Kinetic Resolution of Racemic Allylic Alcohols by Enantioselective Epoxidation. A Route to Substances of Absolute Enantiomeric Purity?†,‡

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We have recently described a titanium alkoxide tartrate epoxidation catalyst which is highly effective for the maiden introduction of chirality into prochiral allylic alcohols.[1,2] One would expect such a selective asymmetric catalyst system to be sensitive to preexisting chirality in an allylic alcohol substrate; however, we were not prepared for the degree of sensitivity which has been observed and is delineated in this report.

Racemic secondary allylic alcohols are very common, and this class of chiral substrates was the first to be examined.[3] The outcome for a few representative cases is indicated in Table I. The first thing to note are the entries in the column headed k_{fast}/k_{slow}. These are the relative rates for the enantiomeric pairs, and they range from about 15 to 140 for the measured cases.[4] Although these relative rate differences are substantial, we were still surprised at the dramatic effectiveness of the kinetic resolution process. Realizing that most of the reactions in Table I were only carried to about 55% completion (~55 ± 5%),[5] the generally high enantiomeric purity (see column headed "obsd % ee") of the recovered allylic alcohol is impressive. The great success of these kinetic resolutions, even for rather modest relative rate differences, defied our intuition. Furthermore, as synthetic chemists, we desired a format for the data which would be handy for making predictions.[6] Taking advantage of pioneering works on mathematical treatments[7] of kinetic resolution,[8] Figure 1 was produced

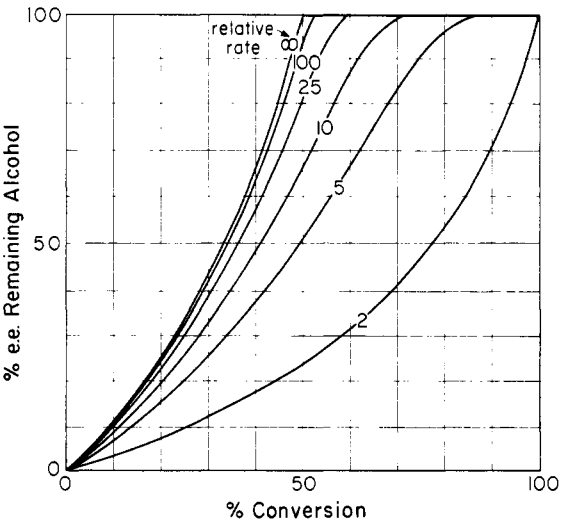
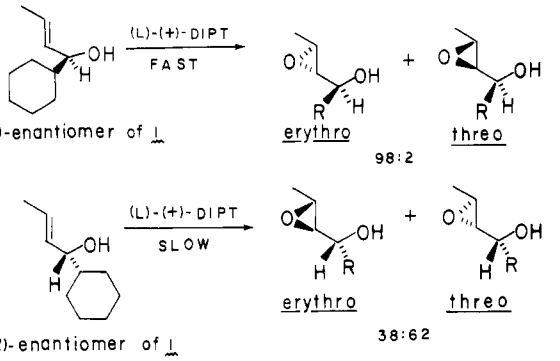


Figure 1. Dependence of enantiomeric excess on relative rate.

Scheme I. Differential Erythro-Threo Selectivity[a] for Enantiomers of **1**



[a] Erythro-threo ratios were determined in separate experiments by using the pure enantiomers.

in a straightforward manner.[9] The usefulness of Figure 1 is apparent. There are three variables: the % ee of the remaining substrate, the % conversion of racemic substrate, and the relative rate. Knowledge of any two of these unknowns allows prediction of the third. Another insight to be gleaned from Figure 1 is that a relative rate difference of only 100 is nearly as effective as a relative rate difference of infinity. Even small relative rate differences (e.g., 5–10) can provide useful amounts of a substance with high enantiomeric purity.

As for the epoxidation of prochiral allylic alcohols,[1,2] the stereochemical outcome of these kinetic resolutions has so far been highly predictable. This is best shown by considering one example in detail. The outcome for racemic (*E*)-cyclohexylpropenylcarbinol (**1**) using L-(+)-diisopropyl tartrate is shown in Scheme I. The allylic alcohol is drawn so that the olefinic carbons and the hydroxyl lie in the plane of the paper, and the carbinol carbon is at the lower right. Recall that for an achiral allylic alcohol drawn in this way L-tartrates mediate delivery of the oxygen atom from

† This communication is dedicated to George Büchi on the occasion of his 60th birthday.

