The product distribution for norbornene oxidation on Rh(111)-p(2×1)-O is consistent with the oxametallacycle intermediate, Scheme I. If a cationic intermediate were formed, it should rearrange to 3-cyclohexene-1-carboxaldehyde on a rapid time scale (Scheme II).[5,6,8,11]

Furthermore, acetone is the sole product of propene oxidation on Rh(111)-p(2×1)-O. A cationic intermediate should afford propanal because of the greater stability of the secondary cation that would be produced from oxygen attack at the 1-position.[12] Steric considerations favor acetone formation for an oxametallacycle intermediate.[3,13]

Epoxidation followed by rearrangement to the norbornanone is likewise ruled out. No norbornanone is detected during reaction of *exo*-2,3-epoxynorbornane on Rh(111)-p(2×1)-O.[14] By ruling out epoxidation, the differences in the oxidation chemistry of Rh(111)-p(2×1)-O and Ag are demonstrated. Norbornene is epoxidized to 2,3-epoxynorbornane by oxygen chemisorbed on Ag(110).[15] The underlying reason for the difference between silver and rhodium is not understood but may be related to their respective abilities to break and form C-H bonds, since norbornanone formation requires a 2,1-hydrogen shift whereas epoxidation does not require any migration of hydrogen.

The difference between the oxide-bound Rh complex and the Rh(111)-p(2×1)-O surface is a clear example of substantially different reaction mechanisms for extended metal surfaces and smaller clusters. The differences in particle size and Rh oxidation state or the presence of acidic sites on the alumina may lead to the different reaction paths on the supported material. Although the supported Rh complex is not well-characterized, an oxidized mononuclear rhodium compound has been proposed.[16] The Rh is nearly zero-valent on Rh(111)-p(2×1)-O since there are no measurable chemical shifts in the Rh(3d) binding energies, although the surface contribution may be difficult to detect. Shifts of 1-2 and 2-4 eV are expected for Rh(I) and Rh(III), respectively. Furthermore, the presence of molecular O_2 on the Rh center was postulated.[5,16] If, indeed, O_2 is present, it could lead to different reactivity; it is clearly not present on Rh(111)-p(2×1)-O. The relative stabilities of ions and radicals may also be different in the vicinity of an extended, conductive surface than when in contact with a cluster containing a few metal atoms due to screening of the charge by the metal conduction electrons. The screening may affect both the time scale and energetics for skeletal rearrangement. Additional information about the supported Rh catalyst and theoretical modeling are necessary to better address these issues.

Acknowledgment. We acknowledge the support of Mitsubishi Kasei. We also thank and acknowledge Jeffrey Schwartz for stimulating discussions leading to this work. Thanks also go to Lily Birladeanu for helpful discussions regarding cation rearrangements.

(10) For example, *tert*-butoxide has an O(1s) binding energy of 530.5 eV on Rh(111)[17] and acetone a binding energy of 531.6 eV on Rh(111)-p(2×1)-O.[18]

(11) It is possible that the rate of norbornanone formation is much more rapid than rearrangement on the extended metal surface than on supported clusters.

(12) McMillan et al.[5] proposed that a glycolate intermediate is formed during propene oxidation on (alumina)Rh(O_2). No acetone is formed from 1,2-propanediol on Rh(111)-p(2×1)-O in preliminary studies; thus, this pathway is excluded.

(13) Addition to the 1-position of a terminal alkene would bring the alkyl group into close proximity to the surface, creating repulsive interactions. This assertion is supported by the substantially lower oxidation yields of internal compared to terminal olefins.[19]

(14) Temperature-programmed reaction of *exo*-2,3-epoxynorbornane on Rh(111)-p(2×1)-O produces CO, CO_2, and H_2O above 350 K, along with *exo*-2,3-epoxynorbornane desorption at 210 and 300 K. No other products are detected.

