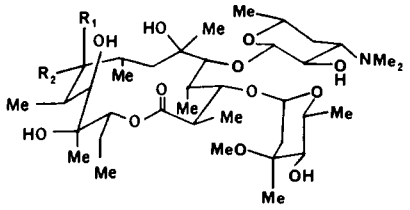
the glycoside **7d** (55% yield based on consumed **7b**; 37% conversion).[17c] The newly introduced anomeric stereochemistry of **7d** was shown to be of the desired α configuration (vide infra). This stereochemical outcome can be attributed largely to participation by the solvent, CH_3CN, which contributes to an overall double inversion during the course of the reaction.[19] These gratifying results enabled us to achieve site-selective introduction of both sugar moieties in a surprisingly simple manner, avoiding the extensive use of protecting groups.

Completion of the synthesis of erythromycin was carried out in the following manner. Simultaneous deprotection of both the C-4″ hydroxyl group of the cladinose moiety and the C-9 amino group in **7d** by Na-Hg/MeOH[13] furnished (9*S*)-erythromycylamine (**10a**) [mp 126-129 °C, $[\alpha]^{25}_D$ -48.1° (*c* 0.59, $CHCl_3$); 75% yield] which was found to be identical with an authentic



10a $R_1 = NH_2$ $R_2 = H$
10b $R_1 = NHCl$ $R_2 = H$
10c $R_1 = R_2 = NH$

sample prepared from natural erythromycin by a known method.[20] Treatment of **10a** with *N*-chlorosuccinimide (1 equiv) in pyridine at 25 °C gave **10b** (mp 166-170 °C with partial melting at 130-134 °C), which was dehydrochlorinated by AgF in HMPA at 70 °C to yield erythromycinimine (**10c**).[20a,b,21] Hydrolysis of **10c** in water at 5 °C afforded the corresponding ketone (40% overall yield from **10a**), which was found to be identical with erythromycin (**2**) in all respects (^1H NMR, mp, mmp, α_D, mass, IR and chromatographic mobility).[22]

Acknowledgment. We are indebted to Professor Yoshito Kishi for his help and encouragement and, in particular, for his acceptance of the role of principal investigator upon Professor Woodward's death. Financial assistance from the National Institutes of Health (GM04229) is gratefully acknowledged. Mass spectra and FT-IR spectra were provided by the facilities supported by the National Science Foundation (Grants CHE-7908590 and CHE-7805150, respectively). The 250-MHz ^1H NMR spectra were measured by the facility supported by the National Science Foundation (Grant CHE-8019562) at the Massachusetts Institute of Technology.

Supplementary Material Available: Physical properties (IR and ^1H NMR spectra, etc.) of selected synthetic substances (including **2**, **6a,b**, **7a-d**, **8a**, **9a**, and **10a,b**) and scheme used for the synthesis of **2** from **3d** (16 pages). Ordering information is given on any current masthead page.

(19) For sterically demanding glycosidation substrates such as **7c**, pronounced participation by CH_3CN was expected.[15f] The presumed intermediate nitrilium species was expected to have the β configuration, due to the "reverse anomeric effect": West, A. C.; Schuerch, C. *J. Am. Chem. Soc.* **1973**, *95*, 1333. Lemieux, R. U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2205.

(20) (a) Wildsmith, E. *Tetrahedron Lett.* **1972**, 29. For other known methods, see: (b) Timms, G. H.; Wildsmith, E. *Ibid.* **1971**, 195. (c) Massey, E. H.; Kitchell, B.; Martin, L. D.; Gerzon, K.; Murphy, H. W. *Ibid.* **1970**, 157.