‡ The early stages of this work were carried out in the Department of Chemistry, Stanford University.

(1) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.

(2) Rossiter, B. E.; Katsuki, T.; Sharpless, K. B. *J. Am. Chem. soc.* **1981**, *103*, 464.

(3) We have also found the kinetic resolution process to be effective with a wide variety of racemic primary allylic alcohols wherein the chirality does not reside at the carbinol carbon. These cases also include examples of axial chirality (e.g., allenic alcohols) and will be reported elsewhere.

(4) With the noted exception, these relative rates were obtained by careful kinetic experiments to determine the absolute rates for each pure enantiomer under pseudo-first-order conditions. Details of these kinetic studies (Woodard, S. S.; Sharpless, K. B., unpublished) will be described in the future.

(5) For the sake of uniformity all the experiments in Table I were performed by using 0.6 equiv of TBHP. This does not mean that 60% of the allylic alcohol was consumed in each case. In fact the percent of completion is not known accurately for any case except entry 6, where it was 55 ± 1%. With only 0.6 equiv of TBHP the reactions slow down dramatically near the end, and it is unlikely, especially for the less reactive substrates, that much more than 55% conversion is realized. For example, on the basis of a relative rate of 16, the 82% ee achieved in entry 5 represents 53% conversion. If one wished to reach 60% conversion with unreactive substrates (i.e., those which require days to react in Table I) then more TBHP (~0.7 equiv) would be needed. Another time-saving approach with sluggish cases (e.g., entries 1, 5, 6, 9, 10) is to use excess TBHP (e.g., 2 equiv) and monitor the degree of conversion by GLC or titration of the remaining TBHP.

(6) Knowing an approximate relative rate for epoxidation of a pair of allylic alcohol enantiomers, a synthetic chemist would typically like to know the extent of conversion necessary to achieve ~98% ee, in the recovered allylic alcohol. Kinetic resolution is just one instance of a relative rate situation of interest in a synthetic context. There are many other cases in synthesis where one would like to make quantitative predictions about product compositions (as a function of % conversion) based on relative rate information.

(7) For other examples of nonenzymatic kinetic resolutions, see: (a) Kuhn, W.; Knopf, E. *Z. Phys. Chem.* Abt. B **1930**, *7*, 292. (b) Newman, P.; Rutkin, P.; Mislow, K. *J. Am. Chem. Soc.* **1958**, *80*, 465. (c) Horeau, A. *Tetrahedron* **1975**, *31*, 1307. (d) Horeau, A. *Tetrahedron Lett.* **1962**, 965. (e) Balavoine, G.; Moradpour, A.; Kagan, H. B. *J. Am. Chem.* Soc. **1974**, *96*, 5152. (f) Meurling, L.; Bergson, G.; Obenius, U. *Chem. Scr.* **1976**, *9*, 9. (g) Brandt, J.; Jochum, C.; Ugi, I.; Jochum, P. *Tetrahedron* **1977**, *33*, 1353. (h) Marckwald, W.; Meth, R. *Chem. Ber.* **1905**, *38*, 801. (i) Okamoto, Y.; Suzuki, K.; Yuki, H. *J. Polym. Sci., Polym. Chem. Ed.*, in press.

(8) For examples of enzymatic kinetic resolutions, see: Jones, J. B.; Beck, J. F. In "Techniques in Chemistry, Vol. 10"; Jones, J. B., Sih, C. J., Perlman, D., Eds.; Wiley: New York, 1976; Chapter 4.

(9) This plot is closely related to Figure 3 in Kagan's paper,[7e] but the variables have been changed to be those most useful for applications to synthetic problems. This graph was computer generated from the equation

$$\frac{k_A}{k_B} = \frac{\ln(A/A_0)}{\ln(B/B_0)} = \frac{\ln(1-C)(1-ee)}{\ln(1-C)(1+ee)}$$

where C is the fraction of consumption of racemate, ee is % ee/100, and A and B refer to the concentrations of the fast and slow reacting enantiomers, respectively.

