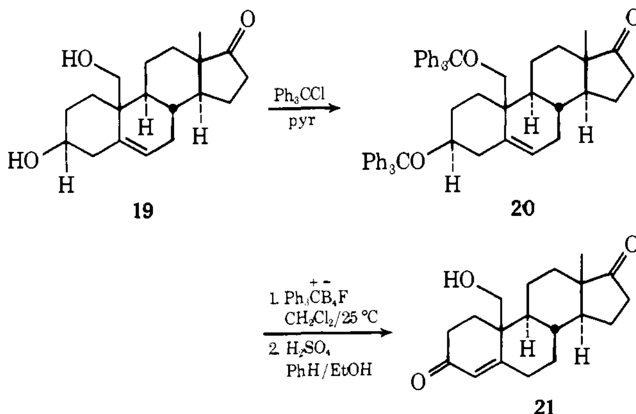
chlorochromate[8] to afford the ketones **12**, **15**, and **18** in very high yields. Thus the overall process for these 1,3-diols results in high yields of the keto alcohol derivative without any chromatographic separation.

One additional diol was successfully oxidized by the bistrityl ether technique. The bistrityl ether **20** of 5-androsten-3β,19-diol-17-one (**19**)[9] could be oxidized by our general procedure. In this case, the strong acid necessary to hydrolyze the primary ether also caused conjugation of the enone system, so that keto alcohol **21** was obtained in good yield. However, this case is somewhat biased toward oxidation at the secondary center due to the extreme steric crowding about the primary ether center (C-19). For this reason, we do not feel this case is a fair test of the general method even though the desired reaction proceeds.



Not all diols could be successfully oxidized by our procedure. For example, straight chain 1,2-diols, e.g., octane-1,2-diol, gave poor results. Despite this limitation, we feel this method does represent a general solution to the problem of selective oxidation of primary, secondary diols.

Acknowledgment. This research was supported by Grant CA18164-01 from the National Cancer Institute of the U.S. Public Health Service.

References and Notes

(1) Presented at the 172nd National Meeting of the American Chemical Society, San Francisco, Calif., Fall 1976, ORGN 139.
(2) W. S. Johnson, J. C. Collins, Jr., R. Pappo, M. B. Rubin, P. J. Kropp, W. F. Johns, J. E. Pike, and W. Bartmann, *J. Am. Chem. Soc.*, **85**, 1409 (1963).
(3) J. Wicha and A. Zarecki, *Tetrahedron Lett.*, 3059 (1974).
(4) See for example (a) R. E. Jones and F. W. Kocher, *J. Am. Chem. Soc.*, **76**, 3682 (1954); (b) T. H. Kritchevsky, D. L. Garmaise, and T. F. Gallagher, *ibid.*, **74**, 483 (1952).
(5) M. E. Jung, *J. Org. Chem.*, **41**, 1479 (1976).
(6) M. P. Doyle, D. J. DeBruyn, and D. J. Scholten, *J. Org. Chem.*, **38**, 625 (1973).
(7) H. C. Beyerman and G. J. Heiszwolf, *Recl. Trav. Chim. Pays-Bas*, **84**, 203 (1965).
(8) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).
(9) O. Halpern, I. Delfin, L. Magana, and A. Bowers, *J. Org. Chem.*, **31**, 693 (1966).

Michael E. Jung,* Laurine M. Speltz
Contribution No. 3712, Department of Chemistry
University of California
Los Angeles, California 90024
Received September 2, 1976

Restricted Rotation of σ-Alkyl Intermediates on a MoS_2 Catalyst

Sir:

The coordinative unsaturation of active sites is an important property of oxide and sulfide catalysts[1,2] as well as of homogeneous catalysts.[3] A proposal has been given that both the isomerization of olefins and the intermolecular hydrogen atom exchange between olefins may occur on the sites to which is bound one hydrogen atom and which have one coordinative vacancy, whereas the hydrogenation of olefins proceeds only on the active sites having three degrees of coordinative unsaturation.[1,2] To shed light on the intermediates formed during the isomerization and of the hydrogen exchange reaction of olefins, a mixture of undeuterated and perdeuterated butenes was allowed to react over a MoS_2 catalyst and the monoexchanged d_1 species formed in these reactions were submitted to microwave spectroscopic analysis. The MoS_2 used here has $2H$ (hexagonal) structure (shown by x-ray diffraction) and a BET surface area of 15 m^2/g. The impurities by atomic absorption analysis were Fe, 0.02; Mg, 0.0015; Ca, 0.0077; Na, 0.012; Mn, 0.0003; Cr, <0.0001; and K, <0.1%.

