Spectroscopic and analytical data[17] suggested that this product was a novel vanadium(IV) dimer **2** formed via the induced internal redox reaction indicated in eq 1. The detailed nature of **2** was

$$2VS_4^{3-}\ (\mathbf{1}) + 2(i\text{-}Bu_2NCS_2)_2 \rightarrow V^{IV}_2(S_2)_2(i\text{-}Bu_2NCS_2)_4\ (\mathbf{2}) + S_x^{2-} \quad (1)$$

established by single-crystal X-ray diffraction.[18,19] Crystals of **2** obtained via evaporation of THF/hexane solutions consist of discrete molecular vanadium(IV) dimers (Figure 1). The vanadium atoms lie on a crystallographic C_2 axis. The V–V distance of 2.851 (1) Å and the observed room temperature diamagnetism of the complex are consistent with the presence of a vanadium–vanadium bond. The vanadium atoms are bridged by two symmetry-related μ-η^2-S_2 ligands, forming a $M_2(\mu\text{-}\eta^2\text{-}S_2)_2$ core similar to that previously found in $Mo_2(S_2)_6^{2-}$ and $Mo_2(S_2)_2Cl_6$.[20,21] The coordination sphere of each vanadium is completed by two bidentate dithiocarbamate ligands. The arrangement of the ligands is simply described as a distorted octahedron, with each S_2^{2-} ligand occupying a single vertex. Although other *molecular* vanadium dimers with S_2 bridges are known,[5,6] the only other $V_2(\mu\text{-}\eta^2\text{-}S_2)_2$ core that has been structurally characterized occurs in the mineral patronite (VS_4). Patronite consists of linear chains of vanadium(IV) ions bridged by S_2^{2-} ligands,[22,23] illustrated in Figure 2. The vanadium ions in patronite associate in pairs with V–V distances alternating between 2.83 and 3.22 Å. There is a remarkable correspondence between the structural parameters of the core in **2** and the core about the tight V–V pairs in patronite. The V–V distances are nearly identical (2.851 (1) Å for **2** vs. 2.83 Å for patronite), as are the S–S distances within the S_2^{2-} ligands (1.998 (2) Å in **2** vs. an average of 2.03 Å in patronite) and the average V–S distances (2.405 Å in **2** vs. 2.40 Å in patronite).

The virtual congruence of the $V_2(S_2)_2$ units in **2** and in patronite presents a vivid confirmation of the persistence of structural units through molecular and solid-state systems. Moreover, the synthesis of **2** by an induced internal redox process reemphasizes the utility of this novel synthetic strategy.

Acknowledgment. We thank Dr. J. Carter Cook for field desorption mass spectra, which were obtained in the Mass Spectrometry Laboratory, School of Chemical Sciences, University of Illinois, supported in part by a grant from the National Institute of General Medical Sciences (GM 27029).

Supplementary Material Available: Crystallographic details, including tables of atomic coordinates, thermal parameters, bond lengths, and bond angles, for $V_2(\mu\text{-}S_2)_2(i\text{-}Bu_2NCS_2)_4$ (14 pages); table of structure factors for $V_2(\mu\text{-}S_2)_2(i\text{-}Bu_2NCS_2)_4$ (14 pages). Ordering information is given on any current masthead page.

---

[17] IR spectrum (KBr pellet): 1485 (s), 1468 (sh), 1438 (m), 1424 (m), 1390 (m), 1370 (sh), 1360 (m), 1341 (m), 1290 (w), 1245 (s), 1205 (m), 1150 (s), 1097 (m), 1003 (m), 940 (w), 922 (m), 882 (w), 809 (m), 630 (m), 620 (w), 590 (m), 535 (vw), 440 (vw), 378 (m) cm^{-1}. Field desorption mass spectrum, base peak corresponds to molecular ion $V_2S_{12}C_{36}H_{72}N_4^+$: m/z obsd (calcd) 1046, 100 (100); 1047, 59 (53); 1048, 79 (67); 1049, 33 (30); 1050, 27 (20); 1051, 8 (8). Anal. Calcd for $V_2S_{12}C_{36}H_{72}N_4$: C, 41.27; H, 6.93; N, 5.35; V, 9.72. Found: C, 42.48; H, 7.40; N, 5.22; V, 9.35. UV–vis λ_{max} (ϵ, 1 mol^{-1}/cm^{-1}): 298 (61 000), 474 (5450).

