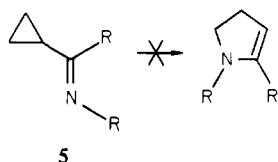


for **1t** is 8.8 kcal mol⁻¹ below that reported for rearrangement of vinylcyclopropane ($\Delta H^\ddagger = 48.5$ kcal mol⁻¹),¹⁸ we suggest that α -azo radicals **3** might be especially stable. The extra stabilization is not that of 1-azaallyl vs. allyl because cyclopropylimines (**5**) do not undergo purely thermal rearrangement.¹⁹ Instead, the



odd electron α to nitrogen appears to be resonance stabilized by the adjacent lone pair, analogous to the effect in α -azo cations.²⁰ It is conceivable that the distant cyclopropane stabilizes **3** by conjugation, a point which could be tested by comparison of activation parameters for vinylcyclopropane and 1,2-dicyclopropylethylene. Although the latter compound is known,²¹ its rearrangement has not been reported. However, 1-cyclopropylbutadiene rearranges only 5.1 kcal mol⁻¹ more readily than vinylcyclopropane.²² Since a cyclopropyl group should be less effective than the additional double bond in stabilizing the radical, most of the 8.8 kcal mol⁻¹ difference between **1t** and vinylcyclopropane is attributed to the above-mentioned three-electron stabilization.²³ Independent evidence for this effect is adduced from the lower E_a for abstraction of H \cdot from azomethane than from ethane.²⁴

Compound **1c** isomerizes over three orders of magnitude slower than the most stable cis acyclic azoalkane reported to date, 1-azobicyclo[2.1.1]hexane² ($\Delta H^\ddagger = 30.3$ kcal mol⁻¹, $\Delta S^\ddagger = 0.8$ eu). Since we have found previously² that the transition-state free energy for azoalkane isomerization is constant at 42.1 kcal mol⁻¹, we can deduce the cis-trans ground-state energy difference for **1** as 42.1-37.8²⁷ = 4.3 kcal mol⁻¹. This energy difference is even smaller than the 7 kcal mol⁻¹ estimated for azoisopropane.^{2,28} One explanation for the low strain energy of **1c** is stabilization by

(17) Milvitskaya, E. M.; Tarakanova, A. V.; Plate, A. F. *Russ. Chem. Rev.* **1976**, *45*, 469. Gutsche, C. D.; Redmore, D. "Carbocyclic Ring Expansion Reactions"; Academic Press: New York, 1968; p 163. See, however: Andrews, G. D.; Baldwin, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 6705. Doering, W. von E.; Sachdev, K. *Ibid.* **1975**, *97*, 5512.

(18) Flowers, M. C.; Frey, H. M. *J. Chem. Soc.* **1961**, 3547. Wellington, C. A. *J. Phys. Chem.* **1962**, *66*, 1671.

(19) Stevens, R. V.; Ellis, M. C.; Wentland, M. P. *J. Am. Chem. Soc.* **1968**, *90*, 5576.

(20) Malament, D. S.; McBride, J. M. *J. Am. Chem. Soc.* **1970**, *92*, 4593. Goldschmidt, S.; Acksteiner, B. *Liebigs Ann. Chem.* **1958**, *618*, 713. Benzing, E. *Ibid.* **1960**, *631*, 1, 10.

(21) Luttke, W.; deMeijere, A. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 512. Köbrich, G.; Merkel, D. *Ibid.* **1970**, *9*, 243.

(22) Frey, H. M.; Krantz, A. *J. Chem. Soc. A* **1969**, 1159.

(23) 2,2'-Dimethoxy-2,2'-azopropane decomposes 6.4 kcal mol⁻¹ more readily than 2,2'-azopropane, suggesting three-electron stabilization by the methoxyl groups. Bandlish, B. K.; Garner, A. W.; Hodges, M. L.; Timberlake, J. W. *J. Am. Chem. Soc.* **1975**, *97*, 5856. See also: Malatesta, V.; Ingold, K. U. *J. Am. Chem. Soc.* **1981**, *103*, 609.

(24) E_a is about 7.9 kcal mol⁻¹ for methyl plus azomethane²⁵ but is 11.8 kcal mol⁻¹ for methyl plus a primary C-H bond.²⁶ See also: Cher, M. *J. Phys. Chem.* **1964**, *68*, 1316.

