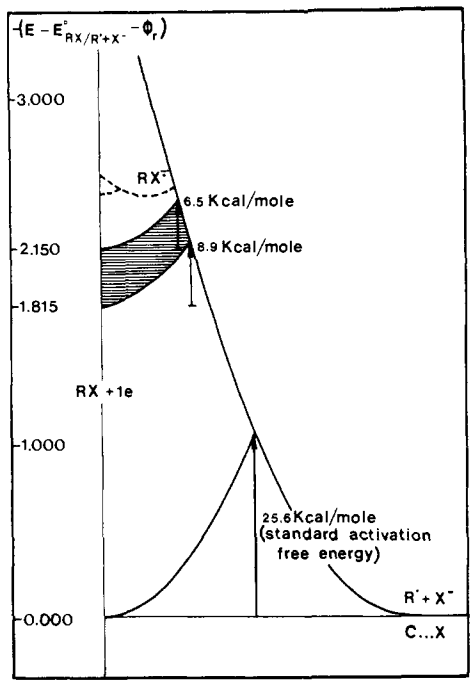
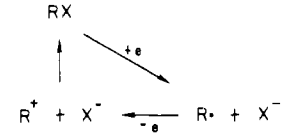


Figure 4. Representation of the potential energy surfaces for the electrochemical reduction (hatched zone, 1 V s^{-1}, cyclic voltammetry) for compound **2** in the context of Marcus theory ($RX + e^- \rightarrow R\cdot + X^-$).

X^-, involving a driving force of at least −2.2 eV (51.3 kcal), i.e., a dissociation constant of 7×10^{37} M.

So far we have assumed that the rate-determining process of the overall $RX + 2e^- \rightarrow R^- + X^-$ is the bond cleavage assisted transfer of one electron leading to R· and X^-, R· being further reduced into R^-. Since the latter reaction has a large driving force (−1.28 V at the peak of the cyclic voltammogram), the question may be raised of the possibility that the transfer of the second electron is concerted with the transfer of the first and the bond cleavage. Analysis of the electrochemical data in the same way as above does not lead to a clear-cut answer: the α predicted by the Marcus relationship (0.23) is much too large as compared to the experimental value (0.125 for a two-electron process) but the α's deriving from the Marcus–Agmon–Levine and the Rehm–Weller relationships (0.16 and 0.09, respectively) are compatible with the experimental value. This possibility is, however, unlikely since the introduction of two electrons in a molecule where the C–X bond is only moderately stretched would result in a very large Coulombic repulsion barrier. It is thus more likely that the second electron enters the system when, the bond being almost broken, it retains the characteristics of the R· radical.

Lastly, it is worth discussing the mechanism of the reverse reaction, i.e., the oxidation of $R^- + X^-$ back into RX. R^- is first reversibly reoxidized into R· without interference of the halide ions. Then R· is reoxidized first into R^+ which reacts with the halide ion regenerating the starting alkyl halide:



The reoxidation pathway is thus not the exact reverse of the reduction pathway. This is not an unprecedented situation. The same occurs in the electrochemistry of vitamin B_{12} derivatives:[38] the reduction of a strongly liganded cobalt(II) complex into the cobalt(I) complex is a one-electron transfer involving the breaking of a cobalt axial ligand bond (analogous to the $RX + e^- \rightarrow R\cdot + X^-$ in the present case) whereas the reoxidation reaction involves first the oxidation of the cobalt(I) complex into a cobalt(II) complex weakly bound with the solvent (analogous to $R\cdot\text{-}e^- \rightarrow R^+$) and then the coordination by the strong ligand (analogous to $R^+ + X^- \rightarrow RX$).

Experimental Section

9-Chloro-9{α-(9-fluorenylidene)}benzylfluorene (**1**) and 9-chloro-9-mesitylfluorene (**2**) were prepared as described in a previous paper.[15b] The procedures for solvent and supporting electrolyte purification are also described there. Due to the extreme hygroscopy of tetrabutylammonium chloride, stock solutions were prepared at the vacuum line and diluted to the desired concentrations. The working electrode was a bright platinum disk of about 0.08 cm^2 surface area. The other electrodes, cell, and instrumentation were the same as previously described.[15b]

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Communications to the Editor

Configuration Entropy of the Alanine Dipeptide in Vacuum and in Solution: A Molecular Dynamics Study†