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(16) Fischer, H. E.; Schwartz, J. *J. Am. Chem. Soc.* **1989**, *111*, 7644.
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(19) Xu, X. Ph.D. Thesis, Harvard University, 1991.

Antibody-Catalyzed Double Stereoselection in Fluorinated Materials

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Recent years have seen breakthroughs in the development of enzymes[1] and/or enzymelike catalysts[2] for asymmetric induction. In particular, molecular recognition by antibodies[3,4] has attracted the interest of synthetic chemists. A class of chiral compounds with multiple stereocenters, namely, diastereomerically pure fluorinated materials, used to differentiate biological properties,[5] has attracted intense interest. To date their preparations have required the separation of diastereoisomeric mixtures or the stereoselective synthesis of fluorinated compounds, both of which may be problematic.[5,6] Therefore, we sought to determine whether it is possible to isolate four optically pure stereoisomers in the maximum 25% yield by direct optical resolution of a diastereoisomeric mixture by an antibody. We have examined the antibody-catalyzed separation of 1,2- or 1,3-diastereoisomeric mixtures, i.e., the possibility of separating each of the four stereoisomers in high optical purity (>97-99% ee).

Enzymelike catalyst design (antibody reagent design) requires the preparation of haptens with structures that would mimic the site of catalytic activity, through transition-state analogues. To form the desired antibody reagents, an immunogenic conjugate was prepared by reaction of a phosphonate, **4**, with a carrier protein (bovin serum albumin and keyhole limpet hemocyanin).[7] To effect the separation of four stereoisomers, four stereochemically related haptens bearing a fluorine atom and a methyl group

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(2) Reviews: (a) Schultz, P. G. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1283. (b) Shokat, K. M.; Schultz, P. G. *Annu. Rev. Immunol.* **1990**, *8*, 335. (c) Schultz, P. G.; Lerner, R. A.; Benkovic, S. J. *Chem. Eng. News* **1990**, *68*(22), 26.

(3) (a) Napper, A. D.; Benkovic, S. J.; Tramontano, A.; Lerner, R. A. *Science* **1987**, *237*, 1041. (b) Benkovic, S. J.; Napper, A. D.; Lerner, R. A. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 5355. (c) Jackson, D. Y.; Jacob, J. W.; Sugasawara, R.; Reich, S. H.; Barlett, P. A.; Schultz, P. G. *J. Am. Chem. Soc.* **1988**, *110*, 4841. (d) Hilvert, D.; Carpenter, S. H.; Nared, K. D.; Auditor, M. T. M. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 4953. (e) Braisted, A. C.; Schultz, P. G. *Ibid.* **1990**, *112*, 7430.

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(5) (a) Bravo, P.; Resnati, G. *Tetrahedron. Asymmetry* **1990**, *1*, 661 and references cited therein. (b) Welch, J. T.; Eswarakrishnan, S. *J. Chem. Soc., Chem. Commun.* **1985**, 186. (c) Vidal-Cros, A.; Gaudry, M.; Marquet, A. *J. Org. Chem.* **1985**, *50*, 3163. (d) Morizawa, Y.; Yasuda, A.; Uchida, K. *Tetrahedron Lett.* **1986**, *27*, 1833. (e) Hanamoto, T.; Fuchikami, T. *J. Org. Chem.* **1990**, *55*, 4969.

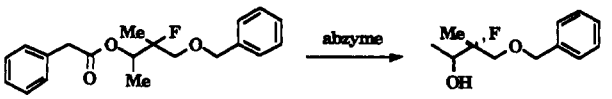
(6) (a) Kitazume, T.; Sato, T.; Kobayashi, T.; Lin, J.-T. *J. Org. Chem.* **1986**, *51*, 1003. (b) Kitazume, T.; Kobayashi, T.; Yamamoto, T.; Yamazaki, T. *Ibid.* **1987**, *52*, 3218. (c) Yamazaki, T.; Yamamoto, T.; Kitazume, T. *Ibid.* **1989**, *54*, 83. (d) Kitazume, T.; Kobayashi, T. *Synthesis* **1987**, 187.