[18] The complete structure determination was carried out by Dr. C. S. Day of Crystalytics Co., Lincoln, NE 68501.

[19] Crystal data: Space group $C2/c$ (No. 15), with $a = 30.268$ (6) Å, $b = 17.484$ (1) Å, $c = 17.523$ (4) Å, $\beta = 143.38$ (1)°, and $Z = 4$. Calculated density 1.258 g cm^{-3}. The structure was solved by a combination of direct methods and difference Fourier techniques. $R_F = 0.038$, $R_{wF} = 0.038$ for 3135 independent reflections with $I > 3\sigma(I)$ and $3° < 2\theta < 50.7°$ (Mo Kα radiation). Anisotropic thermal parameters were used for all non-hydrogen atoms.

[20] Müller, A.; Nolte, W.-O.; Krebs, B. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 279.

[21] Marcoll, J.; Rabenau, A.; Mootz, *D.*; Wunderlich, H. *Rev. Chim. Miner.* **1974**, *11*, 607.

[22] Allman, R.; Baumann, I.; Kutoglu, A.; Rosch, H.; Hellner, E. *Naturwissenschaften* **1964**, *51*, 263. The atomic position reported for S2 (0.763, 0.096, 0.234) is physically unreasonable, lying within 0.3 Å of S_1. The position (0.763, −0.096, 0.234) was used for this figure; this gives a structure qualitatively in agreement with that published, though the reported V–S_2 bond lengths are still not reproduced.

[23] Klemm, W.; Schnering, H. G. *Naturwissenschaften* **1965**, *52*, 12.

NAD(P)$^+$-NAD(P)H Models. 61. An Interconversion between Central and Axial Chiralities as an Evidence for a Functional Model of Chemical Evolution of an Enzyme

Atsuyoshi Ohno,* Meguru Ohara, and Shinzaburo Oka

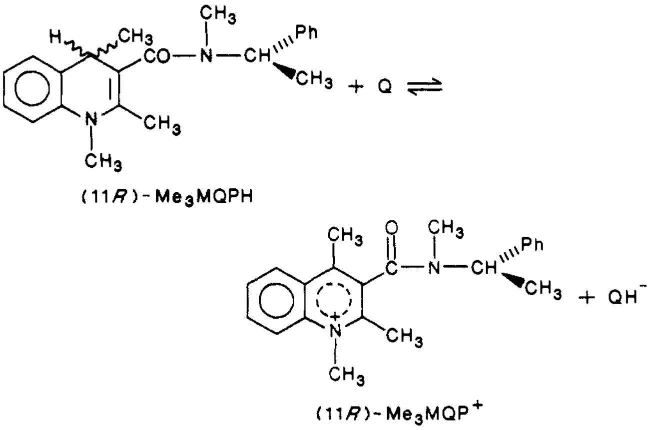
Institute for Chemical Research, Kyoto University
Uji, Kyoto-Fu 611, Japan

Received March 24, 1986

It is well-known that NAD(P)$^+$-dependent dehydrogenases discriminate between the *re* and *si* faces of the coenzyme. Two important and interesting hypotheses were proposed recently to explain the existence of these two opposite stereospecificities. One of the hypotheses proposes that the hydride transfer takes place on the less reactive *re* face of coenzyme when the natural substrate has a thermodynamically unstable carbonyl group and vice versa. The proposal is based on the assumption that during billions of years of chemical evolution, the enzyme has reached the optimal state to catalyze both directions of a reversible reaction most efficiently.[1] Although the proposal was immediately subjected to argument,[2] the basic idea involved in the proposal seems worthy of consideration.[3]