(21) Commonly used methods for oxidation of an amine were unsuccessful when applied to **10a**: (a) Kahr, K.; Berther, C. *Chem. Ber.* **1960**, *93*, 132. (b) Corey, E. J.; Achiwa, K. *J. Am. Chem. Soc.* **1969**, *91*, 1429. (c) Bachmann, W. E.; Cava, M. P.; Dreiding, A. S. *Ibid.* **1954**, *76*, 5554. Ruschig, H.; Fritsch, W.; Schmidt-Thomé, J.; Haede, W. *Chem. Ber.* **1955**, *88*, 883. (d) Bacon, R. G. R.; Hanna, W. J. W. *J. Chem. Soc.* **1965**, 4962. We attribute this failure in part to the hindrance caused by the hydroxyl groups at C-6 and C-11, which are close spatially to the C-9 amino group in **10a**. Thus treatment of **10a** with 3,5-di-*tert*-butyl-1,2-benzoquinone[21b] furnished the corresponding perhydro-1,3-oxazine at C-9/C-11 as a stable product.

(22) The glycoside **3d** (see text) has also been successfully converted to erythromycin: for the sequence employed see the supplementary material. This transformation constitutes another total synthesis of erythromycin, since **3a** (the precursor to **3d**) is derived from erythronolide A[1,2] and the synthesis of erythronolide A has been reported by Corey et al.; see ref 1e in the first paper in this series.

Measurements of Degenerate Radical Ion-Neutral Molecule Electron Exchange by Microsecond Time-Resolved CIDNP. Determination of Relative Hyperfine Coupling Constants of Radical Cations of Chlorophylls and Derivatives[1]

G. L. Closs* and E. V. Sitzmann

Chemistry Division, Argonne National Laboratory Argonne, Illinois 60439 and Department of Chemistry, The University of Chicago Chicago, Illinois 60637

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Chemically induced dynamic nuclear spin polarization (CIDNP) has been shown to be a good method to study photochemical electron transfer.[2] Electron transfer of an excited donor (D) or acceptor (A) molecule produces a geminate radical ion pair which may undergo a back-reaction leaving D and A in their ground states with polarized nuclear spins. It has been pointed out by one of us[3] that if the *only* reaction is electron transfer from D to A followed by back-transfer to regenerate ground states, it may be impossible to observe CIDNP unless the free paramagnetic ions have a relatively long life. This prediction arises directly from the radical pair theory of CIDNP which rigorously requires that at high field the nuclear polarization of the radicals undergoing geminate annihilation is of opposite sign and equal magnitude as that carried by the escaping free ions. If the free ions are converted to the same products as the geminate ions, no observable polarization results *unless* the free ions lose some of their polarization by relaxation, thus making the polarization generated in the geminate process dominant. The conversion of the polarized ions to polarized diamagnetic products can occur by ion annihilation and ion-neutral molecule electron exchange according to (1),

$$*D^+ + D \rightleftarrows *D + D^+ \quad (1)$$

where the asterisks denote nuclear spin polarization. Since the concentration of the neutral molecules is often much higher than that of the ions, this is frequently the most important pathway and leads to failure to observe CIDNP.

In this communciation, we wish to show that fast time-resolved CIDNP spectroscopy can get around this difficulty and give some information on electron exchange kinetics which are difficult to measure directly by other methods.[4] The basis for the success of the time-resolved method is the fact that geminate processes are complete in a fraction of a microsecond, while combination of free ions and/or exchange according to (1) may take tens or hundreds of microseconds depending on concentrations. Thus, if the magnetization is probed, say at 1 μs after the radical ions have been generated by a laser flash, the polarization of products that is probed originates almost exclusively from geminate processes and has not yet been annihilated by the opposite polarization derived from the free ions.

The utility of the method is demonstrated by the photooxidation of chlorophyll and derivatives using quinone. The system had been studied by Roth and collaborators,[5,6] but they failed to observe any polarization of chlorophyll presumably because of rapid exchange according to (1).

Figure 1 shows the pigment polarizations obtainable when a dilute solution ($<10^{-3}$ M) of pigment containing 5×10^{-3} M

* Argonne National Laboratory.

(1) Work performed under the auspices of the Division of Chemical Sciences, Office of Chemical Sciences, Office of Basic Energy Sciences of the U.S. Department of Energy.