(7) Lymphocytes from the spleen of BALC/c mice immunized with each type of the purified antigens (the BSA-phosphonate conjugate or the KLH-phosphonate conjugate) were fused by standard protocols using mouse myeloma cells (P 3-X 63-Ag.8. U-1) as the fusion partner. Antibodies were screened by ELISA for cross-reactivity with the BSA-hapten conjugate, i.e., for inhibition of binding to the BSA-hapten conjugate by free hapten. Six or eight antibodies were obtained for each diastereomer. Antibodies were purified from ascites fluid by protein A Sepharose 4B affinity chromatography and were determined to be >95% homogeneous by sodium dodecyl sulfate polyacrylamide gel electrophoresis.

(8) The antibody (40 μM, Lowry assay, with a molecular weight of 150000 for immunoglobulin G) was incubated at 25 °C in 60 mL of phosphate buffer at pH 7.3. The racemic ester (10 mM) in acetonitrile (6 mL) was hydrolyzed for 15 h at 25-27 °C in this solution. The antibody was removed by Centricon filtration; the mixture was acidified with 1 N HCl, and then the oily materials were extracted with diethyl ether. After determining the hydrolysis ratio by ^{19}F NMR signal intensities, the carbinol and benzyl ester were separated by column chromatography on silica gel.

0002-7863/91/1513-8573$02.50/0

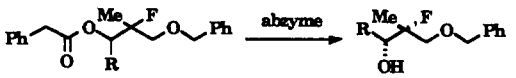
Table I



hapten abs confign	K_{cat},[a] min^{-1}	K_m,[a] μM	hc,[b] %	yield, %	$[\alpha]^{21}_D$, deg (c, MeOH)	op,[c] % ee
2R,3R (+)	0.88 ± 0.3	390 ± 70	23	22	+17.57 (1.14)	99
2S,3S (−)	0.91 ± 0.2	400 ± 70	23.5	21	−17.35 (1.11)	>98.5
2R,3S (+)	0.94 ± 0.2	410 ± 90	23	19	+13.21 (1.21)	98.5
2S,3R (−)	0.86 ± 0.3	380 ± 50	23	19	−13.24 (1.03)	>98

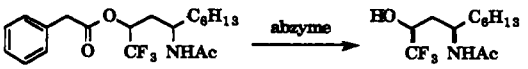
[a] Kinetic constants were determined by the method of initial rate data. Kinetic parameters for the hydrolysis of esters from the Lineweaver–Burk plots were determined. [b] The hydrolysis conversion was determined by ^{19}F NMR signal intensity. [c] The optical purity was determined by GLC after conversion of the compound to its diastereoisomeric ester with optically active MTPA. The analysis was done with Shimadzu GC-14A capillary gas chromatography using an ULBON HR-20M column.

Table II



R	hydrolysis convern, %	de, %	R	hydrolysis convern, %	de, %
Me	48	99	Pr	47.5	99
Et	49	98	Bu	48	>98