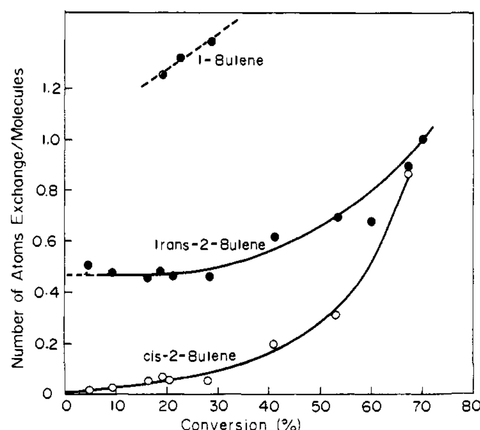
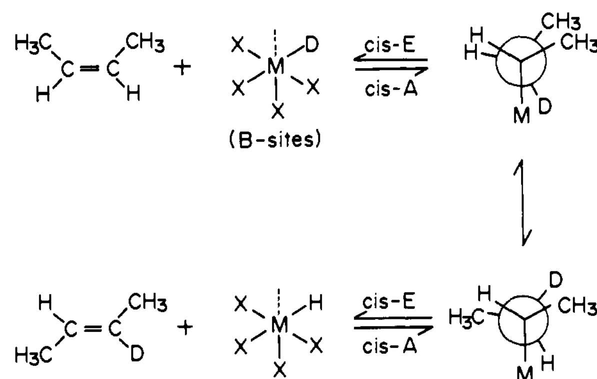


Figure 1. Number of exchanged hydrogen atoms per molecule in the coisomerization of *cis*-but-2-ene-d_0 and *cis*-but-2-ene-d_8 (1:1) in the presence of H_2 and D_2 (1:1) at room temperature.

Figure 1 shows the results of the coisomerization of *cis*-but-2-ene-d_0 and *cis*-but-2-ene-d_8 (1:1) at room temperature, in which the number of hydrogen atoms which have been exchanged was calculated by the method of Hightower and Hall.[4]

$$\text{H atoms exchanged per molecule} = \sum_{i=1}^{4} iN_i + \sum_{i=5}^{8} (8 - i)\ N_i$$

where N_i is the mole fraction of each species containing i deuterium atoms. As shown in Figure 1, the number of exchanged hydrogen atoms per *trans*-but-2-ene molecule is very close to 0.5. This fact indicates that the cis–trans isomerization reaction occurs only with stereospecific hydrogen addition and elimination, which may be analogous to the pure cis stereochemistry observed in the cis addition of hydrogen to methyl acetylene over the MoS_2,[5] where "cis-A" and "cis-E" indicate



cis addition and cis elimination of hydrogen. As the *trans*-but-2-ene-d_1 is inactive for microwave spectroscopic analysis, the *cis*-but-2-ene-d_1 formed in the coisomerization of *cis*-but-2-ene-d_0 and *cis*-but-2-ene-d_8, which was brought about

Table I. Microwave Spectroscopic Analysis of d_1-Butenes

Z-1-d_1 E-1-d_1

2-d_1 2-d_1 1-d_1

(a) *cis*-But-2-ene-d_0 + *cis*-But-2-ene-d_8

Convn in isomerization	66 (%)
cis-But-2-ene-*1*-d_1	0 (%)
cis-But-2-ene-*2*-d_1	100

(b) But-1-ene-d_0 + But-1-ene-d_8

Convn in isomerization	4.2 (%)	9.3 (%)
(Z)-But-1-ene-*1*-d_1	15.9 (%)	24.9 (%)
(E)-But-1-ene-*1*-d_1	16.0	29.1
But-1-ene-*2*-d_1	68.1	46.1

from the *trans*-but-2-ene-d_1 by the reverse process, was subjected to microwave spectroscopic analysis. Nearly 100% of the incorporated D was in the 2 position giving *cis*-but-2-ene-*2*-d_1 as shown in Table Ia, which verifies the isobutyl intermediate formation during the isomerization reaction.