(2) H. D. Roth, "Chemically Induced Magnetic Polarization"; L. T. Muus, P. W. Atkins, K. A. McLauchlan, and J. B. Peterson, Eds., D. Reidel, Dordrect, Holland 1977, pp 35-76.

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(6) The polarized quinone signal is visible even in steady state if the solutions are slightly acidified, thus leading to the protonated semiquinone radical, which exchanges with the quinone on a time scale slow relative to relaxation.

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Table I. Assignments of CIDNP Signals, Hyperfine Coupling Constants (hfs), and Exchange Rate Constants

compd	assignments, ppm[a]	rel signal intensities[b]	rel hfs	CIDNP normalized hfs,[b] G	ENDOR,[8] G	K_{ex}, M^{-1} s^{-1}
chlorophyll *a*						$1.2 \pm 0.9 \times 10^8$
	8 H (4.40)	52.0	1.56	4.17	3.89	
	7 H (4.07)	45.7	1.35	3.60	3.89	
	5 Me (3.62)	100.0	1.00	2.67	2.67	
	1 Me (3.29)	38.0	0.37	0.99	1.00	
	3 Me (3.25)	44.0	0.46	1.23	1.31	
Pyromethyl pheophorbide *a*	8 H(4.49)	71.0	2.31			$4.0 \pm 0.4 \times 10^8$
	7 H (4.29)	76.3	2.39			
	5 Me (3.67)	100.0	1.00			
	1 Me (3.41)	67.0	0.67			
	3 Me (3.25)	58.0	0.62			
Bacteriochlorophyll *a*[c]	1 Me (3.41)	57.9	0.58	1.95	1.70	
	5 Me (3.37)	100.0	1.00	3.37	3.37	
	7, 8 (4.24)	94.7	1.42 (2, H)	5.85	5.86	
	3, 4 (4.01)	57.9	1.74 (1, H)	4.81	4.78	
	3, 4 (3.85)	47.4	1.42 (1, H)	4.61	4.78	
Bacteriopheophytin *a*[c]	3, 8 H (4.28)	137.2	2.06[d]			$1.5 \pm 0.4 \times 10^8$
	4, 7 H (4.01)	142.3	2.13[d]			
	1 Me (3.50)	57.2	0.57			
	5 Me (3.42)	100.0	1.00			
	α H (9.82)	8.1	0.24			
	10 H (6.09)	7.7	−0.23			

[a] Assignments of chlorophyll *a* and derivatives according to G. L. Closs et al., *J. Am. Chem. Soc.*, 85, 3807 (1963). [b] The 5-methyl signal served as the normalization point. [c] The 7, 8, 3, 4 protons in the bacterio system are not assigned unambiguously. [d] Average for 2 protons.

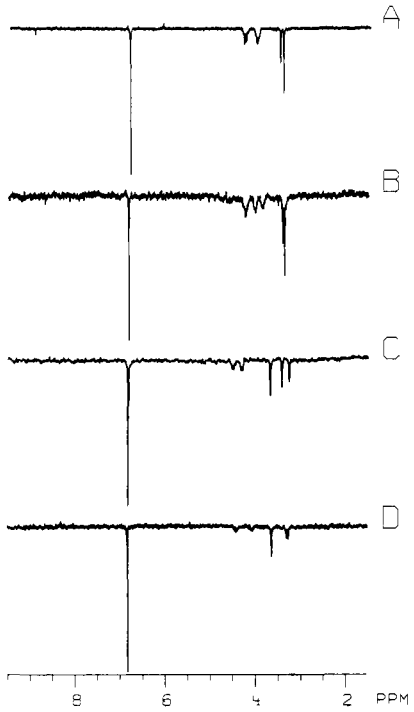

Figure 1. 200-MHz CIDNP spectra of chlorophyll derivatives obtained from solutions containing 5×10^{-3} M benzoquinone with an rf probing pulse of 5-μs duration applied directly after the laser pulse. (A) Bacteriopheophytin *a*, 5×10^{-4} M, (B) Bacteriochlorophyll 3×10^{-4} M, (C) pyromethylpheophorbide *a*, 8×10^{-4} M, (D) chlorophyll *a*, 4×10^{-4} M.