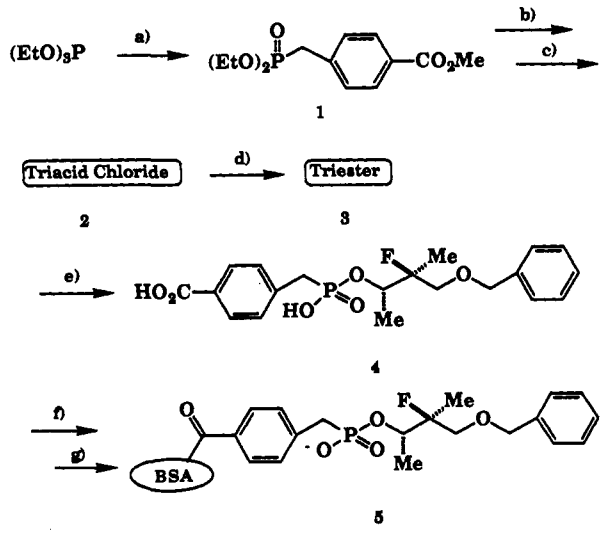
Table III



hapten abs confign	K_{cat},[a] min^{-1}	K_m,[a] μM	hc,[b] %	yield, %	$[\alpha]^{21}_D$, deg c, MeOH	op,[c] % ee
2R,3R (+)	0.79 ± 0.3	410 ± 80	23	19	+18.91 (c 1.01)	>97
2S,3S (−)	0.84 ± 0.2	460 ± 90	24	21	−19.04 (c 1.05)	>97
2R,3R (−)	0.91 ± 0.2	370 ± 60	23	19	−18.45 (c 1.14)	97
2S,3R (+)	0.89 ± 0.3	440 ± 50	23	19	+18.51 (c 1.03)	>98

[a] Kinetic constants were determined by the method of initial rate data. Kinetic parameters for the hydrolysis of esters from the Lineweaver–Burk plots were determined. [b] The hydrolysis conversion was determined by ^{19}F NMR signal intensity. [c] The optical purity was determined by GLC after conversion of the compound to its diastereoisomeric ester with optically active MTPA. The analysis was done with Shimadzu GC-14A capillary gas chromatography using an ULBON HR-20M column.

Scheme I[a]



[a] (a) Arbuzov reaction: triethyl phosphite, methyl 4-(bromomethyl)benzoate, 200 °C. (b) Acidic hydrolysis: concentrated HCl, 50 °C. (c) $SOCl_2$. (d) 1-(Benzyloxy)-2-fluoro-2-methyl-3-butanol, NaH, Et_2O. (e) NaOH (0.1 N), aqueous. (f) Bovine serum albumin (BSA), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride, dilute HCl, pH 5.0. (g) Dialysis, NaCl buffer, pH 7.4.

on adjacent carbons (see Scheme I) were prepared. The antibody[7,8] induced from the syn (threo)[9] hapten acted on the syn diastereoisomer of 1-(benzyloxy)-2-fluoro-2-methyl-3-hydroxybutane with a selectivity of 99% de (hydrolysis conversion 49%), and the antibody from the anti hapten acted on the anti diastereoisomer with a selectivity of >98% de (hydrolysis conversion 49%). These antibody-catalyzed hydrolyses were also effective in separating the four stereoisomers directly from the racemates in a stereospecific manner. (2R,3S)-(+)-1-(Benzyloxy)-2-fluoro-2-methyl-3-hydroxybutane[6d,e] (99% ee; $[\alpha]^{21}_D$ +13.21° (c 1.21, MeOH)) was separated from the racemate by hydrolysis of its ester (conversion 23%) by the antibody generated from the 2R,3S (+) hapten (>98% ee). The enantiomer, (2S,3R)-(−)-1-(benzyloxy)-2-fluoro-2-methyl-3-hydroxybutane (>98% ee), was separated from the recovered ester by use of the antibody generated from the 2S,3R (−) hapten. Then, 2S,3S (−) and 2R,3R (+) isomers could be similarly obtained using the respective antibodies (see Table I).

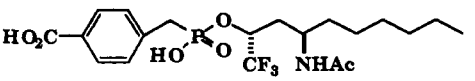


Figure 1.

