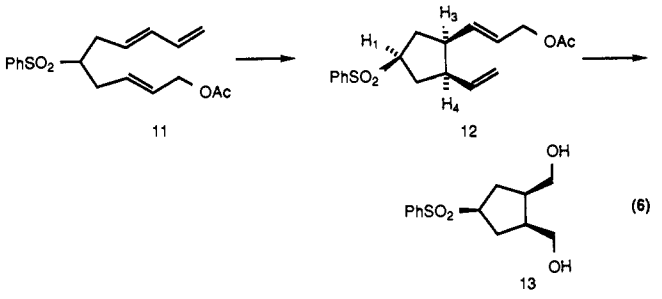
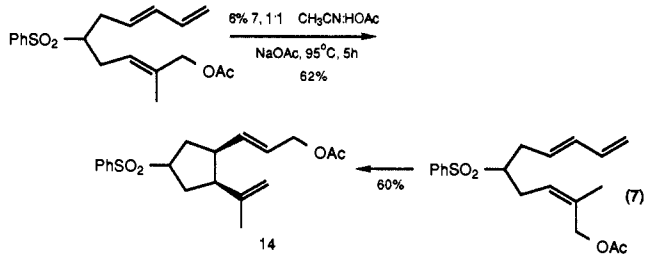
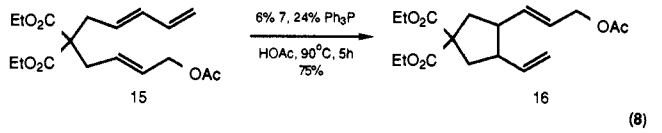


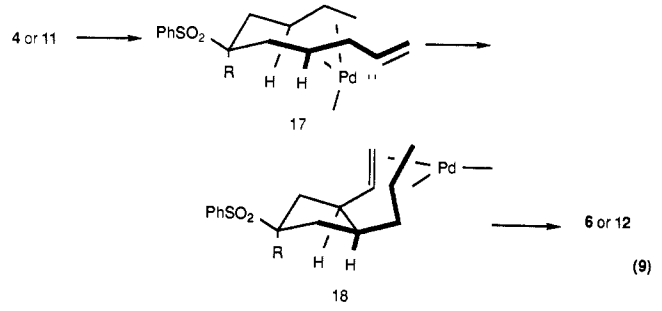
derives from conversion to diol **13**[12] [O_3, CH_2Cl_2, CH_3OH, -78 °C then $NaBH_4$, CH_3OH, 83%]. ^{13}C NMR spectroscopy reveals that **13** has a plane of symmetry [δ 62.69, t, 2 C; 62.57, d, 1 C; 42.91, d, 2 C; 29.08, t, 2 C] which requires the hydroxymethyl groups to be cis. A 7% NOE between H(1) and H(3) + H(4) suggests a cis relationship of these protons and, therefore, the cis stereochemistry of the phenylsulfonyl group. The high diastereoselectivity of this cyclization is independent of the olefin geometry of the starting material (eq 7).



In contrast to the sulfone-substituted substrates, the malonate-derived substrate **15** requires the use of triphenylphosphine for effective cyclization. The source of this difference remains an area of active investigation.



This new synthesis of cyclopentane rings based upon the principle of cyclization via isomerization can provide a stereocontrolled approach to the thermodynamically less stable cis isomers. The high stereoselectivity is in accord with a reorganization in the ligand sphere from one π-allylpalladium–olefin complex such as **17** to another such as **18** with formation of a carbon–carbon bond as shown in eq 9. The interaction of a bulky



R group in **17** with the palladium template would destabilize transition states involving a pathway proceeding through **17** to give **18**. The fact that the trans isomer dominates when R = $PhSO_2$ in **17** and the cis isomer is the exclusive product when R = H suggests that we may have access to either diastereomer depending upon the substitution pattern on the tether.

The fact that the product retains an allyl acetate moiety which is reactive toward the types of catalysts employed makes the success of this cyclization via isomerization rather remarkable. Obviously, the functionality generated in the product offers an opportunity for further structural elaboration.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health, General Medical Sciences Institute, for their generous support of our programs. Mass spectral data was graciously provided through the Mass Spectrometry Facility, University of California—San Francisco, supported by the NIH Division of Research Resources.