The other hypothesis proposed by Buck and his co-workers is mainly based on quantum-mechanical calculations.[4] The carbonyl oxygen in the carbamoyl group at the 3-positon of the enzyme-bound (dihydro)nicotinamide ring is set on the *re* or *si* face of the coenzyme due to prohibited rotation, and a hydride transfers on the face occupied by the carbonyl oxygen. That is, at the transition state of the redox reaction, the migrating hydrogen and the carbonyl oxygen are set in *syn* configuration. X-ray analysis and other physical measurements as well as chemical reactions with well-designed nicotinamide derivatives supported this proposal.[5-7]

In our previous paper, we described how 3-[*N*-methyl-*N*-(*R*)-(α-methylbenzyl)carbamoyl]-1,2,4-trimethyl-1,4-dihydroquinoline [(11*R*)-Me_3MQPh] and its corresponding quinolinium salt [(11*R*)-Me_3MQP^+] stereospecifically interconvert, in agreement with Buck's proposal. The former compound has a central chirality at the 4-position of the dihydroquinoline ring but its side-chain carbonyl group can rotate freely, whereas in the latter



(11*R*)-Me_3MQPH

(11*R*)-Me_3MQP^+

Q = quinone

---

[1] Nambiar, K. P.; Stauffer, D. M.; Lolodziej, P. A.; Benner, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 5886–5890.

[2] Oppenheimer, N. J. *J. Am. Chem. Soc.* **1984**, *106*, 3032–3033.

[3] Benner, S. A.; Nambiar, K. P.; Chambers, G. K. *J. Am. Chem. Soc.* **1985**, *107*, 5513–5517.

[4] Donkersloot, M. C. A.; Buck, H. M. *J. Am. Chem. Soc.* **1981**, *103*, 6554–6558.

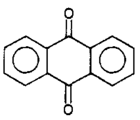
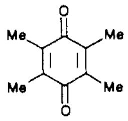
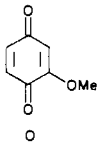
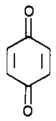
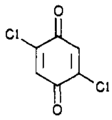
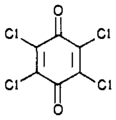
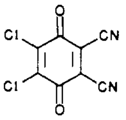
[5] van Lier, P. M.; Donkersloot, M. C. A.; Koster, A. S.; van Hooff, H. J. G.; Buck, H. M. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 119–120.

[6] de Kok, P. M. T.; Buck, H. M. *J. Chem. Soc., Chem. Commun.* **1985**, 1009–1010.

[7] Ohno, A.; Kashiwagi, M.; Ishihara, Y.; Ushida, S.; Oka, S. *Tetrahedron* **1986**, *42*, 961–973.

0002-7863/86/1508-6438$01.50/0

Table I. Reduction of Quinones with Chiral Dihydroquinoline Derivatives

quinone	config at 4-position of Me$_3$MQPH	Mg^{2+} [a]	config at 9-position of Me$_3$MQP$^+$	cy, % [b]	de, %	$E_{1/2}$, V [c]
	*R*	yes	*R*	20	60	−0.94
	*R*	yes	*R*	64	40	−0.84
	S	yes	*S*	31	33	
	*R*	yes	*R*	40	20	−0.62
	*R*	yes	*R*	40	30	−0.51
	R	no			*d*	
	S	yes	*S*	34	27	
	*R*	yes		33	0	−0.18
	*R*	yes	*S*	50	82	+0.01
	R	no	S		58	
	S	yes	*R*		52	
	*R*	yes	*S*	54 [e]	70	+0.51
	R	no	*S*	29	65	

[a] As 1 equiv of perchlorate. [b] Chemical yields observed in ^{1}H NMR spectra with an internal standard. [c] Polarographic half-wave reduction potential observed in acetonitrile in the presence of 0.1 M tetraethylammonium perchlorate (vs. SCE).[11] [d] Bluish green amorphous material was obtained, but its structure has not been elucidated yet. [e] 2,3-Dichloro-5,6-dicyano-*p*-hydroquinone, the reduction product, was obtained in 65% yield.

compound free rotation of the carbonyl group is prohibited. This cation thus produces an axial chirality with respect to this carbonyl group at a sacrifice of the central chirality at the 4-position. That is, self-immolative transfer of central and axial chiralities takes place between Me$_3$MQPH and Me$_3$MQP$^+$.