For the purpose of deriving a basic understanding of the relation between molecular structure and the antibody, we examined the affinity of an antibody, induced by syn hapten **4**, for complex molecules containing various substituents and different-length carbon chains attached to the contiguous asymmetric centers. The diastereoselectivity does not decrease with increasing length of the carbon chain from methyl (99% de) to ethyl (98% de; 49%

(9) In the text, nomenclature of the relative stereochemistry follows the method proposed by Noyori et al. See: Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1983**, *105*, 1598.

hydrolysis conversion), propyl (99% de; 47.5% hydrolysis conversion), or butyl (>98% de; 48% hydrolysis conversion) (see Table II). Not surprisingly, an extreme deterioration in selectivity was observed on changing the substituent from fluorine to another group such as hydrogen or chlorine. The diastereoselectivity decreased from 99% de (48% hydrolysis conversion) to 31% de (with hydrogen) and diastereoisomeric mixture (with chlorine). When a methyl group attached to the tertiary carbon was replaced by other alkyl groups such as ethyl (9% de), propyl (nonselective), or butyl (nonselective), the diastereoselectivity also decreased markedly.

We found that we could similarly achieve a 1,3-double asymmetric selection. In this case, we selected haptens[10] (Figure 1) induced by a 1,3-amino alcohol moiety[11] bearing a trifluoromethyl group at the hydroxyl carbon. (2*R*,3*R*)-(+)-4-(Acetylamino)-1,1,1-trifluoro-2-decanol (>97% ee) was separated from the racemate by hydrolysis of 2-(benzyloxy)-4-(acetylamino)-1,1,1-decane (conversion 23%) by the antibody induced from the 2*R*,3*R* (+) hapten (>98% ee). Then, 2*S*,3*S* (−), 2*R*,3*S*, and 2*S*,3*R* (+) isomers were separated from the recovered ester by use of the respective antibodies (see Table III).

Supplementary Material Available: Experimental details for the synthesis of **5**, **8**, **11**, **14**, **17**, **20**, **23**, and **26** and for asymmetric hydrolysis with antibody (9 pages). Ordering information is given on any current masthead page.

(10) The hapten antigens containing a 1,3-amino alcohol moiety were prepared by using 4-(acetylamino)-1,1,1-trifluoro-2-decanol instead of 1-(benzyloxy)-2-fluoro-2-methyl-3-butanol in Scheme I.

(11) Lin, J.-T.; Yamazaki, T.; Kitazume, T. *J. Org. Chem.* **1987**, *52*, 3211.

*Book Reviews**

Chemistry of Complex Equilibria. By M. T. Beck (Kossuth Lajos University) and I. Nagypál (Jôseph Attila University). Ellis Horwood Ltd.: Chichester, U.K. 1990. 402 pp. $93.50. ISBN 0-85312-143-5.

This book presents a unified treatment of all types of complex equilibria. With a few exceptions, the various subjects presented are well balanced. The most valuable concepts are as follows:

a. Initially, each topic is introduced by means of simple examples. More complex procedures are built on these examples. Thus, a guided tour is available for novices, but the book is also useful for experts.

b. The topics are illustrated with numerous figures (there are 162 figures) making it easier to visualize the sometimes complicated mathematical functions.

c. The book emphasizes the significance of manual (graphical) evaluation of experimental data in order to obtain reliable equilibrium models (e.g., pages 110 and 247). On the other hand, the principles of sophisticated computer programs are also discussed.

d. The authors also demonstrate conceptually that there is no difference between acid–base and complex equilibria (in the earlier literature, this approach did not always prevail). The authors provide valuable guidance to chemists who need to understand complex equilibria for their research.

Chapters 1 and 2 contain basic definitions. The confusion related to concentration, activity, and mixed stability constants is clarified. Chapter 3 is perhaps the best chapter. It discusses basic equilibrium properties of relatively simple systems in considerable detail. It also provides a description of complicated equilibria such as concentration distribution with extrema, systems of unusual concentration distributions, and the like.

Chapter 4 presents a summary of the most important experimental methods. Both the chemical principles and the experimental limitations along with calibration problems are discussed. Chapter 5 gives a reasonable description of both older (graphical) and modern (computer) evaluation techniques. The difficulties with model selection and data transformation are nicely discussed.