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The configurational entropy of biopolymers is an important contribution to their free energy and thus can play an essential role in determining their structure and function.[1-3] In many cases it is appropriate to separate the configurational entropy into two parts, i.e., that contributed by the presence of several accessible minima and that contributed by the flexibility in each of the minima. Evaluation of the latter is the focus of this paper; the former can be obtained by summing over the results for each of the minima with the appropriate statistical weights. Harmonic treatments have been used for the configurational entropy of biopolymers.[3-6] To introduce anharmonicity, the results of

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Table I. Configurational Entropy Differences for the Dipeptide[a,b]

system	ΔS, cal/(mol K)	$T\Delta S$, kcal/mol
C_5(vac, old) to C_7^{eq}(vac, old)	−1.78	−0.53
C_7^{eq}(vac, old) to C_7^{eq}(sol, old)	−1.41	−0.42
P(sol, new) to α(sol, new)	−1.51	−0.45
P(sol, new) to C_7^{eq}(sol, old)	−1.60	−0.48

[a] All values at 300 K. [b] Vac and sol refer to vacuum and solution simulations, respectively. Old and new refer to the type of hydrogen bonding potential that was used. A weaker hydrogen bond potential than employed in the earlier simulation[10] was used in some cases since it appears that the internal C_7^{eq} dipeptide hydrogen bond was too strong relative to the solvent interactions.[9] The entropic effect of this change is negligible; e.g., C_7^{eq}(vac, old) to C_7^{eq}(vac, new) is −0.080 cal/(mol K).

molecular dynamics simulations can be employed to estimate the probability density for the important internal coordinates. If a temperature-dependent multivariate Gaussian probability distribution (quasi-harmonic approximation) is introduced,[7] the resulting entropy difference between two conformations a and b is

$$\Delta S = S_b - S_a = \frac{k_B}{2} \ln \frac{\sigma_b}{\sigma_a} \qquad (1)$$

where σ is the determinant of the covariance matrix σ with elements $\sigma_{ij} = \langle (q_i - \langle q_i \rangle)(q_j - \langle q_j \rangle) \rangle$ and q_i and q_j are individual internal coordinates; the brackets represent averages over the simulation. We report here an evaluation of the configurational entropy change for conformational transitions and the solvation of *N*-methylalanylacetamide, the alanine "dipeptide" $CH_3CONHCHCH_3CONHCH_3$. This small molecule is often used as a model system for polypeptides and proteins because it contains the essential dihedral angles (ϕ,ψ,ω) and the polar groups (C=O, NH) of the peptide bond.

Molecular dynamics simulations were performed on several conformations in vacuo and in aqueous solution. To obtain converged results in vacuum for this relatively harmonic system, 16 independent 20-ps simulations were performed for a given conformation and averaged. To determine the solution behavior, a dipeptide and 195 H_2O molecules with periodic boundary conditions were carefully equilibrated for each conformation and the simulations for analysis were then continued for periods from 6 to 12 ps. All simulations were done at 300 ± 4 K. The configurational entropy differences (eq 1) were determined from the simulations by evaluating the matrix σ with a complete set of bond and dihedral angles.[8] Details of the potential and the simulations are given separately.[9-11]

The vacuum conformations investigated are C_5 (−180, 180) and C_7^{eq} (−70, 80), both of which are local minima on the (ϕ,ψ) surface.[9] In solution the C_7^{eq}, α-helical (−60, −60), and polyproline (−70, 150) configurations were studied. The results given in Table I show that the entropy changes are not large. They may be significant, however, because the present system corresponds to a single amino acid unit and the entropy changes in a polypeptide would scale approximately as the number of amino acids.

Since the entropy changes associated with the transitions are small in magnitude, the signs obtained from the solution simulations are uncertain. Longer simulations are in progress to reduce the statistical errors of these calculations.

The decrease in entropy in vacuum in going from C_5 to C_7^{eq} is expected since the internal hydrogen bond present in the latter restricts configurational freedom. This is illustrated by the trajectories in (ϕ,ψ) space for the two conformers shown in Figure 1. However, the back-bone dihedral angles by themselves do not provide an adequate description of the entropy change.[7] Table II shows for a vacuum example that the average over ϕ,ψ gives less than a third of the entropy difference and that additional important contributions come from the other dihedral angles and from the bond angle and improper torsional terms. Most significant is the result that it is not the individual contributions of the latter but their correlations with the dihedral angles that are important; i.e., adding the dihedral, bond angle, and improper torsion terms gives about half of the total entropy difference.