We now wish to report that Me$_3$MQPH, which afforded the evidence to support Buck's proposal, also yields evidence in favor of Benner's proposal. Thus, there is a possibility that both proposals are interrelated with each other.

In a typical run, 0.005 mmol of (4*R*,11*R*)-Me$_3$MQPH (4*R* isomer)[8] was oxidized by 1.5 equiv of a *p*-quinone as the substrate in 5 mL of anhydrous dioxane in the presence or absence of an equivalent amount of magnesium perchlorate[9] at room temperature in the dark for about 2 days. After usual workup, the materials were subjected to ^{1}H NMR spectroscopy and the diastereomer excess (de) in the quinolinium salt [(11*R*)-Me$_3$MQP$^+$] obtained was measured from the integrations for the methyl groups. The results are listed in Table I together with polarographic half-wave reduction potentials for the quinones used.

Starting from the 4*R* isomer, the quinones that have a potential smaller than −0.2 V afford (9*R*,11*R*)-Me$_3$MQP$^+$ (9*R* isomer)[12] (product from the syn C—H/C═O), whereas the quinones that have a potential larger than 0 V yield the 9*S* isomer (product from the anti C—H/C═O). When the reaction is run with the 4*S* isomer, the unreactive and reactive quinones afford the 9*S* and 9*R* isomers, respectively. Thus, the reaction is stereospecific. The result obtained from the present mimetic system is similar to that observed in a series of dehydrogenase systems.[1,3] At present, it is not clear whether the potential of 0 to −0.2 V is a crucial as well as meaningful value or not; we do not know the oxidation potential of Me$_3$MQPH, for example. However, the result described above clearly indicates that the syn orientation of the carbonyl dipole with respect to the reacting C–H bond is not an intrinsic property of the reaction as has been proposed by Buck and his co-workers. The orientation of the carbonyl dipole is not a major factor in selecting one particular hydrogen for the reaction. Instead, it is highly probable that the orientations of the carbonyl dipole and the reacting C–H bond are independently defined by the same factor which, at least partly, stems from the substrate. The reaction mixture immediately turns green on mixing the two reagents, indicating the formation of a charge-transfer complex between the quinone and Me$_3$MQPH prior to the reaction, and the conformation in this complex seems to be important in determining the orientation. Further studies are in progress in our laboratory to elucidate the mechanism and energetics of this interesting stereospecificity.

---

(8) Both the 4-position of dihydropyridin ring and benzylic carbon on the side chain are in the *R* configuration.

(9) It has been proved that a substrate of this class does not require a magnesium ion for the reduction. Instead, the magnesium ion is rather an inhibitor of the reduction for certain substrates.[10] However, the presence of magnesium ion keeps the reduction free from side reactions and the system stays clean during the reaction.

(10) Ohno, A.; Yasui, S.; Nakamura, K.; Oka, S. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 290–293.

(11) Peover, M. E. *J. Chem. Soc.* **1962**, 4540–4549.

(12) A preliminary result from X-ray crystallography has revealed the absolute configuration with respect to the axial chirality of (11*R*)-Me$_3$MQP$^+$. The 9*S* isomer has a configuration in which the carbonyl dipole points the direction of ring nitrogen in the face above the plane of the molecule. Private communication from Dr. Y. Matsuura of Osaka University.

