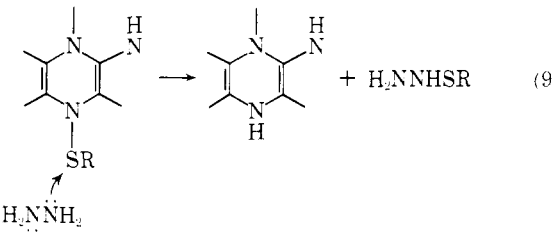


(9)

comparable[10] to the 5H → 4a shift. Hydrazine at concentrations 0.1–0.4 *M* at pH 7.90 had no effect on the rate of reaction. The free radical mechanisms of eq 10 and 11 may

$$RS^- + F_{ox} \overset{K_1}{\rightleftharpoons} RS\cdot + F_{rad}$$
$$F_{rad} + RSH \overset{K_2}{\rightleftharpoons} F_{red} + RS\cdot \quad (10)$$
$$2RS\cdot \xrightarrow{k_3} RSSR$$

$$RSH + F_{ox} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RS\cdot + F_{rad} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} RS^+ + F_{red} \quad (11)$$
$$RS^+ + RS^- \xrightarrow{k_3} RSSR$$

be dismissed since the values of k_{obsd} on both the alkaline and basic side (pH 5.6 and 9.8) of the bell-shaped pH–log k_{obsd} profile were found to be independent of the ratio of oxidized to reduced I at the time of initiation of the reaction. Kinetics indicative of autocatalytic processes were not observed.

The results of a previous study[5] established that a given nucleophile could add to either the 4a- or 5-position of an isoalloxazine ring. The present results point out that both positions may be implicated in flavin catalysis depending on the substrate and, of course, the directional influence of the enzyme.

Acknowledgment. This research was supported by a grant from the National Science Foundation.

References and Notes

(1) D. J. T. Porter, J. G. Voet, and H. J. Bright, *J. Biol. Chem.*, **248,** 4400 (1973).
(2) I. M. Gascoigne and G. K. Radda, *Biochim. Biophys. Acta*, **131,** 498 (1967).
(3) The disappearance of I was followed spectrophotometrically at 443 nm under an argon atmosphere. In practice, a solution of nitroalkane (0.1–1.0 *M*) in 0.1–1.0 *M* aqueous KOH was allowed to sit for 45 min to allow completion of formation of nitroalkane anion; 0.1 ml of this solution was added to 4.8 ml of the appropriate buffer. The resulting solution was degassed and saturated with argon for 30 min, and the reaction was initiated by mixing in a Thunberg cuvet under argon with 0.1 ml of a 2.5×10^{-3} *M* solution of I in CH_3CN. The resulting reaction mixture being 5×10^{-5} *M* in I and 2×10^{-2} *M* in nitroalkane (2% aqueous acetonitrile, v/v, μ = 1.0 with KCl, 30°). At completion of the reaction, admittance of O_2 regenerated I quantitatively. Acetaldehyde was found *via* polarography to be produced quantitatively.
(4) Disappearance of I was followed at 443 nm. All reactions were carried out in Thunberg cuvets under an argon atmosphere employing solution presaturated (for 30 min) with argon. Reactions were initiated by mixing an acetonitrile solution of I with thiophenol in aqueous acetonitrile solution. The reaction solution was 10^{-5} *M* in I and 10^{-3} *M* in thiophenol with buffer concentrations of 0.1–0.5 *M* (20% aqueous acetonitrile, v/v, μ = 1.0 with KCl, 30°). At completion of reaction, admittance of air regenerated I quantitatively. Carried out on a preparative scale 98% yield of $(C_6H_5)_2S_2$ product could be collected as a precipitate (ir, uv, and melting point).
(5) T. C. Bruice, L. Hevesi, and S. Shinkai, *Biochemistry*, **12,** 2083 (1973).
(6) G. A. Russell and R. K. Norris, *Rev. Reactive Org. React.*, **1,** 65 (1972); R. C. Kerber, G. W. Urry, and N. Kornblum, *J. Amer. Chem. Soc.*, **87,** 4520 (1965).
(7) A similar mechanism has been proposed for the oxidation of glutathione by 2,6-dichloroindolphenol: D. S. Coffey and L. Hellerman, *Biochemistry*, **3,** 394 (1964).
(8) W. Haas and P. Hemmerich, *Z. Naturforsch. B*, **27,** 1035 (1972).
(9) W. H. Walker, P. Hemmerich, and V. Massey, *Eur. J. Biochem.*, **13,** 258 (1970).
(10) D. Clerin and T. C. Bruice, *J. Amer. Chem. Soc.*, **96,** 5571 (1974).
(11) The observation of general-base catalysis in the oxidation of lipoic acid by oxidized flavin [ref 2] is in accord with the mechanism of eq 8 where k_{ga} is rate determining. E. Loechler and T. Hollocher (private communication) present cogent arguments in support of the mechanism of eq 8. These include a change in rate-determining step from k_3 to k_{ga} in going from a monoalkylthiol to dithiothreitol.
(12) C. Steelink, M.S. Thesis in Chemistry, 1949, University of Southern California.
(13) Postdoctoral Fellow, University of California, Santa Barbara, California 93106.