Registry No. 2, 116997-87-6; **3**, 116997-88-7; **4**, 116997-89-8; **5**, 116997-90-1; *cis*-**6a**, 116997-99-0; *trans*-**6a**, 117065-70-0; *cis*-**6b**, 116998-00-6; *trans*-**6b**, 117065-71-1; *cis*-**8**, 116998-01-7; *trans*-**8**, 117065-72-2; **9a**, 116997-93-4; **9b**, 116997-94-5; **10**, 117024-47-2; **11**, 116997-96-7; **12**, 116998-04-0; **13**, 116998-05-1; **14**, 116998-02-8; **15**, 116997-98-9; **16**, 116998-03-9; $PhSO_2CH_2SO_2Ph$, 3406-02-8; (*E*,*E*)-H_2C=CHCH=CHCH_2C(SO_2Ph)$_2$CH_2CH=C(CH_3)CH_2OAc, 116997-91-2; (*Z*,*E*)-H_2C=CHCH=CHCH_2C(SO_2Ph)$_2$CH_2CH=C(CH_3)CH_2OAc, 116997-92-3; (*E*,*E*)-H_2C=CHCH=CHCH_2CH(SO_2Ph)CH_2CH=C(CH_3)CH_2OAc, 116997-95-6; (*Z*,*E*)-H_2C=CHCH=CHCH_2CH(SO_2Ph)CH_2CH=C(CH_3)CH_2OAc, 116997-97-8; 3,4-epoxy-1-butene, 930-22-3; 3,4-epoxy-1-cyclohexene, 6705-51-7.

Supplementary Material Available: Spectral data for **6a**, **6b**, **8**, **10**, **12**, **14**, and *trans*-**16** (4 pages). Ordering information is given on any current masthead page.

Does the Conformation of Hydrocarbon Chains Depend on Solvation?

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Received July 22, 1988

Modern theoretical and instrumental methods have failed to resolve many simple yet significant chemical questions. This communication addresses one of them: How are the conformations of hydrocarbon chains affected by solvation? The question is significant because hydrocarbon chains embedded in solvent are among the most important structural units in chemistry and biology. Within a crystal, aliphatic hydrocarbons assume extended, all-trans geometries.[1] On the other hand, *n*-butane in the gas phase contains about 25% gauche rotamer.[2] Only 16% of gaseous *n*-heptane is all-trans.[3] Matters are, however, far less definitive with the liquid state. The origins of the trans/gauche energy difference are not completely understood,[4] and even less is known about how solvation influences the controlling elements. Access to chain behavior in solution has been hampered by computational complexities and a poor experimental approachability.

Conformational data on hydrocarbon chains in solution are, of course, available although often in conflict. Thus, Jorgensen et al.[5] have repeatedly found in Monte Carlo simulations that hydrocarbons (e.g., butane, pentane, and hexane) do not experience conformational changes upon transfer from the gas phase to neat liquids. In contrast, spectroscopic studies[6-8] indicate a marked phase-sensitivity for *n*-butane. According to computations of Pratt et al.,[9] the more globular gauche form is favored in the condensed phase where molecules are close enough for repulsive interactions

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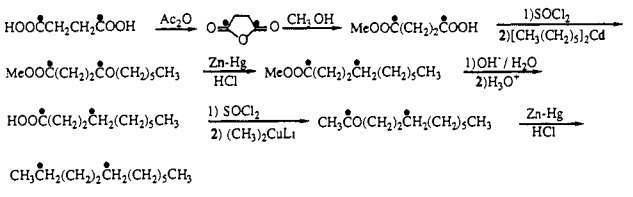
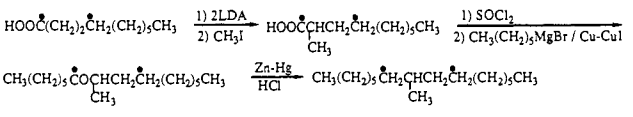
Scheme I

1. Synthesis of Undecane-2,5-di-^{13}C

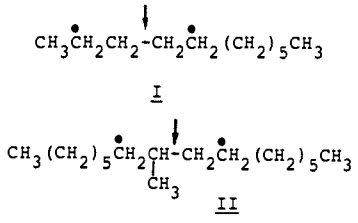


2. Synthesis of 8-Methylhexadecane-7,10-di-^{13}C



to predominate. With regard to solvent effects on chain conformation, Rosenthal et al.[10] find, via Raman spectroscopy, that trans/gauche energy differences vary little when *n*-butane is transferred from pure liquid to CH_2Cl_2 or CCl_4. In contrast, IR work of Casal et al.[11] on *n*-tridecane-7,7-d_2 shows that the average gauche fraction increases from 35% to 60% when the solvent is changed from *n*-heptane to hexadecane. To compound the uncertainties, trans/gauche ratios have never been determined in polar solvents. No one knows how flexible chains acquiesce to the constraints (if such exist) imposed by various solvent shells.[12]

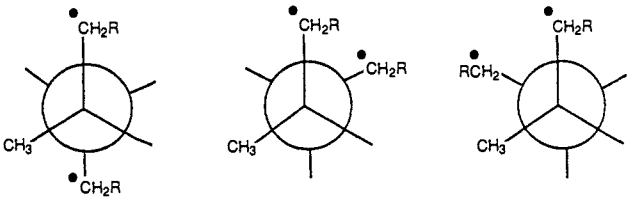
We have exploited the di-^{13}C-labeling method (already applied to several chemical and biological systems[13-15]) to conformational changes in hydrocarbons I and II dissolved in diverse solvents.