If one accepts Benner's evolutionary optimization theory,[13] the present result seems to provide a possibility that the evolution is not a consequence of naturally occurring random phenomena but rather that it lies in the line of scientific inevitability.

---

(13) Hanson, K. R.; Rose, I. A. *Acc. Chem. Res.* **1975**, *8*, 1-10.

An Artificial Visual Pigment with Restricted C_9-C_{11} Motion Forms Normal Photolysis Intermediates

M. Sheves*† and A. Albeck

Department of Organic Chemistry, Weizmann
Institute of Science, Rehovot 76100, Israel

M. Ottolenghi

Department of Physical Chemistry
The Hebrew University of Jerusalem
Jerusalem 91904, Israel

P. H. M. Bovee-Geurts and W. J. De Grip

Department of Biochemistry
Center for Eye Research, University of Nijmegen
6500 HB Nijmegen, The Netherlands

C. M. Einterz, J. W. Lewis, L. E. Schaechter, and
D. S. Kliger*

Department of Chemistry, University of California
Santa Cruz, California 95064

Received June 16, 1986

The primary event in the photolysis of visual pigments leads to the formation of a new species, bathorhodopsin (batho), characterized by a spectrum which is red-shifted relative to the parent pigment.[1] Batho is stable at temperatures below −140 °C[2] but at higher temperatures is thermally converted in the dark to a series of other intermediates. The sequence of thermal reactions of these intermediates results in an activated form of the pigment which directly initiates visual transduction.[3] There is much evidence that the formation of batho involves a cis-trans isomerization of the 11-*cis*-retinylidene chromophore of the pigment.[4] It has been suggested, however, that such an isomerization would involve a large chromophore geometry change which would be difficult to rationalize with a restricted chromophore pocket of the protein. Thus, models have been proposed in which a number of bonds undergo concerted motions. Warshel has proposed a "bicycle pedal" motion involving several bond rotations which result in isomerization with limited overall shape change of the chromophore.[5] More recently, Liu proposed a model for the isomerization process[6] based on a concerted rotation of the C_{10}—C_{11} single bond and isomerization of the adjacent C_{11}=C_{12} double bond. An analogous approach has been applied to the photocycle of bacteriorhodopsin, suggesting a concerted isomerization (trans → cis) about C_{13}=C_{14} and rotation around C_{14}—C_{15} of its *all-trans*-retinylidene chromophore.[7]

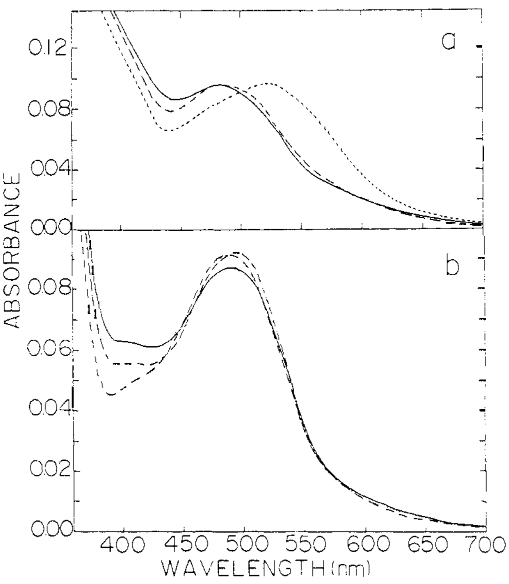
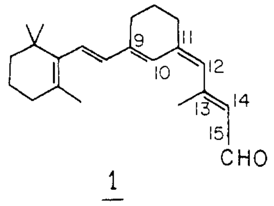


Figure 1. (a) 436-nm illumination of pigment **I** (2% ammonyx/66% glycerol mixture; pH 6.5) at −130 °C. (—) Spectrum of pigment at −130 °C; (- - -) illumination for 30 s; (— — —) warming to −85 °C and recooling to −130 °C to monitor the spectrum. (b) 436-nm illumination of pigment **I** at −85 °C. (—) Absorption of pigment at −85 °C; (— — —) illumination for 5 min at −85 °C; (—·—) warming to −75 °C and recooling to −85 °C, (···) warming to −55 °C and recooling to −85 °C.