Ichiro Yokoe,[13] T. C. Bruice*
Department of Chemistry, University of California Santa Barbara, Santa Barbara, California 93106
Received August 12, 1974

A Novel Route to Bicyclo[3.3.1]non-1-ene. Supporting Evidence for Wiseman's Postulate

Sir:

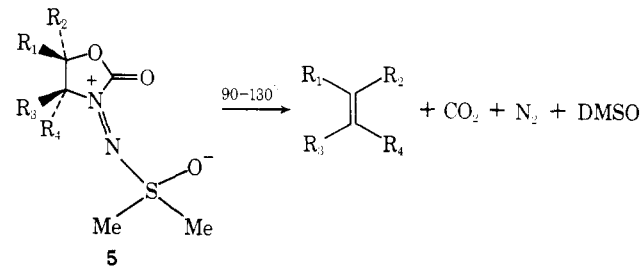
The failure of Bredt's rule, as formulated in the quantitative expression ("S number") of Fawcett, to account for differences in strain between isomeric bridgehead olefins, *e.g.*, **1** and **2,** represents a serious shortcoming of this numerical approach.[1] In contrast, the proposal by Wiseman[2] that the strain in bridgehead alkenes is closely related to the strain of the corresponding trans cycloalkene accounts well for the properties of known bridgehead olefins and leads to the clear-cut prediction that the bridgehead double bond will be more stable when it is oriented trans in the larger ring. Thus, *Z* isomer **2** (*trans*-cyclooctene) should be more stable than the *E* isomer **1** (*trans*-cyclohexene).

1, X = CH_2 2, X = CH_2
3, X = SO_2 4, X = SO_2

Support for the Wiseman postulate comes from the synthesis of several "anti-Bredt" bridgehead olefins,[3-6] including bicyclo[3.3.1]non-1-ene[7-9] and certain heterocyclic derivatives.[10,11] Except for the sulfones **3** and **4,** where the presence of *E* and *Z* isomers was inferred from the stereochemistry of Diels–Alder adducts,[10] the methods of synthesis provide no information concerning the preferred geometry of these bridgehead olefins. A study of the thermal decomposition of sulfoximines (**5**) derived from *N*-aminooxazolidones has led to the finding that these substances extrude CO_2, N_2, and DMSO at 90–130° with liberation of the olefin stereospecifically (cis elimination) and in high yield (Scheme I).[12] It was therefore of interest to apply this olefin synthesis to *E* (**1**) and *Z* (**2**) isomers of bicyclo[3.3.1]non-1-ene.