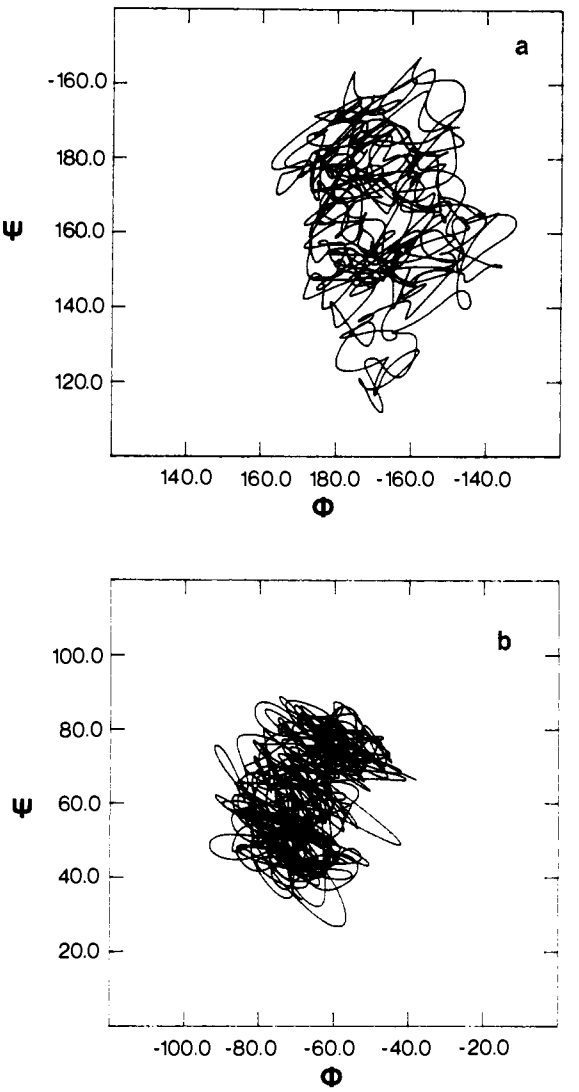

Figure 1. Vacuum dipeptide trajectories in (ϕ,ψ) space at 300 K; (a) C_5 conformer, 6 ps of dynamics; (b) C_7^{eq} conformer, 6 ps of dynamics.

Table II. Vacuum C_5 to C_7^{eq} Entropy Difference Decomposition[a]

coordinate subset	full matrix	diagonal elements
complete	−1.78	−1.25
ϕ,ψ	−0.52	−0.51
all dihedrals	−0.94	−1.32
bond angles	−0.43	−0.42
improper torsions	0.49	0.49

[a] All values in cal/(mol K).

The entropic stabilization of C_5 (−0.53 kcal/mol at 300 K) relative to C_7^{eq} in vacuum is more than counter-balanced by the enthalpy of the transition. From the simulation, ΔH for C_5 to C_7^{eq} is −4.15 kcal/mol and the calculated free energy difference is −3.6 kcal/mol; this is nearly the same as the potential energy difference at the two minima (−3.52 kcal/mol) on the surface used.

The transfer of the dipeptide from vacuum to aqueous solution shows a configurational entropy change of −1.4 cal/mol K (−0.42

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kcal/mol at 300 K). This change is small compared with the calculated solvation enthalpy (−23 kcal/mol) at infinite dilution.[10]

Comparison of the internal entropy differences of the conformers in solution shows that the values are of the same magnitude as those found in vacuum (see Table I). The solvated polyproline conformation appears to have somewhat less freedom than the α-helical conformer, which is very similar in entropy to the C_7^{eq} conformer.

This study of a peptide model system has demonstrated that molecular dynamics simulations can be used to estimate the configuration entropy differences in conformational transitions and in solvation processes. Such internal entropy changes have to be included in any calculations of the free energy differences between conformers.[12,13]

Acknowledgment. We thank B. Brooks, M. Pettitt, W. Reiher, P. Rossky, and S. Swaminathan for helpful discussions. Part of the calculations reported here were performed at the Rowland Institute and Los Alamos National Laboratory.

Registry No. $CH_3CONHCHCH_3CONHCH_3$, 22715-68-0.

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Intramolecular Reductive Elimination of Methane from a Dinuclear Palladium Complex Containing Methyl and Hydride on Adjacent Palladium Centers

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Dinuclear elimination of groups from two different metal atoms involving the formation of metal-metal bonds or bridged metal centers is an important step in many reactions that are catalyzed by transition metals.[1] Although intermolecular dinuclear reductive elimination mechanisms have been established for several reactions,[2] only rarely have the corresponding intramolecular eliminations been investigated.[3] We report herein the preparation, isolation, and structure of a dinuclear palladium complex containing methyl and hydride on adjacent palladium atoms and its facile 1,1-dinuclear intramolecular elimination of methane.