To test the need for adjacent bond rotation in the photolysis of bovine rhodopsin, we have prepared an artificial visual pigment (**I**) derived from a chromophore (**1**) whose C_{10}—C_{11} rotation is



1

severely hindered by a six-membered ring linking C_9 to C_{11}. A similar approach was first applied by Akita et al.[8] for testing the C_{11}=C_{12} isomerization model. The synthesis of modified retinal **1** has been previously described.[9] Its absorption spectrum in hexane has a λ_{max} of 355 nm and its protonated Schiff base in methanol has a λ_{max} at 445 nm. The extinction coefficients of these transitions are small, about 9500 M^{-1} cm^{-1}. This 11-*cis*-retinal readily forms a pigment when incubated with bovine opsin by standard procedures.[10] No excess of the retinal is needed to form the pigment. The artificial pigment, which absorbs maximally at 485 nm, is stable in 0.1 M hydroxylamine at 20 °C (pH 6.5) and bleaches on exposure to light. The extinction coefficient at 485 nm is about 13000 M^{-1} cm^{-1}, one-third that of native bovine rhodopsin. This extinction coefficient is estimated from the ratio of the 280- and 485-nm absorbances after opsin has been precipitated from an octyl glucoside suspension. This ratio is 3 times as great for the artificial pigment as the equivalent ratio for purified bovine rhodopsin. The "opsin shift" of the artificial pigment, defined as the energy difference between the absorption maximum of a protonated Schiff base in methanol and that of the corresponding pigment,[11] is 1850 cm^{-1}, which approaches that of the native pigment (2650 cm^{-1}) and that of the 11-cis-locked pigment (1950 cm^{-1}).[8] A competition study showed that once a

---

* Authors to whom correspondence should be addressed.

† Incumbent of the Morris and Ida Wolf Career Development Chair.

(1) (a) Honig, B. *Annu. Rev. Phys. Chem.* **1978**, *29*, 31-57. (b) Ottolenghi, M. *Adv. Photochem.* **1980**, *12*, 97-200.

(2) Yoshizawa, T.; Wald G. *Nature (London)* **1963**, *197*, 1279-1286.

(3) Wald, G.; Brown, P. K. *Science (Washington, D.C.)* **1958**, *127*, 222.

(4) Birge, R. R. *Annu. Rev. Biophys. Bioeng.* **1981**, *10*, 315-354.

(5) Warshel, A. *Nature (London)* **1976**, *260*, 679-683.

(6) Liu, R. S. H.; Asato, A. E. *Proc. Natl. Acad. Sci. U.S.A.* **1985**, *82*, 259-263.

(7) (a) Schulten, K.; Tavan, P. *Nature (London)* **1978**, *272*, 85-86. (b) Orlandi, G.; Schulten, K. *Chem. Phys. Lett.* **1979**, *64*, 370-374. (c) Liu, R. S. H.; Mead, D.; Asato, A. E. *J. Am. Chem. Soc.* **1985**, *107*, 6609-6614.

(8) Akita, H.; Tanis, S. P.; Adams, M.; Balogh-Nair, V.; Nakanishi, K. *J. Am. Chem. Soc.* **1980**, *102*, 6370-6372.

(9) Albeck, A.; Friedman, N.; Sheves, M.; Ottolenghi, M. *J. Am. Chem. Soc.*, in press.

(10) Horwitz, J. S.; Lewis, J. W.; Powers, M. A.; Kliger, D. S. *Photochem. Photobiol.* **1983**, *37*, 181-185.

(11) Nakanishi, K.; Balogh-Nair, V.; Arnaboldi, M.; Tsujimoto, K.; Honig, B. *J. Am. Chem. Soc.* **1980**, *102*, 7945-7947.

0002-7863/86/1508-6440$01.50/0