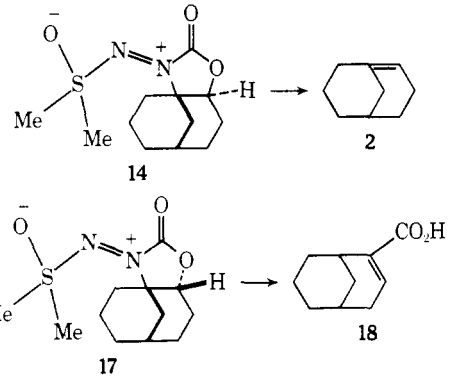
Ketoester **6** was reduced under Meerwein-Ponndorf conditions to a mixture of exo (**7**) and endo (**8**) alcohols, which were separated by gas chromatography.[9] The minor exo al-

Scheme I

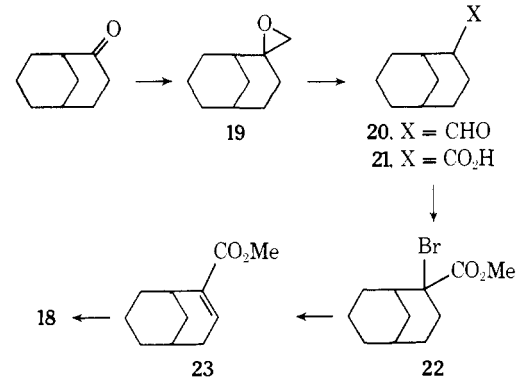


5

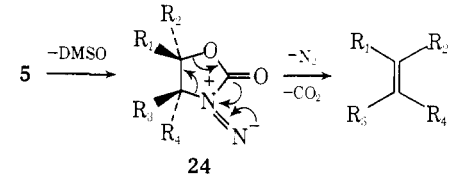
Scheme II



Scheme III

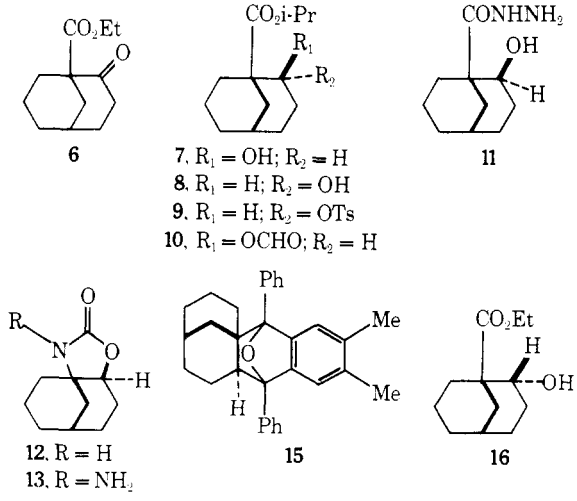


Scheme IV



cohol **7** was augmented by conversion of the endo isomer **8** to its tosylate **9** (mp 92–95°, 99%) with tosyl chloride in pyridine (0°, 30 hr), followed by displacement with tetraethylammonium formate (DMF, 80°, 83 hr).[13] The resulting exo formate **10** was partially saponified with $NaHCO_3$ in MeOH (25°, 6 hr) to give after chromatography (silica gel, hexane–ether) pure **7** in 28% yield. Treatment of **7** with $H_2NNH_2 \cdot H_2O$ in dioxane (sealed tube, 150–160°, 110 hr) afforded the hydrazide **11** (mp 155–159°, 76%), which underwent nitrosation ($NaNO_2$, HCl) and cyclization of the intermediate hydroxy isocyanate to produce oxazolidone **12** (mp 121–123°; ir 3350, 1760 cm^{-1}; nmr δ 4.43 (C*H*O, d of d, J = 9 Hz), 6.40 (N*H*, broad)) in 92% yield.[14] Amination of 12 *via* its lithio derivative (*n*-BuLi, THF) with *O*-(2,4-dinitrophenyl)hydroxylamine[15] yielded **13,** which was oxidized immediately with $Pb(OAc)_4$ in DMSO to sulfoximine **14** (mp 109–110°; ir 1750 cm^{-1}; nmr δ 3.17 (6 H),[16] 4.26 (C*H*O, t, J = 6 Hz).[17] Upon warming **14** in DMSO to 120–130°, a brisk evolution of CO_2 and N_2 took place with liberation of bicyclo[3.3.1]non-1-ene (**2**) in excellent yield. Distillation afforded *ca.* 50% of pure **2** which was identified by comparison of its nmr spectrum with that reported[7] and by formation of a Diels–Alder adduct **15** (mp 212–214°) with 1,3-diphenyl-5,6-dimethylisobenzofuran[18] (Scheme II).

