

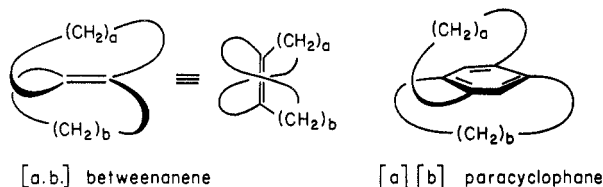
trans-Cycloalkenes and [a.b]Betweenanenes, Molecular Jump Ropes and Double Bond Sandwiches

JAMES A. MARSHALL

Department of Chemistry, Northwestern University, Evanston, Illinois 60201

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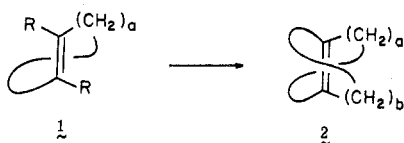
"[a.b]Betweenanene" is a descriptive name for a novel class of compounds in which a pair of *trans*-cycloalkenes shares a common tetrasubstituted double bond.¹ This



arrangement forces the bridging chains of the smaller ring members of the series to loop above and below the double bond, thereby creating a sandwich structure ("ene" between "anes"). The numerical prefixes *a* and *b* indicate the length of each bridge. Geometrically, betweenanenes closely resemble their aromatic counterparts, the [a][b]paracyclophanes.²

We became interested in betweenanenes in 1966 while developing new methodology for the synthesis of *trans*-cyclododecenes.³ At the time we thought we were the first to conceptualize the bicyclic structure but later found that Cahn, Ingold, and Prelog had formulated "bis(*trans*-hexamethylene)ethylene" ([6.6]betweenanene by our nomenclature system) as a hypothetical molecule possessing planar chirality.⁴ The first actual synthesis of such a compound, [10.10]betweenanene (2, *a* = *b* = 10), was achieved in 1977 by Morris Lewellyn in our laboratory at Northwestern.¹ That same year Nakazaki and his group at Osaka described a photochemical approach to the [10.8] and [8.8] homologues.⁵

Much of our betweenanene synthetic program has been concerned with *trans*-1,2-disubstituted cycloalkenes such as 1 with a view toward the structurally defining synthesis 1 → 2. These studies have proven



intrinsically interesting and have provided valuable insight to certain common features of cycloalkenes 1 and 2. We therefore begin this account with a brief survey of pertinent *trans*-cycloalkene chemistry.⁶

trans-Cycloalkenes

In 1948 Stoll and co-workers separated the ethylene ketal of civetone (*cis*-10-cycloheptadecenone) from the *trans* isomer by fractional crystallization and thereby isolated the world's first *trans*-cycloalkene.⁷ Shortly

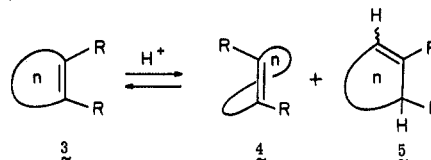
James A. Marshall was born in Oshkosh, WI, in 1935. He received a B.S. degree from the University of Wisconsin and a Ph.D. degree from the University of Michigan under the direction of Robert E. Ireland. After postdoctoral work with William S. Johnson at Stanford, he joined the faculty of Northwestern University where he is currently Professor of Chemistry.

Table I
Acid Catalyzed Isomerization of Cycloalkenes

<i>n</i>	R, R	<i>K</i> cis/trans	<i>n</i>	R, R	<i>K</i> cis/trans
8	H, H	"very large"	11	H, H	0.4
9	H, H	232	12	H, H	0.5
9	CH ₃ , H	>5000	12	CH ₃ , H	1.5
10	H, H	12.2	12	CH ₃ , CH ₃	4
10	CH ₃ , H	>2000			

thereafter Ziegler and Wilms recognized that the "more reactive form" of cyclooctene must possess a *trans* double bond.⁸ Subsequent work by Blomquist⁹ and Cope¹⁰ established synthetic routes to *trans*-cycloalkenes and elaborated some of their properties. At the same time a number of essential oils were found to contain sesquiterpenes with nine- to eleven-membered *trans*-cycloalkene carbon skeletons.¹¹ Thus within only a few years of their initial discovery *trans*-cycloalkenes became relatively commonplace substances.

