,**b** R_f 0.19, **7a**,**b** R_f 0.34 (55:45 hexane–AcoEt); HPLC: **6a** Rt = 14–15 min, **6b** Rt = 16–18 min, silica gel 60–5 μm, 7.5 o.d × 300 mm, 3.0 mL/min, 6% *i*-PrOH–hexane.

(17) Miller, J. G.; Kurz, W.; Untch, K. G.; Stork, G. *J. Am. Chem. Soc.* **1974**, *96*, 6774.

(18) When the reaction was carried out at 100 °C in dioxane, the tetracyclic product resulting from the transannular Diels–Alder reaction was formed in ca. 10% yield.

(19) Macrocyclic **2a**: NMR ($CDCl_3$, 500 MHz) 0.86 (s, 18-Me), 1.48 (d, $J = 0.6$ Hz, 19-Me). Tricyclic **1**: NMR ($CDCl_3$, 90 MHz) 0.95 (s, 18-Me, lit.[20] 0.94), 0.99 (s, 19-Me, lit. 0.99), 5.62 (br s, C(6,7)-olefin, lit. 5.57); CMR ($CDCl_3$, 22.5 MHz) 219.92, 212.15, 130.23, 127.09, 49.87, 48.44, 44.13, 43.74 (2 × C), 36.49, 36.29, 35.90, 34.66, 33.81, 31.92, 21.67, 21.28, 20.37, 13.97.

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Fischer Carbene Mediated Conversions of Enynes to Bi- and Tricyclic Cyclopropane-Containing Carbon Skeletons

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The reaction of Fischer carbene complexes with enyne substrates represents a potentially valuable strategy for the construction of bicyclic (or tricyclic if the carbene is tethered to the enyne) carbon skeletons (cf. **9**, Scheme I) through a coupling of the well-established mode of carbene/alkyne reactions to generate presumed vinylcarbene intermediates (cf. **1** → **2** → **3**)[2] with the less often exploited reaction of carbenes with alkenes to generate cyclopropanes (cf. **3** → **4** → **9**). The latter process of this pair is admittedly suspect of having limitations since *inter*molecular cyclopropane formation by donor-atom-substituted carbenes (e.g., $R(MeO)C{=}M(CO)_5$) is general only with electron deficient alkenes;[3] simple or electron rich olefins often suffer competitive reactions such as metathesis via presumed metallacyclobutane intermediates (cf. **4** → **8**).[4] Indeed, neither of two previous reports of reaction between carbene complexes and enynes has described the formation of cyclopropane-containing products. In one,[5] the (catalytic) conversion of 2-alkynyl-2′-alkenylbiphenyls to 5-alkenylphenanthrenes proceeded by metathesis which was driven by generation of the aromatic phenanthrene skeleton. In the other,[6] the parent hept-6-en-1-yne produced bicyclic cyclobutanones and simple furans. Carbon monoxide insertion into the vinyl carbene (cf. **3** → **7**) to provide a vinyl ketene (an intermediate which has also been proposed in naphthol formation when aryl-substituted carbenes are reacted with alkynes) followed either by an internal 2 + 2 cycloaddition (cf. **7** → **5**) or by rearrangement (cf. **7** →

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(1) (a) 3M Graduate Fellow, 1986–1987. (b) Fellow of the Alfred P. Sloan Foundation, 1985–1989. (c) Lando-SOHIO Undergraduate Research Fellow, summer 1986.

(2) For excellent overviews of both synthetic and mechanistic aspects of the chemistry of Fischer and other electrophilic carbenes, see (a) Dotz, K. H.; Fischer, H.; Hofmann, P.; Kreissl, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Weinheim, 1983. (b) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; pp 783–811.

(3) (a) Fischer, E. O.; Dotz, K. *Chem. Ber.* **1970**, *103*, 1273. (b) Dotz, K. H.; Fischer, E. O. *Chem. Ber.* **1972**, *105*, 1356.

(4) For reviews, see (a) Syatkovskii, A. I.; Babitskii, B. D. *Russ. Chem. Rev.* (*Engl. Transl.*) **1984**, *53*, 672. *Usp. Khim.* **1984**, *53*, 1152. (b) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919. (c) Doyle, M. P. *Acc. Chem. Res.* **1986**, *19*, 348. (d) Brookhart, M.; Studabaker, W. B. *Chem. Rev.* **1987**, *87*, 411. However, several examples of *intra*molecular cyclopropanation of simple alkenes are known: (e) Casey, C. P.; Shusterman, A. J. *J. Mol. Catal.* **1980**, *8*, 1. (f) Toledano, C. A.; Levisalles, J.; Rudler, M.; Rudler, H. *J. Organomet. Chem.* **1982**, *228*, C7. (g) Casey, C. P.; Shusterman, A. J.; Vollendorf, N. W.; Haller, K. J. *J. Am. Chem. Soc.* **1982**, *104*, 2417. (h) Casey, C. P.; Vollendorf, N. W.; Haller, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 375. (i) Toledano, C. A.; Rudler, H.; Karan, J.-C.; Jeannin, Y. *J. Chem. Soc., Chem. Commun.* **1984**, 574. (j) Casey, C. P.; Shusterman, A. J. *Organometallics* **1985**, *4*, 736.

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(6) Wulff, W. D.; Kaesler, R. W. *Organometallics* **1985**, *4*, 1461.