Endo hydroxy ester **16,** prepared by reduction of **6** with $NaBH_4$,[9] was transformed *via* a parallel sequence to that



described above[19] to sulfoximine **17** (mp 131–132°; ir 1755 cm^{-1}; nmr δ 3.20 (6 H),[16] 4.15 (C*H*O, t, J = 6 Hz). The sulfoximine **17** was significantly more resistant to thermal decomposition than its stereoisomer **14** and gave no trace of bicyclo[3.3.1]non-1-ene up to 130°. At 150–160° **17** underwent conversion in 49% yield to a single, nonpolymeric product identified as bicyclo[3.3.1]non-2-ene-2-carboxylic acid (**18;** mp 73–77°; ir 3400–2600, 1680 cm^{-1}; nmr δ 7.08 (1 H, t, J = 6 Hz), 11.5 (1 H, broad)) by means of an independent synthesis (Scheme III). Thus, bicyclo[3.3.1]nonan-2-one[20] upon treatment with dimethylsulfonium methylide[21] gave epoxide **19** (δ 2.50, 2 H, s), which was rearranged to aldehyde **20** (ir 2770, 1730 cm^{-1}; nmr δ 9.62 (1 H)) in the presence of $BF_3 \cdot Et_2O$. Oxidation of **20** (Ag_2O) afforded the corresponding carboxylic acid **21** (1710 cm^{-1}). Bromination of **21** (Br_2, PBr_3) followed by methanolysis of the intermediate α-bromoacyl bromide[22] yielded ester **22** which, without purification, was heated in quinoline at 170° (3 hr). The resulting $\alpha\beta$-unsaturated ester **23** (δ 3.67 (3 H, s), 7.05 (1 H, t, J = 2 Hz) was saponified to give **18.**

Formation of olefins from sulfoximines of type **5** is presumed to occur *via* dissociation to a diazene **24**[23] followed by a concerted cycloelimination (Scheme IV). The difference in behavior between sulfoximines **14** and **17** is obviously related to the rigid requirement for cis elimination in this process[12] and the ease with which a double bond can be accomodated at a bridgehead in the bicyclo[3.3.1]nonene system. Cis elimination from exo sulfoximine **14** leads directly to the (*Z*)-bicyclononene **2,** whereas the corresponding sequence applied to **17** would lead to the more energetic *E* alkene **1.** Whether carboxylic acid **18** arises by trapping of the transient (diradical ?) **1** with extruded CO_2 or by some other mechanism is unclear at present. However, these results do suggest that geometrically isomeric, bridgehead olefins may be of substantially different energy in the direction predicted by Wiseman's hypothesis.[24]

References and Notes

(1) For a recent review, see G. L. Buchanan, *Chem. Soc. Rev.*, **3,** 41 (1974).
(2) J. R. Wiseman and W. A. Pletcher, *J. Amer. Chem. Soc.*, **92,** 956 (1970).
(3) J. R. Wiseman, H. F. Chan, and C. J. Ahola, *J. Amer. Chem. Soc.*, **91,** 2812 (1969).
(4) J. A. Chong and J. R. Wiseman, *J. Amer. Chem. Soc.*, **94,** 8627 (1972).
(5) R. Keese and E. P. Krebs, *Angew. Chem., Int. Ed. Engl.*, **10,** 262 (1971).
(6) A. D. Wolf and M. Jones, *J. Amer. Chem. Soc.*, **95,** 8209 (1973).
(7) J. A. Marshall and H. Faubl, *J. Amer. Chem. Soc.*, **89,** 5965 (1967).
(8) J. R. Wiseman, *J. Amer. Chem. Soc.*, **89,** 5966 (1967).
(9) J. A. Marshall and H. Faubl, *J. Amer. Chem. Soc.*, **92,** 948 (1970).
(10) C. B. Quinn and J. R. Wiseman, *J. Amer. Chem. Soc.*, **95,** 1342, 6120 (1973).
(11) C. B. Quinn, J. R. Wiseman, and J. C. Calabrese, *J. Amer. Chem. Soc.*,