Early studies on the acid-catalyzed isomerization of *trans*-cycloalkenes revealed an interesting behavior pattern (Table I). For the unsubstituted alkenes, the *cis* isomer markedly predominates in rings of ten or fewer members whereas the *trans* isomer is favored in



eleven and larger membered rings.¹² Later work has shown that methyl substituents on the double bond decrease the stability of the *trans* relative to the *cis* isomer.¹⁰ Thus, *trans*-cyclododecene is favored over *cis*-

(1) Marshall, J. A.; Lewellyn, M. E. *J. Am. Chem. Soc.* 1977, 99, 3508-10. An account of early efforts and considerations is given in: Runquist, A. W. "Synthetic Approaches to Betweenanenes"; Ph.D. Thesis, Northwestern University, 1974.

(2) Cf.: Nakazaki, M.; Yamamoto, K.; Tanaka, S. *J. Org. Chem.* 1976, 41, 4081-86.

(3) Cf.: Marshall, J. A.; Scanio, C. J. V.; Iburg, W. J. *J. Org. Chem.* 1967, 32, 3750-54.

(4) Cahn, R. S.; Ingold, C.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* 1966, 5, 385-415. See p 402.

(5) Nakazaki, M.; Yamamoto, K.; Yanagi, J. *J. Chem. Soc., Chem. Commun.* 1977, 346-47; *J. Am. Chem. Soc.* 1979, 101, 147-51.

(6) Some background material is included in the excellent review on the stereochemistry of many-membered rings. Sicher, J. *Prog. Stereochem.* 1962, 3, 210-13.

(7) Stoll, M.; Hulstkamp, J.; Rouve, A. *Helv. Chim. Acta* 1948, 31, 543-53.

(8) Ziegler, K.; Wilms, H. *Justus Liebigs Ann. Chem.* 1950, 567, 1-43.

(9) Cf.: Blomquist, A. T.; Liu, L. H.; Bohrer, J. C. *J. Am. Chem. Soc.* 1952, 74, 3643-7.

(10) Cf.: Cope, A. C.; Amros, D.; Ciganek, A.; Howell, C. F.; Jacura, Z. *J. Am. Chem. Soc.* 1959, 81, 3153-4.

(11) Cf.: Dev, S. *Tetrahedron* 1960, 9, 1-9. Dawson, T. L.; Ramage, G. R.; Wilson, B. *Chem. Ind. (London)* 1951, 464-5; *J. Chem. Soc.* 1951, 3382-86. Sorm, F.; et al. *Collect. Czech. Chem. Commun.* 1958, 23, 2033-44.

(12) Cope, A. C.; Moore, P. T.; Moore, W. R. *J. Am. Chem. Soc.* 1959, 81, 3153.

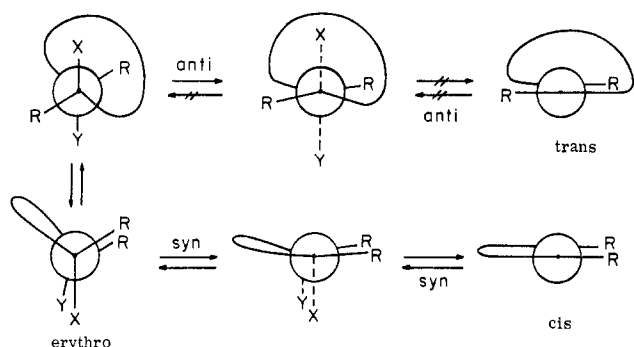


Figure 1. Elimination/additions involving *erythro*-cycloalkane systems.