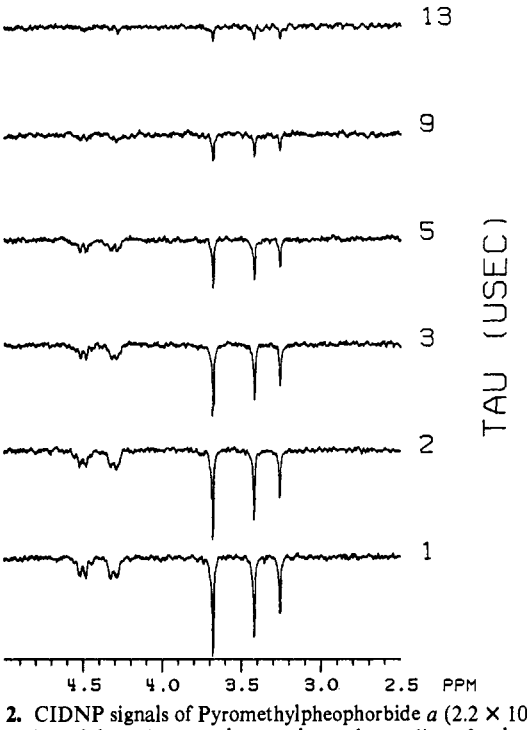

Figure 2. CIDNP signals of Pyromethylpheophorbide *a* (2.2×10^{-4} M) as a function of delay between laser pulse and sampling rf pulse.

quinone in methanol–chloroform (1:3 v/v) is excited by a frequency doubled Nd:YAG laser pulse (532 nm) followed at a short and variable time interval, τ, by a rf pulse. Collction of the FID, signal averaging (50 pulses), and Fourier transformation completes the experiment. All equilibrium polarization had been destroyed by a sequence of random phase pulses prior to laser excitation so that only CIDNP signals are visible in the spectra. Figure 2 shows the decay of the signals as a function of τ. The intensities can be fitted to an exponential with a time constant which was found to be inversely proportional to the pigment concentration proving that process (1) is destroying the geminate polarization. The bimolecular exchange rate constants obtained from runs at several different concentrations are listed in Table I.[7] The method yields signs and relative magnitudes of hyperfine coupling constants when the signal intensities are compared with theoretical intensity calculations. The values obtained compare well with ENDOR results.[8] Our method is complementary to ENDOR studies

(7) The relative hyperfine coupling constants were calculated with a computer program on CIDNP intensities kindly provided to us by Dr. R. Kaptein.

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because of the ease of NMR assignments even for complicated molecules such as chlorophylls. On the other hand, just as in NMR line broadening studies,[9] it yields only ratios of hyperfine coupling constants and needs at least one ENDOR frequency to convert the ratios to absolute values.

Acknowledgment. Part of this work was supported by National Science Foundation Grant NSF CHE 7821789. The NMR spectrometer was purchased with the aid of a Department of Energy Grant DE AC 02-79 ER 10415.

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Hydrophobic-Hydrophilic Interactions in Sodium Dodecyl Sulfate Micelles. Stilbene-Viologen Complex Formation as a Probe of the Micelle Interior[1]

John C. Russell and David G. Whitten*

Department of Chemistry, University of North Carolina Chapel Hill, North Carolina 27514

André M. Braun

Department of Chemistry Swiss Federal Institute of Technology, Ecublens CH 1015 Lausanne, Switzerland