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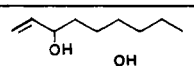
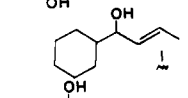
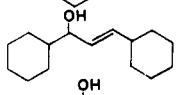
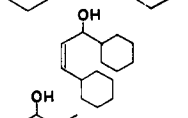
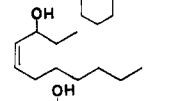
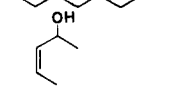
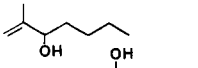
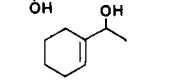
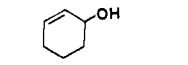
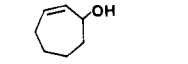
Table I. Kinetic Resolution of Racemic Allylic Alcohols[a]

	allylic alcohol	time[b]	unreacted allylic alcohol[c] config[d]	% ee obsd[e]	% ee calcd[f]	rel rate,[4] k_{fast}/k_{slow}	epoxy alcohol product E/T [g]	Ti(O-*i*-Pr)$_4$ TBHP[h] E/T	VO(acac)$_2$ TBHP[i] E/T
(1)		12 days	*R*	>96	100	83	99/1	53/47	75/25
(2)		15 h	*R*	>96	100	104	97/3	38/62	80/20
(3)		15 h	*R*	>96			97/3	37/63	79/21
(4)[j]		15 h	*S*	~10			2/98	2/98	16/84
(5)		2 days	*R*	82[k]	95.2	16	40/60	4/96	22/78
(6)		6 days	*R*	91		~20[l]	81/19	5/95	25/75
(7)		15 h	*R*	>96	100	138	98/2	83/17	98/2
(8)		15 h	*R*	>96	100	83	98/2	88/12	91/9
(9)[j]		4 days	*R*	30					
(10)		4 days	*R*	80					

[a] Typically performed as follows: 1.0 equiv of Ti(O-*i*-Pr)$_4$ [*x* mL], 1.2 equiv of DIPT, and 1.0 equiv of allylic alcohol are stirred in dry CH_2Cl_2 (10 mL/mmol of allylic alcohol) at -20 °C. Then 0.6 equiv of anhydrous TBHP (ca. 4-6 M in CH_2Cl_2)[13] is added, and the homogeneous reaction mixture is maintained at -20 °C (in a freezer) for the prescribed time (reaction times vary according to olefin substitution). After completion, the cold reaction mixture is poured into a precooled (-20 °C) solution consisting of ca. 2 volumes of reagent grade acetone containing *x* mL of H_2O. The resulting mixture is stirred and allowed to warm to ambient temperature. Stirring is continued until filtration gives a clear solution. Concentration and tartrate hydrolysis[1] followed by a chromatographic step yields the products. [b] In the case of sluggish substrates much shorter reaction times are needed if more TBHP is used (see ref 5). [c] The maximum yield in a kinetic resolution is 50%. In the 10 cases reported here the isolated yield of recovered allylic alcohol ranged from 30-45%. [d] All absolute configurations were proven by chemical correlations (see supplementary material). [e] The enantiomeric excesses were determined by conversion to the MTPA ester (Mosher ester) followed by ^1H or ^{19}F NMR analysis and/or by conversion to the acetate followed by ^1H NMR analysis in the presence of Eu(hfbc)$_3$. An entry of >96 means the allylic alcohol was at least that pure and that NMR signals for the minor enantiomer were not detected. [f] These are the enantiomeric excesses calculated (see Figure 1 and ref 9) from the known relative rates and assuming 60% conversion. In each case where "100" appears, it results from rounding off a string of nines. The shortest string (7 nines) occurs for entry 1 and the longest string (13 nines) occurs for entry 7. [g] These erythro-threo ratios were measured by GLC during the early stage (i.e., 25% or less conversion) of each reaction and thus closely resemble the E/T ratio for the fast-reacting enantiomer. [h] These are the E/T ratios in the absence of tartrate ligand but under otherwise identical conditions to those described above.[a] [i] Performed at 25 °C in the usual[13] manner. [j] In this case 1.5 equiv of DIPT and 1.0 equiv of TiO(*i*-Pr)$_4$ were used. [k] This % ee is calculated[9] to occur at 53% conversion. [l] In this case the degree of conversion was determined to be 55 ± 1%. This fact, along with the observed % ee, allows one to estimate a relative rate of about 20.