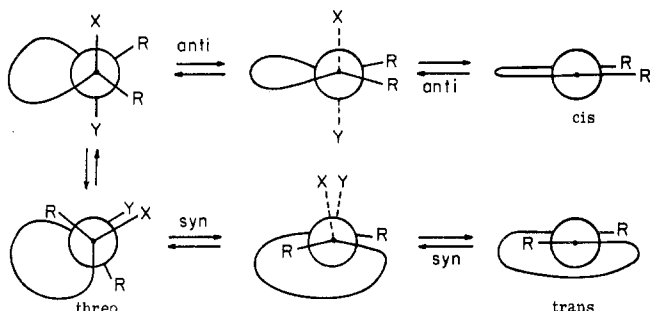


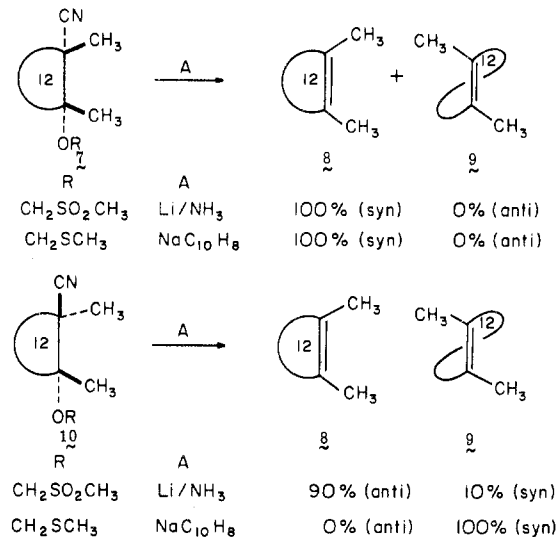
Figure 2. Elimination/additions involving *threo*-cycloalkane systems.

by a factor of two, but *cis*-1-methylcyclododecene predominates over the *trans* isomer 1.5:1.¹³ The 1,2-dimethylcyclododecenes show a *cis/trans* preference of 4.¹³ In fact, the double bond in the latter system actually prefers the trisubstituted position (5). While the *cis/trans* preference can be understood in terms of steric interactions between the methyl substituent and the *trans*-bridging chain, the preference for trisubstitution in the 1,2-dimethyl case has yet to be explained.

Ring Chain Effect in *trans*-Cycloalkenes

The foregoing equilibration data illustrate an important property of *trans*-cycloalkenes which distinguishes them from *cis* isomers or acyclic counterparts, especially for smaller ring members of the series. For these substances the ring chain spans the double bond, thereby causing varying degrees of strain. The effects are most striking for *trans*-cyclooctene and, expectedly, drop off as ring size increases. The point at which the reactivity of the *trans*-cycloalkenes approximates the *cis* isomer or an acyclic analogue depends upon the type of reaction and the double bond substituents. The bridging chain can also exert a steric influence on reactions leading to and from *trans*-cycloalkenes. Figures 1 and 2 show, with the aid of Newman projection formulas, *syn* and *anti* eliminations leading to *cis*- and *trans*-cycloalkenes and the reverse reactions. A major steric problem can be seen in *anti* eliminations of *erythro* disubstituted cycloalkanes (Figure 1), especially for the smaller ring members, owing to interactions between the leaving group X and the bridging ring chain. Likewise, *anti* additions to *trans*-cycloalkenes will suffer from the same type of steric interaction between the ring chain and the entering nucleophile X. Similar problems would arise for internal displacement

Scheme I Reduction-Elimination of *vic*-Cyanohydrin Derivatives



reactions such as those affording oxiranes (17 → 18). The actual feasibility of such processes will depend upon the ability of the bridging chain to swing away from the face of the double bond (additions) or the leaving group X (eliminations). This, in turn, will depend upon interactions between the bridging chain and the double bond substituent, R. A similar type of interaction prevents racemization of certain optically active *trans*-cycloalkenes (see below).