Chapter 6 does not appear to be very well focused. Some of the subjects are discussed in considerably more detail in widely used reference books. Perhaps Section 6.4 could have been discussed more appropriately in Chapter 2.

Generally speaking, the biographical citations are current through 1985 with several isolated examples of more recent citations.

Gilbert Gordon, *Miami University*

Chemical Modeling of Aqueous Systems II. ACS Symposium Series 416. Edited by Daniel C. Melchoir and R. L. Bassett. American Chemical Society: Washington, D.C. 1989. xvi + 556 pp. $89.95. ISBN 0-8412-1729-7.

A group of 41 papers given at a symposium, held during the National Meeting of the ACS in Los Angeles in 1988, make up this volume. They are arranged under eight headings: Aqueous Thermodynamics and Theoretical Advancements, Code Development and Documentation, Applications to Modeling: Equilibrium and Mass Transfer, Applications to Modeling: Transport and Coupled Codes, Applications to Modeling: Surface Chemistry, Advancements in Modeling: Modeling Sensitivities, Advancements in Modeling: Thermodynamic and Kinetic Advances, and Advancements in Modeling: Organic Compounds. A thorough index completes the book.

Nuclear Measurements in Industry. Studies in Physical and Theoretical Chemistry 61. By S. Rózsa (Institute of Isotopes of the Hungarian Academy of Sciences). Elsevier: Amsterdam and New York. 1989. xiv + 310 pp. $134.25. ISBN 0-444-98873-4.

Radiometric measurements, by which trace amounts of radioactive isotopes can be used to monitor technological processes for such characteristics as flow, composition, thickness of coatings, and package filling. All aspects of the subject are treated, including basic concepts, detection and measuring instruments, and various applications.

Bubble Wake Dynamics in Liquids and Liquid–Solid Suspensions. By Liang-Shih Fan and Katsumi Tsuchiya. Butterworths: Stoneham, MA. 1990. xv + 363 pp. $95.00. ISBN 0-409-90286-1.

Chemical reactions and mass transfer that accompany the movement of the gas bubbles through fluids are the subject of this book. The wake behind a moving bubble may have a dominating influence. The fundamental phenomena are addressed in the nine chapters. The viewpoint is that of the chemical engineer, but the subject has obvious significance in some biological systems.

Progress in C_1 Chemistry in Japan. Edited by The Research Association for C_1 Chemistry. Elsevier: Amsterdam and New York. 1989. 408 pp. $156.00. ISBN 0-444-98848-3.

The seven chapters in this typescript volume are strongly oriented toward the catalytic conversion of synthesis gas into commercially important chemicals such as ethanol, ethylene glycol, acetic acid, and olefins.

Advances in Polymer Science. Volume 97: Synthesis, Mechanism, Polymer Drugs. With contributions by M. Akashi, H. K. Hall, C. Lee, T. Li, W. Kamińska, P. Penczek, A. D. Pomogailo, K. Takemoto, and I. E. Uflyand. Springer-Verlag: New York. 1990. vi + 165 pp. $85.00. ISBN 3-540-52834-2.

Volume 97 of this popular series is comprised of four papers encompasing a broad range of topics, from synthetic and mechanistic aspects of polymer science to polymeric drugs. Contributions are from China, Poland, the U.S.S.R., and Japan. Each paper stands independently of the others in the book and includes a reasonable introduction and review of the pertinent scientific literature. The entire volume is indexed, enhancing its usefulness as a reference work.

The titles of the four papers included in this work are the following: The Role of Tetramethylene Diradicals in Photo-induced 'Charge-Transfer' Cycloadditions and Copolymerization; Polyfunctional Cyanate Monomers as Components of Polymer Systems; Polymers Containing Metallochelate Units; and New Aspects of Polymer Drugs.

For the researcher with a specific interest in one of these areas or for the scientist keeping up with developments in polymer science, this book

*Unsigned book reviews are by the Book Review Editor.