In contrast, the intermolecular exchange of vinyl hydrogens of α-olefins such as propene and but-1-ene occurs much more rapidly than does double bond migration on the MoS_2 catalyst, although the exchange between D_2 and the olefins is negligibly slow at room temperature.

As a result, the number of exchanged hydrogen atoms per but-1-ene molecule is large as observed in Figure 1.

In order to obtain information about the intermediates involved in such rapid hydrogen exchange reactions, the exchange reaction between but-1-ene-d_0 and -d_8 and between propene-d_0 and -d_6 was performed at room temperature. The results of microwave spectroscopic analysis of the d_1-species generated in the exchange reactions are shown in Table Ib and in Figure 2, which confirms that the rapid hydrogen exchange in these α-olefins involves only their vinyl hydrogens.

Kondo, Saito, and Tamaru[6] proposed a method to distinguish the intermediates involved in the intermolecular hydrogen exchange reaction of propene. They assumed that these may be n-propyl, isopropyl, σ-allyl, or π-allyl species, or that the exchange proceeds via a concerted mechanism. According to this method, the extremely slow formation of propene-*3*-d_1 in Figure 2 probably excludes σ-allyl and/or π-allyl intermediates as well as the concerted mechanism.

The approximately constant ratio of propene-*1*-d_1 to propene-*2*-d_1 (3:7) found at low exchange conversion may imply that the σ-alkyl intermediates are about 70% n-propyl and 30% isopropyl. It is surprising at a first glance that the value of (propene-*3*-d_1)/(propene-*1*-d_1) is abnormally small, since the ratio should become about 3/2 for an ordinary isopropyl intermediate providing that the two methyls are equivalent. This fact, accordingly, implies that the two methyls of the isopropyl intermediate are not equivalent in the exchange reaction on the MoS_2 catalyst.

Similar nonequivalence of the two methyl groups of an isopropyl intermediate has been reported only on the EDA complexes of phthalocyanine with alkali metals,[7] of which the largest value of (propene-*1*-d_1)/(propene-*3*-d_1) was 3.0 for $[Co(phthalocyanine)]^{3-}\cdot 3Na^+$, and 2.5 for $[Ni(phthalocyanine)]^{3-}\cdot 3Na^+$, respectively. The value of (propene-*1*-d_1)/(propene-*3*-d_1) obtained in this experiment on the MoS_2 is larger than 15 at low exchange conversion.

If one hydrogen atom and one propene molecule are bound to one active site, then the stereospecific hydrogen addition taking place on this site makes a coordinated propyl and one vacant coordination site. In the reverse change, the vacant coordination site will accept a hydrogen atom from the propyl intermediate in the stereospecific manner.

Figure 2. Distribution of the geometrical isomers of propene-d_1 formed in the hydrogen exchange reaction between propene-d_0 and propene-d_6 in the presence of hydrogen at room temperature. d_i is the percent of $C_3H_{6-i}D_i$.

Accordingly, if the rotation of the isoalkyl intermediates on such unsymmetric active sites is restricted with respect to rotation around the coordination bond, then the two methyls of the isopropyl intermediate may not be equivalent in the hydrogen exchange reaction, which is shown schematically as follows;

H_3C-CH=CH_2 + X_4M-D → CH_3-CH-CH_2(M···D) → CH_3-CH=CHD (1-d_1-propene)

Rotation

CH_2D-CH-CH_2(M···H) → CH_2D-CH=CH_2 (3-d_1-propene)

A similar restricted rotation may be noted in the isobutyl intermediate on the MoS_2 catalyst.

As described above, the cis–trans isomerization of but-2-ene on MoS_2 undoubtedly proceeds through an isobutyl intermediate, and a part of the rapid hydrogen exchange reaction of but-1-ene also occurs via an isobutyl intermediate. However, the double bond isomerization reaction, in which the isobutyl intermediate has been verified, is quite slow compared with the cis–trans isomerization or the hydrogen exchange reaction.

This slow double bond isomerization may correspond to the slow formation of propene-*3*-d_1 discussed above.