the underside.[1,2] Table I reveals that the titanium alkoxide tartrate catalyst strongly favors erythro products. Note that with cyclohexylpropenylcarbinol (**1**) these two effects (i.e., the preference for α attack and erythro selectivity) are consonant for the *S* enantiomer but are dissonant for the *R* enantiomer. Experimentally the *S* enantiomer is observed to react 104 times faster than the *R* enantiomer (entry 2, Table I) and to give an erythro–threo ratio of 98:2. It is interesting that the *R* enantiomer of **1** gives preferentially the threo product. In this instance the preference for α attack is marginally favored over the tendency for erythro selectivity.[10]

All but one[11] of the secondary allylic alcohols (ca. 20 cases) we have examined conform to the following reactivity pattern: when using L-(+)-tartrates the fast-reacting enantiomer is the one related to the *S* enantiomer of **1** (the *R* and *S* designation may vary, but it is the enantiomer in which the substituent on the carbinol carbon is up when the allylic alcohol moiety is drawn as in Scheme I).[12]

The last column in Table I gives the erythro–threo ratios observed in epoxidations by the achiral vanadium catalyst system [VO(acac)$_2$, *tert*-butyl hydroperoxide (TBHP), CH_2Cl_2].[13] *The vanadium catalyst had been the most erythro-selective method known. It is apparent from Table I that the titanium alkoxide tartrate system is substantially more erythro selective than is the vanadium system.* What makes this selectivity even more interesting is the dramatic change it represents over the selectivity seen with titanium isopropoxide in the absence of tartrates (next to last column in Table I). As revealed in Table I, Ti(O-*i*-Pr)$_4$ alone is generally threo selective.[14] For an example of an es-

(10) The observed erythro/threo ratio is not always an accurate measure of the actual erythro/threo selectivity. This is especially true for the slow reacting enantiomer (see note 16).

(11) Examination of the results in Table I reveals that (*Z*)-allylic alcohols (entries 3–5) are relatively poor substrates. One also notes for the *Z* substrates that selectivity decreases as the (*Z*)-β-vinyl substituent gets larger. For a cyclohexyl substituent (entry 4) almost no kinetic resolution occurs, and the small selection which is observed is opposite (i.e. *R* enantiomer reacts faster than the *S* enantiomer) to that for all other secondary allylic alcohols we have studied.

(12) This empirical selectivity rule is very useful due to its simplicity. The selectivity is also explained by what we believe to be the mechanism for these epoxidations. The complex subject of the detailed mechanism will be dealt with in a future publication.[4]

(13) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* **1979**, *12*, 63 and references cited therein.

pecially dramatic turnaround in erythro–threo selectivity for Ti(O-*i*-Pr)$_4$ with and without tartrate see entry 6, Table I (81/19 → 5/95). The highest threo selectivity for free Ti(O-*i*-Pr)$_4$ occurs with (*Z*)-allylic alcohols (entries 4–6, Table I); with this class of allylic alcohols, it appears to be as threo selective as organic per acids.[13]

The enantiomeric purity of the epoxy alcohol products is often very high. Consider, for example, the epoxidation of racemic allylic alcohol **1** to ~50% conversion and 100% conversion. When an epoxidation of **1** [−20 °C, (+)-diisopropyl tartarate] was monitored by GLC and quenched at 52% conversion, the yield of *erythro*-epoxy alcohol was 49% (calcd 49%),[15] with an optical purity of >96% ee (calcd 96.5% ee). [15] In another experiment an otherwise identical epoxidation of **1** was carried to 100% conversion, and the erythro and threo products, following acetylation, were separated chromatographically. The yield of *threo*-epoxy alcohol was 20% (calcd 32%),[15] and it possessed an enantiomeric excess of 92% (calcd 93.5%).[15,16] Therefore, the epoxy alcohol products of these kinetic resolutions also have good potential for use in asymmetric syntheses.

It was found that increasing the size of the alkyl group in the tartrate ester significantly increases the rate difference for epoxidation of the *S* and *R* enantiomers.[17] The relative rates (k_S/k_R) for allylic alcohol **1** were found to be 19, 36, and 104 for (+)-dimethyl tartrate (DMT), (+)-diethyl tartrate (DET), and (+)-diisopropyl tartrate (DIPT), respectively. A similar increase in selectivity was also observed on changing from DET to DIPT for two other secondary allylic alcohols. For this reason DIPT is regarded as the tartrate of choice for kinetic resolutions.