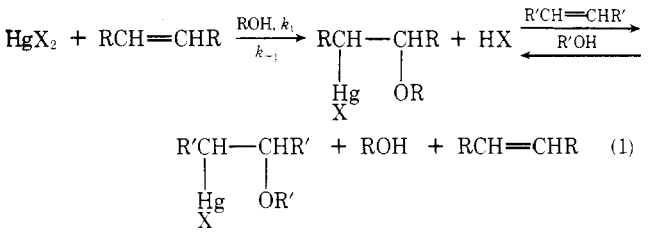
95, 6121 (1973).
(12) J. D. White and M. Kim, *Tetrahedron Lett.*, 3361 (1974).
(13) M. Harnik, *Steroids*, **3**, 359 (1964).
(14) M. S. Newman and T. B. Patrick, *J. Amer. Chem. Soc.*, **91**, 6461 (1969).
(15) Y. Tamura, J. Minamikawa, K. Sumoto, S. Fujii, and M. Ikeda, *J. Org. Chem.*, **38**, 1239 (1973).
(16) Two closely spaced singlets of 3 H each.
(17) C. W. Rees and M. Yelland, *Chem. Commun.*, 377 (1969).
(18) J. D. White, M. E. Mann, H. D. Kirshenbaum, and A. Mitra, *J. Org. Chem.*, **36**, 1048 (1971).
(19) (a) Hydrazinolysis ($H_2NNH_2 \cdot H_2O$, EtOH, 150°, 12 hr) hydrazide (mp 100–107°), (b) nitrosation oxazolidone (mp 87–89.5°; 3450, 1760 cm^{-1}; δ 4.18 (*CHO*, t, J = 8 Hz), 5.90 (*NH*, broad), (c) amination (*O*-mesitylenesulfonylhydroxylamine,[15] (d) oxidation ($Pb(OAc)_4$, DMSO).
(20) K. H. Baggaley, J. R. Dixon, J. M. Evans, and S. H. Graham, *Tetrahedron*, 23, 299 (1967).
(21) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1353 (1965).
(22) C. F. Allen and M. J. Kalm, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N.Y., 1963, p 608.
(23) D. J. Anderson, T. L. Gilchrist, D. C. Horwell, and C. W. Rees, *Chem. Commun.*, 146 (1969).
(24) Support of this work by grants from the National Science Foundation (GP- 36941 and GP-41510X) is gratefully acknowledged.

Moon-geu Kim, James D. White*
Department of Chemistry, Oregon State University
Corvallis, Oregon 97331
Received August 19, 1974

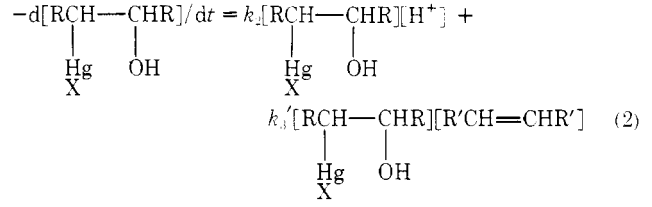
Mechanism of Alkene Exchange Reactions with Oxymercurials

Sir:

The reaction of a mercuric salt in a protic solvent with an alkene affords an oxymercurial. It has recently been shown that oxymercurials with ionic ligands undergo facile exchange reactions with alkenes and alkoxy and hydroxy