This peculiar phenomenon suggests that the isobutyl found from but-1-ene (isobutyl-I) and that from but-2-ene (isobutyl-II) should be distinguishable over the MoS_2 catalyst. If the rotation of the isobutyl-I and/or isobutyl-II is restricted on the unsymmetric active sites, these two isobutyl intermediates may be distinguished from each other as shown in the scheme shown below. In this reaction scheme, the rapid exchange of vinyl hydrogens and the cis–trans isomerization can proceed without the rotation, but the double bond migration occurs only with the rotation around the coordination bond. As a result, the double bond isomerization reaction is controlled by the restricted rotation of the isobutyl intermediate. To explain the

But-1-ene + X_4M-D ⇌ CH_3-CH_2-CH-CH_2(M···D) (iso-butyl-I)

Rotation

But-2-ene + X_4M-H ⇌ CH_2D-CH-CH-CH_3(M···H) (iso-butyl-II)

extensive hydrogen mixing of the 1-butene formed in the coisomerization of *cis*-2-butene-d_0 and *cis*-2-butene-d_8 on the iron film, Touroude and Gault[8] conjectured slow rotation of the half-hydrogenated intermediates along the σ-carbon–metal bond in comparison with the carbon–carbon bond.

For establishing the restricted rotation, however, some direct evidences to exclude the dissociative mechanism should be required. On the MoS_2 catalyst, the hydrogen exchange reaction between (*Z*)-propene-*1*-d_1 and propene-d_6 was performed in the presence of hydrogen. If the dissociative mechanism would participate in the exchange reaction, propene-*1,1*-d_2 and (*Z*)-propene-*1,2*-d_2 should be formed; in contrast with this, the associative mechanism will give the (*E*)-propene-*1,2*-d_2 and the propene-*1,1*-d_2.[6] The result clearly confirmed the pure associative mechanism via the half-hydrogenated species being composed of 70% *n*-propyl and 30% isopropyl species.[9]

Such unusual properties of the σ-alkyl intermediates formed on the MoS_2 catalyst may originate from the 2*H* layer structure (hexagonal) of the MoS_2. The active sites having two degrees of coordinative unsaturation may be on the side of the sandwich-like crystal of MoS_2, and the σ-alkyl intermediates formed on these active sites are strongly inhibited from rotating with respect to the coordination bond.

Acknowledgment. The authors are indebted to Dr. T. Kondo and Dr. S. Saito of Sagami Chemical Research Center for microwave spectroscopic measurements, and also thank professor K. Tamaru of the University of Tokyo for his stimulating discussions.

References and Notes

(1) S. Siegel, *J. Catal.*, **30**, 139 (1973).
(2) A. Takeuchi, K. Tanaka, and K. Miyahara, *Chem. Lett.*, 171, 411 (1974); A. Takeuchi, K. Tanaka, I. Toyoshima, and K. Miyahara, *J. Catal.*, **40**, 94 (1975); A. Takeuchi, K. Tanaka, and K. Miyahara, *ibid.*, **40**, 101 (1975); T. Okuhara, S. Sato, K. Tanaka, and K. Miyahara, *ibid.*, **43**, 360 (1976).
(3) J. P. Collman, *Acc. Chem. Res.*, **1**, 136 (1968).
(4) J. W. Hightower and W. K. Hall, *Chem. Eng. Prog., Symp. Ser.*, **63**, 122 (1967).
(5) Unpublished data.
(6) T. Kondo, S. Saito, and K. Tamaru, *J. Am. Chem. Soc.*, **96**, 6857 (1974).
(7) S. Naito, M. Ichikawa, S. Saito, and K. Tamaru, *J. Chem. Soc., Faraday Trans. 1*, **69**, 685 (1973).
(8) R. Touroude and F. G. Gault, *J. Catal.*, **32**, 294 (1974).
(9) Submitted for publication.

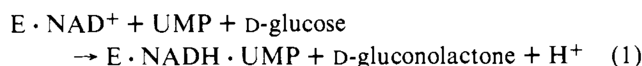
Toshio Okuhara, Ken-ichi Tanaka*
Research Institute for Catalysis, Hokkaido University
Sapporo, Japan
Received May 24, 1976

UDPgalactose 4-Epimerase Catalyzed Oxygen Dependent Reduction of a Free Radical Substrate Analogue by Two Electron Reducing Agents[1]

Sir:

In the course of our studies on the mechanism of action of *Escherichia coli* UDPgalactose 4-epimerase (E.C. 5.1.3.2), which catalyzes the interconversion of UDPgalactose and UDPglucose, we have discovered a new reaction catalyzed by this enzyme in which NAD^+ mediates the transfer of two electrons from a reducing agent such as $NaBH_4$ or D-glucose to two one-electron acceptors, O_2 and uridine-5′-(2,2,6,6-tetramethyl-4-piperidin-1-oxyl diphosphate) I. I is a stable nitroxide free radical described by Wong and Berliner[2] as a paramagnetic structural analogue of UDP-sugars.