On the other hand, *syn* eliminations and additions can proceed without undue steric encumbrance since the reacting groups (X and Y) can both occupy space opposite (Figure 2) or to one side of (Figure 1) the bridging chain. In contrast to the *trans* systems (Figure 1), *anti* eliminations and additions leading to and from *cis*-cycloalkenes (Figure 2) are not subject to unusual bridging chain steric interactions. In summary, *erythro/syn/cis* and *threo/anti/cis* processes are sterically favorable for all ring sizes, *threo/syn/trans* is possible in rings of eight or more members, and *erythro/anti/trans* processes are sterically disfavored.

Support for this picture comes from recent studies on reduction-eliminations of *threo*- and *erythro*-cyanohydrin derivatives 10 and 7 (Scheme I). Cyanohydrin 10 shows a 9:1 preference for *anti* over *syn* elimination (*threo/anti/cis* vs. *threo/syn/trans*) whereas 7 undergoes exclusive *syn* elimination (*erythro/syn/cis*) upon Li/NH₃ reduction. Interestingly, both 7 and 10 give only *syn*-elimination products (8 and 9, respectively) upon reduction with sodium naphthalenide.¹³ It is noteworthy that early preparations of *trans*-cycloalkenes employed *syn* elimination reactions (Figure 2, R = X = H; Y = Me₂N→O).¹⁴

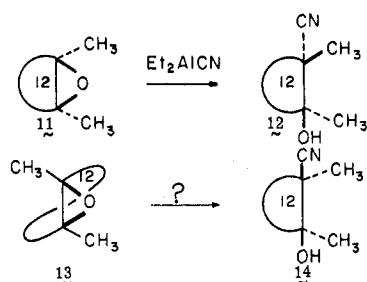
Epoxides and cyclopropanes should also be subject to ring-chain steric control since they are geometrically similar to alkenes. Thus, while the *cis*-epoxide 11 affords the *threo*-cyanohydrin 12 (*cis/anti/threo*) upon treatment with diethylaluminum cyanide,¹³ the *trans* isomer 13 would be expected to be unreactive toward S_N2 opening (Scheme II).

Studies on ring closure reactions also support this analysis. The *threo*-2-trimethylammoniocycloalkanol

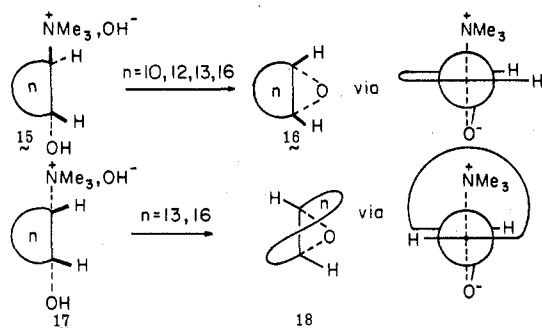
(13) Marshall, J. A.; Karas, L. J.; Royce, R. D., Jr. *J. Org. Chem.* **1979**, *44*, 2994-99. See footnote 7.

(14) Cf.: Cope, A. C.; McLean, D. C.; Nelson, N. H. *J. Am. Chem. Soc.* **1955**, *77*, 1628-31.

Scheme II
S_N2 Opening of Bicyclic Oxiranes



Scheme III
Internal Displacements Leading to Bicyclic Oxiranes



15 readily cyclize (threo/anti/cis) to the corresponding *cis*-epoxides 16. In the analogous *erythro* series, 17, cyclization to the *trans*-epoxide (erythro/anti/trans) fails for $n = 10$ and proceeds in low yield for $n = 12$.¹⁵ Clearly, encapsulation of the departing amine grouping as shown in Scheme III would retard epoxide formation in the smaller ring cases.