The importance of using an excess of tartrate ligand in these reactions needs to be emphasized. In our report on the asymmetric epoxidation of prochiral allylic alcohols,[1] we recommended a tartrate ligand to Ti(O-*i*-Pr)$_4$ ratio of nearly 1:1. Because of the greater steric requirements of secondary allylic alcohol substrates, the kinetic resolution is more vulnerable to the incursion of epoxidation pathways involving titanium alkoxide species which are not ligated to tartrate.[18] To minimize the threat of epoxidation by such achiral titanium catalysts *we now routinely use a tartrate–titanium ratio of 1.2:1.0*, but even higher ratios (e.g., 1.5:1.0) may be beneficial in some cases.[19] For example, the two poorest substrates in Table I (entries 4 and 9) gave essentially no kinetic resolution when a ratio of 1.0:1.0 was tried, but when the ratio was raised to 1.5:1.0 at least detectable resolution (10 and 30% ee) did occur. Furthermore, *against the advice in our earlier report*[1] *we now recommend that even for prochiral allylic alcohols the tartrate–titanium ratio should never be less than 1.1:1.0.*[20]

Like epoxidations of prochiral allylic alcohols,[1] these kinetic resolutions can also be effected under catalytic conditions. Thus 2-methylhept-1-en-3-ol was very effectively (>96% ee) resolved by using only $^1/_4$ the amount of titanium/tartrate complex employed in entry 7 of Table I. The only other difference in conditions from those in entry 7 was that the reaction was allowed to proceed for 3 days.

Cyclohexanol is one of the poorest kinetic resolution substrates listed (entry 9) in Table I. Fortunately, substituted cyclohexenols[21a] and other ring sizes, such as cycloheptenol (entry 10) and cyclopentenol,[21b] appear more promising.

Even with its limitations this new kinetic resolution process is remarkably general[3] and should in many cases provide the best, if not the only, route to optically pure allylic alcohols.[22] Another noteworthy aspect of this approach to chiral materials is that virtually any degree of enantiomeric purity can be obtained. For example, if the epoxidation of 2-methylhept-1-en-3-ol (entry 7) is carried to 60% conversion, the enantiomeric excess is calculated to be 99.999999999%,[23] and one can go much higher than this simply by proceeding to higher conversions. Such extreme enantiomeric purities are of interest in studying physiological responses to *pure* enantiomers.[24]

For the production of enantiomerically pure substances, kinetic resolution is generally regarded as a poor cousin to asymmetric synthesis. Kinetic resolution suffers from the disadvantage that at least half of the starting material is lost. However, we believe this work makes clear one striking advantage kinetic resolution holds over asymmetric synthesis. The enantiomeric excess realized in an asymmetric synthesis is simply a consequence of the energy difference ($\Delta\Delta G^{\ddagger}$) between two diastereomeric transition states; the only way to improve the % ee is to increase that energy difference. Kinetic resolution too depends on there being an energy difference between diastereomeric transition states, but the manner in which that energy difference is expressed is unique to kinetic resolutions. The energy difference, manifested as a relative rate difference, represents a constant and unrelenting differential pressure upon the two enantiomers. This winnowing should continue until the last molecule of the more reactive enantiomer is swept away, and one is left with a substance possessed of absolute enantiometric purity.[25]

(14) Oshima has recently described an aluminum alkoxide epoxidation catalyst which is also threo selective (Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1980**, 1657).

(15) These calculations were made by using the erythro/threo selectivities for each enantiomer (given in Scheme I), a relative rate of 104, and the equation in ref 9.

(16) We have found that the erythro/threo ratios may vary depending on the substrate and the reaction conditions. Time is an especially important variable, and in the case of **1**, if the reaction is allowed to stand after reaching 100% conversion, the erythro/threo ratio increases. We have traced this effect to selective opening of the *threo*-epoxy alcohol by the titanium tartrate catalyst [for examples of titanium alkoxide catalyzed reactions of epoxy alcohols, see: Morgans, D. J.; Sharpless, K. B.; Traynor, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 462]. The opening process is also enantioselective and exhibits a great preference for the *threo*-epoxy alcohol enantiomer which arises from the slow-reacting enantiomer of **1**. This new epoxy alcohol kinetic resolution process is now being studied.