(25) Grieg, G.; Thynne, J. C. *J. Trans. Faraday Soc.* **1966**, *62*, 3338.

(26) Kerr, J. A. In "Free Radicals"; Kochi, J. K., Ed.; Wiley: New York, 1973; p 15.

(27) This figure is ΔG^\ddagger (490 K) calculated from data in Table I. Free energies are used for consistency with our earlier work.²

(28) Fogel, L. D.; Rennert, A. M.; Steel, C. *J. Chem. Soc., Chem. Commun.* **1975**, 536.

cyclopropyl groups and another is reduction of alkyl group steric repulsion by "tying back" the methyls of azoisopropane. Although we have previously assumed that the cis-trans energy gap in azoisopropane would be close to the "inherent" value, the severe crowding found in *cis*-azomethane¹³ suggests that values below 7 kcal mol⁻¹ are possible. Unfortunately, the potentially enlightening experimental determination of activation parameters for *cis*-azomethane isomerization is rendered difficult by its facile tautomerization. Theoretically calculated cis-trans gaps are of little help because they span a broad range¹.

In summary, we have found that both *cis*- and *trans*-azocyclopropane are extraordinarily stable azoalkanes. While heating **1c** at >200 °C causes isomerization to **1t**, thermolysis of **1t** gives mostly diazavinylcyclopropane rearrangement. The activation enthalpy for this rearrangement suggests three-electron stabilization of α -azo alkyl radicals. Finally, the cis-trans energy gap (4.3 kcal mol⁻¹) estimated for azocyclopropane is the lowest discovered to date.

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Vanadium-Catalyzed Epoxidations. 2. Highly Stereoselective Epoxidations of Acyclic Homoallylic Alcohols Predicted by a Detailed Transition-State Model¹

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The area of stereoselective synthesis of acyclic molecules has been expanding rapidly in recent years to meet the considerable challenges posed by such complex natural products as the ionophore, macrolide, and ansamycin antibiotics.² Epoxidations of straight-chain olefinic alcohols have been crucial to the successful completion of a number of these synthetic efforts,³ and the exceptional versatility of the epoxide functionality in synthesis makes further advances in stereoselective acyclic epoxidations of particular interest. Recently, a remarkably enantioselective epoxidation of allylic alcohols has been reported.⁴ Although mechanistic details are yet to be established, it is now possible to unequivocally predict the direction of asymmetric induction in this system irrespective of substrate substitution. Surprisingly, the same is *not* true for the widely used vanadium/*tert*-butyl hydroperoxide procedure ($V^{5+}/TBHP$) when applied to acyclic systems. Although "preferred-angle" proposals have been made for some open-chain allylic alcohols,⁵ a general solution applicable to all acyclic olefinic alcohols has been lacking. In a recent paper⁶

(1) This work was presented at the First IUPAC Symposium on Organometallic Chemistry Directed toward Organic Synthesis at Ft. Collins, CO, on Aug 4, 1981.

(2) (a) For recent reviews, see: Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2-72. Kishi, Y. *Aldrichim. Acta* **1980**, *13*, 23-30. (b) For interesting recent examples see: Still, W. C.; Darst, K. P. *J. Am. Chem. Soc.* **1980**, *102*, 7385-7387. Snider, B. B.; Duncia, J. V. *Ibid.* **1980**, *102*, 5926-5928. Trost, B. M.; Klun, T. P. *Ibid.* **1981**, *103*, 1864-1865. Evans, D. A.; Bartroli, J.; Shin, T. L. *Ibid.* **1981**, *103*, 2127-2129. Evans, D. A.; McGee, L. R. *Ibid.* **1981**, *103*, 2876-2878 and references cited.

(3) (a) Rifamycin S: Nagaoka, H.; Rutsch, W.; Schmid, G.; Iio, H.; Johnson, M. R.; Kishi, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7962-7965. (b) Monensin: Fukuyama, T.; Wang, C.-L. J.; Kishi, Y. *Ibid.* **1979**, *101*, 260-262. (c) Lasalocid: Nakata, T.; Schmid, G.; Vranesic, B.; Okigawa, M.; Smith-Palmer, T.; Kishi, Y. *Ibid.* **1978**, *100*, 2933-2935.

(4) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974-5976. (b) Rossiter, B. E.; Katsuki, T.; Sharpless, K. B. *Ibid.* **1981**, *103*, 464-465.