Although a relatively large number of dinuclear platinum complexes containing two bridging bis(diphenylphosphino)methane ligands and alkyl groups σ-bonded to platinum are known, there are relatively few examples of similar dinuclear palladium complexes.[4-6] The reaction of an equimolar amount of trimethylaluminum with the palladium(I) chloride dimer $Pd_2Cl_2(\mu\text{-dppm})_2$ [dppm=bis(diphenylphosphino)methane] (**1**)[7] at −78 °C in methylene chloride gave an intermediate (**2**) which could not be isolated (Scheme I) but was characterized by its ^1H and $^{31}P\{^1H\}$ spectra. The $^{31}P\{^1H\}$ spectrum of **2**, analyzed as an AA′BB′ spin system, is shown (Figure 1) along with the calculated spectrum.

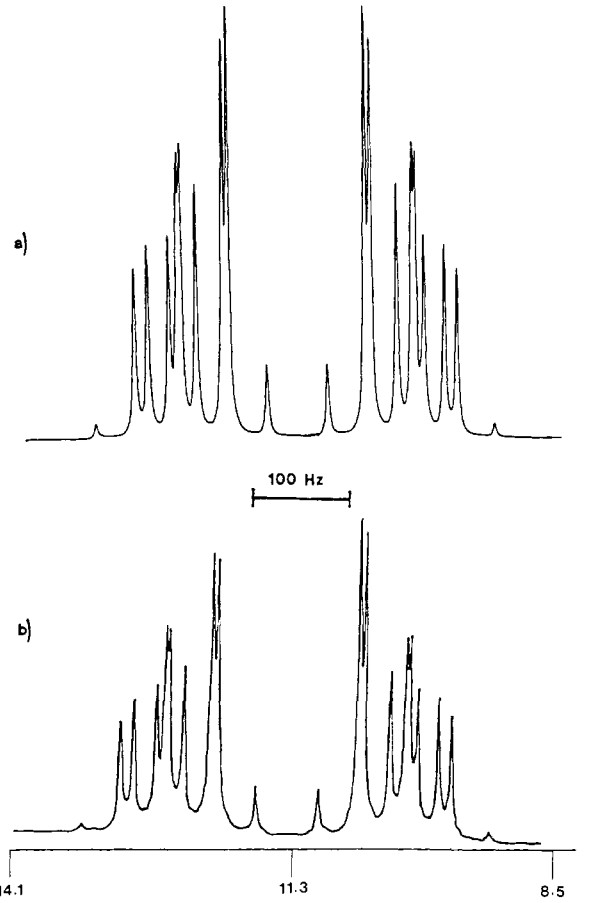

Figure 1. $^{31}P\{^1H\}$ NMR (81.015 MHz) of **2**. (a) Simulated spectrum; (b) spectrum of **2** at −80 °C in CD_2Cl_2.

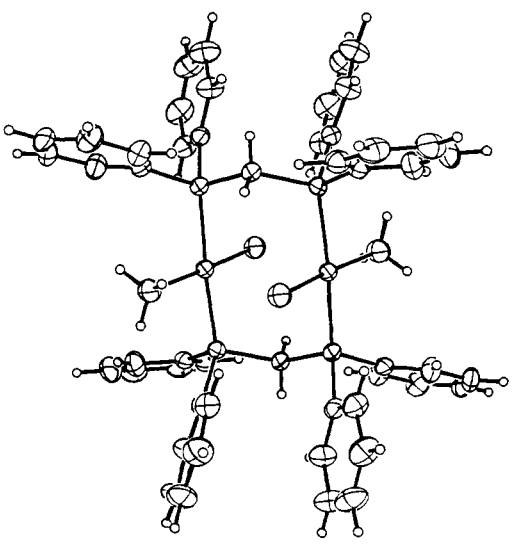

Figure 2. X-ray Structure of **3**.

An ambient temperature, **2** disproportionated to a palladium(0) complex (**4**) and **3**. The X-ray structure of **3** (Figure 2) verified a face-to-face dimer with methyl groups in the anti geometry. The palladium(0) complex **4** reacted with methylene chloride to give the A-frame methylene-bridged dimer **5**. The reaction of methylene chloride with $Pd_2(dppm)_3$ to form **5** has been reported to proceed very slowly.[7b] A faster reaction with **4** was observed, apparently because it is a more coordinatively unsaturated palladium(0) species. Complex **3** is not available via the oxidative addition of methyl chloride to $Pd_2(dppm)_3$.

Intermediate complex **2** reacted with ethanol at −78 °C to give the dinuclear palladium complex **6**-H, containing methyl and

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