(17) This effect appears to arise principally from a further retardation in the rate of the slow-reacting enantiomer.

(18) Under the reaction conditions titanium alkoxides undergo rapid ligand exchange processes. These dynamic equilibria are essential for the catalysis but can also give rise to significant concentrations of achiral titanium alkoxide catalysts (much unpublished evidence[4] supports this view).

(19) We have found that the use of excess tartrate ligand effectively suppresses epoxidation by titanium species not bound to tartrate. One should be aware that the use of excess tartrate diminishes the rate of epoxidation by reducing the concentration of the active monotartrate catalyst:

$$\underset{\text{"active"}}{\text{Ti(OR)}_2\text{(tartrate)}} \xrightarrow{\text{tartrate}} \underset{\text{"inactive"}}{\text{Ti(tartrate)}_2} + 2\text{ROH}$$

Therefore, the amount of excess tartrate to use will always be a compromise between the joint considerations of enantiomeric excess and rate.

(20) The original one-to-one recipe[1] was simply a matter of cutting it too close. For epoxidations of prochiral allylic alcohols we now use a tartrate–titanium ratio of 1.1:1.0 for stoichiometric applications and a 1.2 or 1.3:1 ratio for catalytic applications and stoichiometric applications with hindered prochiral allylic alcohols.

(21) (a) Yamada, Y.; Martin, V. S.; Sharpless, K. B., unpublished results. (b) Dr. E. D. Mihelich of Proctor and Gamble informed us of his success in using this process for kinetic resolution of 2-cyclopenten-1-ol.

(22) We have recently performed kinetic resolution of racemic 5-phenyl-1-penten-3-ol on a 1-mol scale with no difficulty.

(23) Professor John W. Cornforth has pointed out to us an effect which under certain conditions will cause the observed enantiomeric excess to be slightly less than this calculated value. This effect will be discussed in a future publication.[4] We are very grateful to Professor Cornforth for his assistance and insight.

(24) For example, we are now applying the kinetic resolution process to producing very high purity chiral insect pheromones. Chiral pheromone research has been hampered by the lack of reference standards of "100%" enantiomeric purity.

(25) This concept of being able to achieve absolute enantiomeric purity in kinetic resolutions by removal of the "last molecule" of the fast-reacting enantiomer is intriguing. The hypothesis that this or any other kinetic resolution process can actually reach absolute optical purity is far beyond the possibility of testing with existing methods for assaying enantiomeric purity. The realization that kinetic resolutions can lead to extremely high, if not absolute, optical purities is either stated or implicit in a number of the works cited in ref 7 and 8.

(26) **Notes Added in Proof**: (a) In order to obtain good results in these kinetic resolutions they *must* proceed to at least 50 to 60% conversion. In our laboratory and others, substandard results (i.e., poor % ee with a substrate expected to have a sizable enantiomeric rate difference) have most often been traced to an inadequate extent of conversion. Thus, we strongly recommend that the reactions be monitored so that the intended degree of conversion is actually realized. (b) It should be noted that the relative epoxidation rates for enantiomeric pairs of allylic alcohols can never exceed the ratio of enantiomers in the tartrate ester. For example, a tartrate ester enantiomeric excess of 99% leads to a relative rate ceiling of 199.

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Supplementary Material Available: Erythro-threo and absolute configuration correlations (5 pages). Ordering information is given on any current masthead page.

Restricted Gearing and Residual Stereoisomerism in Bis(1,4-dimethyl-9-triptycyl)methane

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In accord with predictions,[1] bis(2,3-dimethyl-9-triptycyl)-methane (**1**) exhibits residual diastereoisomerism and a high barrier to gear slippage under the constraint of dynamic gearing.[2,3] Furthermore, empirical force-field (EFF) calculations show that correlated disrotation of the 2,3-dimethyl-9-triptycyl groups in **1** is virtually unhindered within each diastereomer [meso (**1a**) and DL (**1b**)].[4] *We now describe the first molecular gear system in which two experimentally observable barriers, one to gearing and the other to gear slippage, lead to residual stereoisomerism.*

The compound chosen for this study, bis(1,4-dimethyl-9-triptycyl)methane (**2**), was prepared by addition of an excess of 3,6-dimethylbenzyne (from 3,6-dimethylanthranilic acid[11] and isoamyl nitrite) to bis(9-anthryl)methane.[12] Purification by column chromatography on silica, eluant 99:1 pentane/ether, yielded as the only detectable product **2a**,[13] mp 351-354 °C.