(5) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Tetrahedron Lett.* **1979**, 4733-4736.

(6) Mihelich, E. D., *Tetrahedron Lett.* **1979**, 4729-4733.

Table I. V⁵⁺/TBHP Epoxidations of Homoallylic Alcohols^{a,j}

entry	homoallylic alcohol ^b	major epoxy alcohol ^c	selectivity ^d	yield, ^e %	entry	homoallylic alcohol ^b	major epoxy alcohol ^c	selectivity ^d	yield, ^e %
1			>400:1	90	9			104:1	92
2			24:1	93 ^f	10			>400:1	97
	R = (CH ₂) ₇ CO ₂ CH ₃								
3			1.4:1	99	11			70:1	73 ^g
4			12:1	83	12			85:1	70
5			4.6:1	50	13			2.1:1	91 ^h
6			4.8:1	98	14			15.9:1	81
7			3:1	88	15			211:1	95
8			5:1	88 ⁱ					

^a Epoxidations were carried out by adding the olefin (1–16 mmol), vanadium(IV) oxide bis(2,4-pentanedionate) (1–2 mol%), and anhydrous 1 M *tert*-butyl hydroperoxide (1.5 equiv) to anhydrous methylene chloride (~0.1 M in olefin) at ice bath temperature followed by stirring at room temperature overnight (16 h). The less reactive substrates required longer times: entry 11 (24 h), entry 12 (96 h), entry 13 (41 h). ^b Noncommercial substrates were prepared as follows: entry 1, deconjugative alkylation of 2-pentenoic acid (LDA, MeI, THF) followed by reduction (LAH) and chromatography; entry 4, by Lindlar reduction of the corresponding acetylene (ChemSampCo.); entries 5–8, by the method of Hiyama^{12e} [see: Buse, C. T.; Heathcock, C. H. *Tetrahedron Lett.* 1978, 1685–1688]; entries 9–15, by Me₂AlC≡CR opening of the appropriate epoxide [see: Fried, J.; Lin, C.-H.; Ford, S. H. *Tetrahedron Lett.* 1969, 1379–1381] followed by chromatography and hydrogenation over Lindlar catalyst. ^c Assigned as follows: entry 1, the benzyl ether (BzI₂Br, KH), on reaction with vinyl cuprate (CH₂=CHMgBr, CuI), gave the known, substituted hexenol;^{12b} entries 2 and 3, acidic ring opening (HCO₂H, CH₂Cl₂) of the trifluoroacetate derivative followed by methanolysis (NaOMe, MeOH) afforded the known 9,10,12-triol [Abbot, G. G.; Gunstone, F. D. *Chem. Phys. Lipids* 1971, 7, 279–289] resulting from γ -C–O cleavage of the oxirane; entries 5 and 8, LAH reduction yielded the *meso*-diols (by ¹³C NMR); entries 10 and 13, LiCuMe₂ reaction afforded the *meso*-diol and *d,l*-diol, respectively (by ¹³C NMR): Major isomer assignments for the other cases rely on the ¹³C NMR chemical shift and GC and TLC mobility comparisons with the stereochemically defined examples. ^d Determined by ¹³C NMR spectroscopy and capillary gas chromatography (12 m × 0.32 mm WCOT silicone column; used for selectivities >50:1). Authentic diastereomeric mixtures were obtained in all cases by peracid epoxidation (MCPBA). ^e Isolated yields of distilled or chromatographed epoxy alcohols uncorrected for recovered starting material. All products gave satisfactory spectral and analytical data. ^f Recovered starting material, 3.4%. ^g Recovered starting material, 9%. ^h Recovered starting material, 3.5%. ⁱ Run at 0 °C to avoid destruction of minor isomer. ^j All materials are racemic with the exception of entries 2 and 3 which have the 12*R* configuration.

we postulated that the direction of asymmetric induction observed during the V⁵⁺/TBHP epoxidation of certain acyclic allylic alcohols could be explained by a vanadate ester transition state⁷ in which the metal was tetrahedrally coordinated. We now report further studies which indicate this transition-state formulation

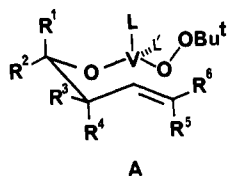
is broadly useful for predicting not only the direction but also the degree of relative asymmetric induction in the V⁵⁺/TBHP epoxidation of acyclic olefinic alcohols.