The method is based on the Karplus-like responses of $^3J_{CC}$ to the relative disposition of the two ^{13}C atoms about the central bond. Thus, when trans rotates to gauche, $^3J_{CC}$ decreases from 4 to 2 Hz. Once the labeled compounds were in hand (Scheme I),[17] securing the couplings, and hence the conformational preferences, was trivial; we merely had to measure separation between members of the two doublets looming above the natural abundance peaks.

NMR runs on hydrocarbon I were performed at 25 °C with 0.5 and 2.0 M solutions of 10% dilabeled material with 400 aquisitions at a sweep-width of 1600 Hz on an IBM 200 MHz instrument. A $^3J_{CC}$(obsd) of 3.6 ± 0.1 Hz was obtained consistently in four solvents of widely differing polarity: chloroform, ether, ethanol, and 13% water-in-ethanol. The coupling of 3.6 Hz corresponds to 24% gauche and 76% trans (calculated from J_g = 2.0 Hz and J_t = 4.1 Hz[16] and by assuming that $^3J_{CC}$(obsd) is a weighted average of the two). Since the couplings in the four solvents are constant (within the precision of the experiments that allowed detection of $a \geq 10\%$ change in gauche value), it is clear that the conformation of I about the C_3–C_4 bond is unaffected by solvation phenomena. Note that only one of the four distinct C/C dihedral angles in undecane has been probed. There is no reason to suspect, however, that the C_3–C_4 linkage behaves atypically among its neighbors although further work on this point is required.

Dilabeled hydrocarbon II was investigated because, according to molecular mechanics calculations (MODEL), two of its major rotamers (trans T and gauche G_1) possess virtually identical steric



T G_1 G_2

energies (12.7 kcal/mol). Since interconversion costs little or no "conformational energy", solvation effects could conceivably dictate the equilibria in the solution phase. Such is not the case however. Long-range couplings of 2.8 ± 0.1 Hz were observed with neat II and with material dissolved in hexane, cyclohexane (spectra traced normally and with an INADEQUATE pulse sequence), xylene, chloroform, acetone, ethanol, and 14% water-in-ethanol. The remarkable insensitivity of chain conformation to surroundings was further demonstrated by MM2 dihedral driver computations from which we deduced populations of 62% (G_1 + G_2) and 38% T. These numbers, along with J_g = 2.0 Hz and J_t = 4.1 Hz, gave a calculated $^3J_{CC}$ = 2.8 Hz in the gas phase—the *identical* value found in various solvents including aqueous ethanol.

Hydrocarbon folding in 100% water remains an unknown (insolubility prevented the experiment). Extrapolating our results to water would, of course, be reckless despite the wide range of solvent polarities employed. Water's unique behavior, like its natural purity, must be respected.

Acknowledgment. This work was supported by the National Institutes of Health.

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(17) The cost of the dilabeled succinic acid (MSD Isotopes) and the length of the synthesis required that the yield of each step be optimized with unlabeled materials on an equivalent scale.

Structure of Aranorosin, a New Antibiotic of a Novel Skeletal Type†

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A novel antibiotic, designated aranorosin (**1**) has been isolated from a fungal strain, *Pseudoarachniotus roseus*. The compound is active against Gram-positive bacteria and fungi and also shows antitumor properties.[1] The antibiotic, present in both the mycelium and culture filtrate, is extractable and purified by repeated chromatography over silica gel.[2] In this paper we report

† Dedicated to Prof. N. S. Narasimhan of the University of Poona on the occasion of his 60th birthday.

(1) Minimum inhibitory concentration (μg/mL) of aranorosin against a few selected test organisms: *Staphylococcus aureus* 209P, 1.5; *Streptococcus faecalis*, 3.0; *Bacillus subtilis*, 1.5; *Pseudomonas aeruginosa* ATCC 9027, >100; *Candida albicans*, 30; *Aspergillus niger*, 7.5; *Penicillium italicum*, 30; *Microsporum gypseum*, 3.0.

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