Under conditions of rapid cogwheeling, and in the absence of gear slippage, two diastereomers (meso and DL) are expected[1] for

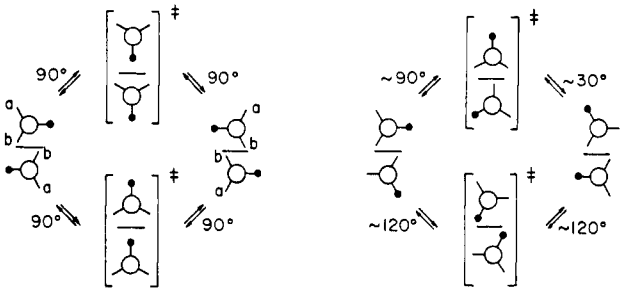

Figure 1. Conformational gearing circuits for the meso (*dl*) (left) and D or L (right) isomers of bis(1,4-dimethyl-9-triptycyl)methane (**2**). The schematic projections follow a previously adopted convention.[1,2] Structures in brackets are transition states. The diastereotopic benzene rings in the *dl* conformers are situated in sites a and b.

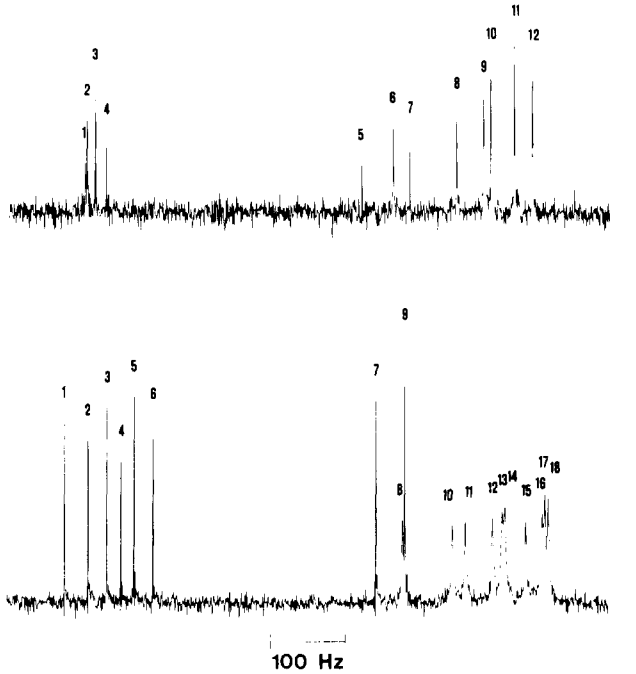

Figure 2. Aromatic $^{13}C\{^1H\}$ NMR region of the spectrum for **2a** at high temperature (top, 100 °C) and low temperature (bottom, -50 °C).

2. EFF calculations[14] show that the perturbation due to the 1-(peri-)methyl groups results in drastic alteration of the energy hypersurface for gearing (Figure 1). The meso isomer consists of a *dl* pair of conformers with C_2 symmetry which interconvert through a C_s transition state 16.5 kcal mol^{-1} higher in energy. The D or L isomer consists of a pair of asymmetric homomers which interconvert through C_1 and C_2 transition states 3.5 and 22.8 kcal mol^{-1} higher in energy, respectively. These computational predictions are consistent with the NMR behavior exhibited by **2a**. At low temperature (-50 to -60 °C) the aromatic region of the ^1H NMR spectrum features 2 ABCD spin systems and the aromatic $^{13}C\{^1H\}$ NMR region 18 lines (Figure 2),[15a] whereas at high temperature (90-100 °C) 1 ABCD spin system and 12 lines[15b] are observed in the two spectra.[16] This site exchange phenomenon