Application of the tetrahedral vanadate ester transition-state model to homoallylic alcohols immediately suggested that high asymmetric inductions should be attainable for a wide variety of substitution patterns. Although predictions are best done with the aid of Dreiding molecular models,⁸ A illustrates a chair

(7) (a) Chong, A. O.; Sharpless, K. B. *J. Org. Chem.* 1977, 42, 1587–1590. (b) Curci, R.; Difuria, F.; Modena, G. In "Fundamental Research in Homogeneous Catalysis"; Ishii, Y., Tsutsui, M., Eds.; Plenum Press: New York, 1978; Vol. 2, pp 255–274. (c) Itoh, T.; Jitsukawa, K.; Kaneda, K.; Teranishi, S. *J. Am. Chem. Soc.* 1979, 101, 159–169.

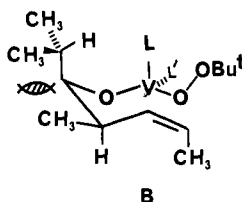
(8) We use a silicon unit for the vanadium atom and a V–O–O angle of ~60° for these studies.

conformation which is quite useful for discussion purposes. We



have investigated six different substitution types and our results are summarized in Table I. In all cases, the observed selectivity is in accord with that form of A which minimizes steric interactions among the various substituents according to commonly accepted principles of conformational analysis. We believe the very high asymmetric inductions that we have obtained for a number of these substrates are entirely predictable on the same grounds.

Entries 1, 9, and 10 show selectivities of >100:1 since the favored transition state in these cases has $R^1 = R^4 = H$ and $R^3 = R^5 = \text{alkyl}$. Formation of the minor isomer requires a severe 1,3-interaction ($R^4 = R^5 = \text{alkyl}$) and is, therefore, highly disfavored. The same is true for entries 11-15 even though R^1 is now constrained to be alkyl in order to avoid a severe R^4-R^5 interaction. For $R^1 = \text{Me}$, this appears to be well tolerated although the reaction rate slows considerably. However, with $R^1 = i\text{-Pr}$ (entry 13) no chair conformation is free of a severe 1,3-interaction (see B) and competition with boat conformations leads



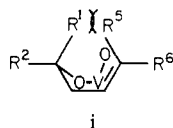
to a much poorer asymmetric induction. Removal of the indicated Me-Me interaction by changing R^1 from iso-propyl to *n*-pentyl (entry 14) again allowed highly selective epoxide formation (94:6 product ratio).

The above cases fit the category of 1,2-relative asymmetric induction in Bartlett's terminology.^{2a} Entries 2 and 4 indicate that high 1,3-induction is also possible in the V^{5+}/TBHP system. This selectivity is lost in the case of the corresponding (*E*)-olefin (entry 3) since energetically competitive boat forms are possible.⁹

Finally, we were especially interested in the structure type characterized by entries 5-8. The possibility exists that vanadium could be trigonal bipyramidal in these reactions, and a preliminary predictive model has been formulated on this basis.¹⁰ Such a model fails when applied to this substrate class. The tetrahedral vanadate ester formulation, on the other hand, nicely accounts for the ~5:1 selectivity observed on the basis of preferred chain form A ($R^2 = R^3 = \text{alkyl}$).¹¹

We have found the principles outlined here to be consistent not only with our own experimental results but also with those previously reported in the literature.^{10,12} In particular, the bis-

(9) In boat conformation i, a severe R^1-R^5 interaction occurs ($R^5 = \text{alkyl}$) as long as a lone pair of the coordinated peroxide oxygen is aligned in the plane of the olefin π cloud as has been suggested by Sharpless¹⁰ for peracid epoxidations.



Without this requirement, it is difficult to account for the substantial selectivities observed for entries 2 and 4. Consequently, we employ this constraint when evaluating the transition-state models for every substrate.

(10) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* 1979, 12, 63-73.

(11) At this point in time, we can only view the tetrahedral vanadate ester formulation as a very highly successful predictive model. However, we do feel our results lend support to the proposed mechanism for this reaction (Scheme III in ref 10) with the added refinement of an early (reactant-like) transition state.

homoallylic alcohol cases studied by Kishi^{12a} are easily rationalized in terms of a similar 7.5-membered-ring^{7c} transition state.¹³

Our results now open the door to rational synthetic planning based on this efficient epoxidation methodology. The facility with which four contiguous chiral centers have been assembled in a predictable manner with virtually complete stereocontrol (entries 9-12 and 15) testifies to the power of this synthetic approach. Numerous applications in complex acyclic synthesis will undoubtedly follow.