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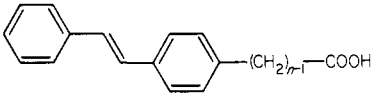
The formation of organized assemblies such as micelles, vesicles, and other bilayer systems is commonly attributed to hydrophobic effects which result in the organized media existing as a microheterogeneous phase separate from the bulk solution and consisting of discrete hydrophobic and hydrophilic regions.[2-6] Although there has been controversy as to the distinctness of these regions and the site of various species solubilized in or interacting with them, it is clear that these organized assemblies can act variously as carriers, barriers, or reaction media toward different reagents. Unresolved problems concerning micelles in particular center around features such as the size, shape, amount of water incorporated in hydrophobic regions, and "tightness", or integrity of the structure.[3-5] In recent studies we have used surfactant molecules incorporating relatively nonpolar chromophores as probes for the hydrophobic regions of micelles, vesicles, and other assemblies.[7-10] A molecule of particular utility has been the surfactant *trans*-stilbene, S_{16}, which can be incorporated into a variety of media and whose fluorescence and photoisomerization behavior provides a sensitive index of the microenvironment.[10] In the present paper we report a study of complex formation between a series of surfactant stilbenes, S_n, and the organic dication dimethyl viologen, MV^{2+}, in micellar media. In the generally accepted model for micelle structure the stilbene chromophore in most, if not all, of these compounds would be expected to be buried relatively deep in a hydrophobic hydrocarbon core, while the viologen dication should be located in the more polar surface region or Stern layer.[2-4] However, much recent work has suggested that most polar molecules and even aromatic hydrocarbons tend to occupy surface sites or at least regions moderately polar.[5,11-13] This has been attributed variously to the high surface/volume ratio present in the micelle and the inadequacy of the headgroups to "cover" the surface as well as to a high internal Laplace pressure within the micelle interior.[5,11] The results of this study are noteworthy in that we find complex formation occurs readily regardless of where the stilbene chromophore is located in the surfactant molecules. This, together with other results presented herein, indicates that the entire micelle is available for complex formation and is in accord with a developing picture that in many cases micelles have a very open structure with extensive hydrocarbon-water interfaces.

Table I. Stern-Volmer Constants for Quenching of Surfactant Stilbene Fluorescence by Methyl Viologen (MV^{2+}) in SLS Micelles

trans-stilbene derivative[a]	K_{sv}[20]	r
S_4	2150 ± 200[b]	0.992
S_5	2060	0.997
S_6	2440	0.997
S_7	2120	0.998
S_{10}	2250	0.996
S_{12}	1870	0.998
S_{16}	1020	0.999
trans-stilbene	2450	0.997

[a] Surfactant stilbene concentration 5×10^{-5} M in each case, [SLS] = 0.028. [b] Error limits in each case are ±200 or less.

The synthesis of the surfactant *trans*-stilbenes, S_n, was relatively straightforward. Toluene was acylated under Friedel-Crafts



S_n, n = 4-6, 7, 10, 12, 16

conditions with the acid chloride monomethyl ester of the appropriate diacid to give the toluene keto ester precursors of S_4, S_5, S_6, S_{10}, and S_{16}. In the case of S_7 and S_{12}, the Grignard reagent from 4-bromotoluene was condensed with cycloheptanone and cyclododecanone, respectively, and the resulting tertiary alcohol dehydrated by relfuxing with *p*-toluenesulfonic acid in toluene. The cyclic styrene thus formed was cleaved by ozonolysis and the product refluxed in methanol-sulfuric acid to give the toluene keto ester. The keto esters were brominated at the aromatic methyl with *N*-bromosuccinimide and then treated with triphenylphosphine to give Wittig reagents. Condensation with benzaldehyde by using potassium carbonate yielded the corresponding *trans*-stilbene keto esters which were reduced to the S_n esters by refluxing with zinc amalgam in hydrochloric acid. The esters were saponified by refluxing with potassium hydroxide in aqueous acetone. Satisfactory NMR, IR, and UV spectra and elemental analyses were obtained for all the stilbene acids or the corresponding methyl ester precursors for those acids too insoluble to analyze as such. Sodium dodecyl sulfate (SLS, Biorad) was recrystallized once from ethanol. Methyl viologen dichloride hydrate (Aldrich) and LTAC were used as received. The surfactant *N*-methyl-*N'*-hexadecyl-4,4'-bipyridinium^{2+} ($MV16^{2+}$) was synthesized as described previously.[14]

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