(1) Hounshell, W. D.; Johnson, C. A.; Guenzi, A.; Cozzi, F.; Mislow, K. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 6961.
(2) Cozzi, F.; Guenzi, A.; Johnson, C. A.; Mislow, K.; Hounshell, W. D.; Blount, J. F. *J. Am. Chem. Soc.* **1981**, *103*, 957.
(3) Bis(3-chloro-9-triptycyl) ether exhibits similar behavior: Kawada, Y.; Iwamura, H. *J. Am. Chem. Soc.* **1981**, *103*, 958.
(4) Preliminary calculations had indicated a C_s ground state for bis(9-triptycyl)methane and a gearing transition state with C_2 symmetry lying ca. 1.0 kcal mol^{-1} above the ground state.[1] Using a different force field, a C_2 ground state was calculated, with a C_s transition state ca. 0.1 kcal mol^{-1} higher in energy.[5] However, these energy differences are well within the error limits of the EFF method, and it is now evident that the C_2 and C_s structures are essentially isoenergetic, i.e., the potential-energy hypersurface is virtually flat along the gearing coordinate.[8] Our calculations clearly predict that the barrier heights to gearing in bis(9-triptycyl)methane and related compounds are well below the limits of detection by NMR experiments; indeed, no line broadening has been observed in bis(9-triptycyl)methane and bis(9-triptycyl) ether (to -94 °C),[10] bis(9-triptycyl)carbinol (to -80 °C),[1] and **1a** (to -50 °C).
(5) The force field employed was that of Allinger's MM2 program (*QCPE* **1980**, *11*, 395) with two modifications designed for C_{ar}-C_{ar} bonds (l^o = 1.3937 Å and k_s = 8.0667 mdyn Å^{-1}).[6] Unconstrained geometry optimization was achieved with a modified version of BIGSTRN-2[7] utilizing analytical first and second derivatives of energy and full-matrix Newton-Raphson minimization. Examination of the eigenvalues of the force constant matrix of the final structures confirmed that the C_2 form of bis(9-triptycyl)methane was a minimum while the C_s form was a single partial maximum.
(6) For example, see: Ōsawa, E.; Onuki, Y.; Mislow, K. *J. Am. Chem. Soc.*, in press.
(7) Iverson, D. J.; Mislow, K. *QCPE* **1981**, *13*, 410.
(8) A $\pi/3$ disrotation of both 9-triptycyl moieties in the C_s or C_2 conformations leads to pseudorotation[9] of the whole molecule.
(9) Kilpatrick, J. E.; Pitzer, K. S.; Spitzer, R. *J. Am. Chem. Soc.* **1947**, *69*, 2483.
(10) Kawada, Y.; Iwamura, H. *J. Org. Chem.* **1980**, *45*, 2547.
(11) Newman, M. S.; Cella, J. A. *J. Org. Chem.* **1973**, *38*, 3482.
(12) Applequist, D. E.; Swart, D. J. *J. Org. Chem.* **1975**, *40*, 1800.
(13) NMR and high-resolution mass spectra were consistent with the assigned constitution.
(14) Calculations were carried out with use of BIGSTRN-2.[7]
(15) (a) $^{13}C\{^1H\}$ NMR (25.2 MHz) in [$^2H_2$]dichloromethane (-50 °C) δ 148.1, 146.8, 145.8, 145.1, 144.4, 143.4, 131.5, 130.1, 130.0, 127.4, 126.7, 125.3, 124.8, 124.6, 123.5, 122.7, 122.5, 122.3 (aromatic carbons); 57.1 (quaternary carbon); 50.8 (methine carbon); 28.0 (methylene carbon); 25.6, 19.4 (methyl carbons). (b) $^{13}C\{^1H\}$ NMR in [1,2-$^2H_2$]tetrachloroethane (100 °C) δ 147.00, 146.97, 146.5, 145.9, 132.3, 130.7, 129.8, 127.3, 125.8, 125.4, 124.2, 123.2 (aromatic carbons); 58.5 (quaternary carbon); 52.3 (methine carbon); 29.3 (methylene carbon); 26.0, 19.5 (methyl carbons).
(16) This behavior is unprecedented for this class of compounds and is traceable to the presence of the methyl groups in the 1-positions of the triptycyl moieties. As shown in pioneering studies by Ōki and co-workers,[17] bulky substituents in these positions are capable of slowing torsional processes at the 9-position of triptycene.

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