Acknowledgment. We thank Professor D. A. Evans for introducing us to the exceptional utility of fused silica capillary gas chromatography columns for determining isomer distributions.

(12) (a) Fukuyama, T.; Vranesic, B.; Negri, D. P.; Kishi, Y. *Tetrahedron Lett.* 1978, 2741-2744. (b) Johnson, M. R.; Nakata, T.; Kishi, Y. *Ibid.* 1979, 4343-4346. (c) Johnson, M. R.; Kishi, Y. *Ibid.* 1979, 4347-4350. (d) Kozikowski, A. P.; Schmiesing, R. J.; Sorgi, K. L. *Ibid.* 1981, 2059-2062. (e) Hiyama, T.; Kimura, K.; Nozaki, H. *Ibid.* 1981, 1037-1040.

(13) Analysis of this considerably more flexible system is simplified by minimizing steric interactions between the *tert*-butyl of the hydroperoxide and the alkyl groups on the more substituted side of the double bond. This again emphasizes the importance of considering all ligand-substrate interactions in these reactions.⁶

Theoretical Studies of S_N2 Transition States. 1. Geometries

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The establishment of rate-equilibrium¹ or structure-reactivity² relationships is a common feature of experimental investigations of reaction mechanisms. Extensive experience has led to the view that such phenomenological effects provide information concerning the structures and properties of transition states if it is valid to postulate that these properties are related in some well-defined manner to properties of the reactants and the products. In this and the following communication we present relationships between the calculated geometries and energies of S_N2 transition states and calculated properties of the reactions. There is remarkable agreement between these theoretical results and the postulates of physical organic chemistry.

Our work was inspired by the outstanding series of experimental contributions by Brauman and his co-workers³ concerning the

* Fellow of the Alfred P. Sloan Foundation, 1981-1983.

(1) Brønsted, J. N. *Chem. Rev.* 1928, 5, 231-338. (b) Hammett, L. P. *Ibid.* 1935, 17, 125-136. (c) Leffler, J. E.; Grunwald, E. "Rates and Equilibria of Organic Reactions"; Wiley: New York, 1963.

(2) (a) Olson, A. R. *J. Chem. Phys.* 1933, 1, 418-423. (b) Ogg, R. A.; Polanyi, M. *Trans. Faraday Soc.* 1935, 31, 604-620. (c) Evans, M. G.; Polanyi, M. *Ibid.* 1935, 31, 875-894. (d) Bell, R. P. *Proc. R. Soc., Ser. A.* 1936, 154, 414-429. (e) Evans, M. G.; Polanyi, M. *Trans. Faraday Soc.* 1936, 32, 1333-1360. (f) Evans, M. G.; Polanyi, M. *Ibid.* 1938, 34, 11-29. (g) Wigner, E. *Ibid.* 1938, 34, 29-41. (h) Evans, M. G. *Ibid.* 1938, 34, 49-57. (i) Hughes, E. D. *Ibid.* 1938, 34, 185-202. (j) Leffler, J. E. *Science (Washington, D.C.)* 1953, 117, 340-341. (k) Hammond, G. S. *J. Am. Chem. Soc.* 1955, 77, 334-338. (l) Burgi, H.-B. *Angew. Chem., Int. Ed. Engl.* 1975, 14, 460-473. (m) Chapman, N. B.; Shorter, J., Eds. "Correlation Analysis in Chemistry. Recent Advances"; Plenum Press: New York, 1978.

(3) (a) Brauman, J. I.; Olmstead, W. N.; Lieder, C. A. *J. Am. Chem. Soc.* 1974, 96, 4030-4031. (b) Farneth, W. E.; Brauman, J. I. *Ibid.* 1976, 98, 7891-7898. (c) Olmstead, W. N.; Brauman, J. I. *Ibid.* 1977, 99, 4219-4228. Inversion of configuration in gas-phase S_N2 reactions has been observed by: Wolf, A. P.; Schueler, P.; Pettijohn, R. R.; To, K.-C.; Rack, E. P. *J. Phys. Chem.* 1979, 83, 1237-1241. To, K.-C.; Rack, E. P.; Wolf, A. P. *J. Chem. Phys.* 1981, 74, 1499-1500.