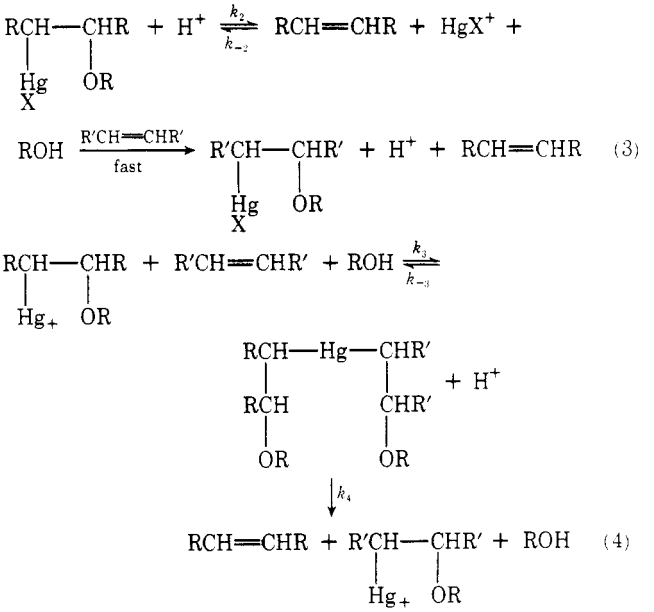


groups in protic solvents[1-3] (eq 1). The alkoxy exchange has been shown[2] to exhibit pseudo-first-order kinetics while the alkene exchange reaction of hydroxymercurials in aqueous medium has been established by Halpern[1] to accurately obey the rate law described in eq 2. The two terms in the



rate law were ascribed to a reversible deoxymercuration reaction (eq 3, OR = OH) and the formation of a covalently bonded transient bisoxymercurial intermediate (eq 4, OR = OH). A similar mechanism for alkene exchange was considered by Pritzkow[3] in an extensive kinetic investigation that also was unable to distinguish between a bimolecular exchange mechanism or one that involved a bisoxymercurial intermediate as in eq 4.

Our previous study showed that alkoxy exchange was facilitated by both protic acid and an excess of alkene in solution. To explain the rate enhancement due to the presence



of an alkene, we postulated a mechanism involving nucleophilic attack by the exchanging alkene on the mercury atom of the oxymercurial. However, our data could not exclude the mechanism given in eq 4. We therefore elected to use an optically active oxymercurial in an exchange reaction with a racemic alkene. The resulting diastereomeric transition states involved in this exchange have afforded unequivocal evidence that *both* the optically active oxymercurial and the exchanging alkene are coordinated to the mercury in the rate limiting step. Our experiments provide a unique mechanistic probe that supplements the existing kinetic data on exchange reactions with both hydroxy-[1] and alkoxymercurials.[3] We also report evidence that precludes the formation of a bisoxymercurial (eq 4) as a major pathway in the exchange reaction of an alkoxymercurial.

The methoxymercuration of optically active bornylene (**1**), $[\alpha]D$ −24°, with $Hg(NO_3)_2$ and HgO (1:1) in methanol (16 hr) afforded the methoxymercurials **2** and **3** in a ratio of 2 to 1.[4] One equivalent of 1-octene was added and after 1 hr at 25° 7% exchange (eq 1) had occurred affording **1** and **4** (Scheme I). The reaction was quenched by the addition of basic $NaBH_4$. Optically active **1** was recovered from the reaction mixture and the isolated 2-methoxyoctane (**5**) had $[\alpha]D$ +2.0°.[5] A repeat of this experiment employing **1** and $Hg(NO_3)_2$ in CH_3OH (2 hr) afforded **2** and **3** in the presence of 1 eqiv of HNO_3.[4] Exchange with 1-octene (0.8 equiv) was 5–6% complete after 10 min and the resulting methyl ether **5** had $[\alpha]D$ +4.2°. The optical purity of **4**[6] was dependent upon the reaction time since the degenerate exchange of 1-octene with **4** resulted in loss of optical activity. However, optical yields of **5** as high as 36%[6] were observed when the exchange reaction was not allowed to go to completion.

Induced asymmetry was also observed when 1 equiv of racemic 1-phenylnorbornene (**6**) was added to a mixture of **2** and **3** in CH_3OH. Analysis by glpc indicated that about 8% exchange has occurred in 5 min when 1 equivalent of HNO_3 was present. The methoxy ethers **9** and **10** ($[\alpha]D$ −0.6°) were produced in a ratio of 1 to 9.6.[8] Recovery of the unreacted alkene **6** showed that it was also optically active and had $[\alpha]D$ −1.1°.

The observation of enantiomeric enrichment of the oxymercurials resulting from exchange of an alkene with optically active **2** and **3** precludes the reversible oxymercuration-deoxymercuration pathway (eq 3) as being the dominant exchange mechanism in good agreement with the ki-