The NAD^+ tightly bound to this enzyme is reversibly reduced to NADH by substrates in the epimerization process,[3] and it can be reduced by $NaBH_4$, $NaBH_3CN$, or any of a variety of sugars including D-glucose in reactions which require or are markedly accelerated by the presence of uridine nucleotides.[4] The resultant epimerase·NADH complexes are inactive and contain tightly bound uridine nucleotide, as indicated in eq 1 for D-glucose and UMP as the reducing system. These reactions involve direct hydrogen transfer.



$$\mathrm{E \cdot NAD^+ + UMP + D\text{-}glucose} \rightarrow \mathrm{E \cdot NADH \cdot UMP + D\text{-}gluconolactone + H^+} \quad (1)$$

Free radical I oxidizes epimerase·NADH complexes in an O_2-dependent reaction. When coupled to reduction of epimerase·NAD^+ by $NaBH_4$ or by D-glucose in the presence of UMP the enzyme acts catalytically to destroy the ESR signal of I. Curve A in Figure 1 shows the loss of ESR signal associated with 3.9 μM I in the presence of 0.77 μM enzyme and excess $NaBH_4$. This establishes the catalytic action of epimerase·NAD^+ in the destruction of the free radical. Neither $NaBH_4$ nor NADH alone act on I at rates detected under Figure 1 conditions. Oxygen dependence in the destruction of I is established by curve B in Figure 1, in which the reducing system is D-glucose plus UMP. The loss of ESR signal requires the simultaneous presence of UDPgalactose 4-epimerase, O_2, and either $NaBH_4$ or D-glucose plus UMP. Moreover, it appears to involve binding of I at the active site because the ESR signal of 2,2,6,6-tetramethyl piperidin-1-oxyl-4-ol is stable under the conditions of Figure 1. I is a good competitive reversible inhibitor of the catalytic activity of epimerase·NAD^+, K_I = 0.2 mM.

In Figure 1 the epimerase·NAD^+ would have been reduced to epimerase·NADH by the reducing systems present, suggesting that the disappearance of the ESR signal resulted

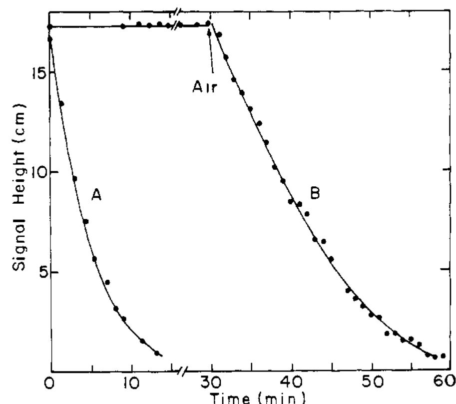
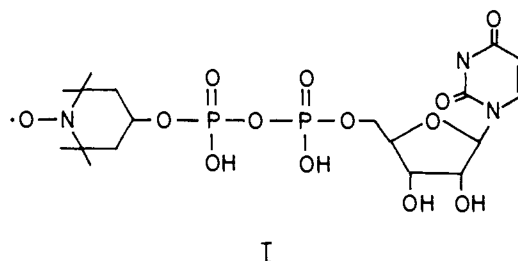


Figure 1. Time course for disappearance of ESR signal of I. In the experiment depicted by curve A the reaction mixture consisted of 3.9 μM I, 0.5 mM $NaBH_4$, and 117 units of UDPgalactose 4-epimerase[3] in 0.2 ml of 0.1 M sodium bicinate buffer at pH 8.5 and ambient temperature. The reaction was initiated at zero time by addition of enzyme. In the experiment depicted by curve B the complete reaction mixture containing 3.5 μM I, 65.6 μM UMP, 90 mM D-glucose, and 585 units of enzyme in 0.2 ml of 0.1 M sodium bicinate at pH 8.5 was prepared in an anaerobic box under N_2 and sealed inside a capillary tube. The capillary was then placed in the cavity of the ESR spectrometer at ambient temperature and the ESR signal monitored. After 30 min the capillary was opened to the atmosphere. Plotted are the ESR signal amplitudes of I measured in a Varian E-4 ESR spectrometer.



I