Optical Activity of *trans*-Cycloalkenes

Blomquist noted that *trans*-cycloalkenes are chiral and tried unsuccessfully to resolve *trans*-6-cyclononene.⁹ Cope resolved *trans*-cyclooctene¹⁶ and showed the levorotatory enantiomer to have the *R* configuration through chemical correlation with (+)-tartaric acid.¹⁷ The chirality of *trans*-cycloalkenes stems from the double bond whose two faces are distinguished by the spanning ring chain. The chirality sense of this arrangement is determined by the criss-cross orientation of the ring chain relative to the double bond. The absolute configuration of a *trans*-cycloalkene is determined as follows:⁴ The most preferred (highest priority) atom directly attached to the double bond is selected according to the sequence rules. The next attached atom, designated the "pilot atom", is oriented toward the viewer and the path from the pilot atom back to the double bond is traced (Figure 3). If this path follows a clockwise direction, the configuration is *R*; a counterclockwise path defines the *S* enantiomer.

trans-Cycloalkenes owe their optical stability to restricted rotation of the bridging chain past the double bond substituent, R (Figure 3). This barrier is substantial for *trans*-cyclooctene¹⁶ but falls off rapidly for

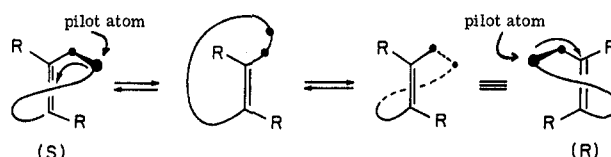
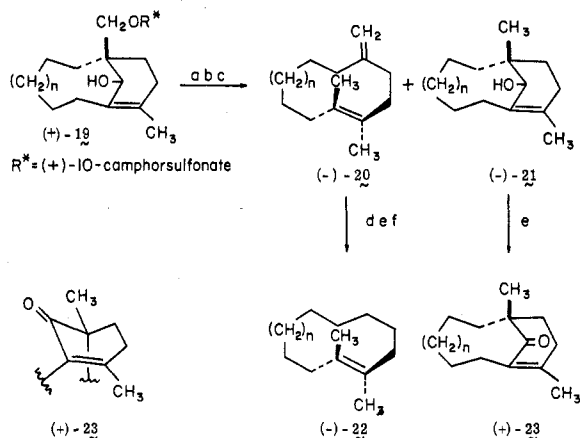


Figure 3. Chirality designation and racemization in *trans*-cycloalkenes.

Chart I
Synthesis of Optically Active *trans*-Cycloalkenes



(a) LiAlH_4 , $\text{MeOCH}_2\text{CH}_2\text{OMe}$ (b) Ac_2O , $\text{C}_6\text{H}_5\text{N}$ (c) Li , NH_3

(d) SiAm_2BH ; H_2O_2 , NaOH (e) $\text{ClCrO}_3\text{H} \cdot \text{C}_6\text{H}_5\text{N}$ (f) $(\text{Ph}_3\text{P})_3\text{RhCl}$, C_6H_6

trans-cyclononene and higher homologues.¹⁸ Efforts to isolate optically active *trans*-cyclodecenes have not succeeded.¹⁹ The R/ring-chain interaction responsible for the aforementioned rotational barrier may also influence the ease of anti-periplanar internal reactions (double constraint processes) of erythro-1,2-disubstituted cycloalkanes (Figure 1).

As noted above (Figure 3), double bond substituents as well as ring size should influence the racemization of *trans*-cycloalkenes. In accord with this prediction we have found that 1,2-dialkyl-*trans*-cyclodecenes (20, 22; $n = 1$)²⁰ and cycloundecenes (20, 22; $n = 2$) can be prepared in optically active form.²¹ The crucial breakthrough here was our ability to resolve the bicyclic alcohols 19 ($n = 1, 2$; $\text{R}^* = \text{H}$) through their crystalline camphorsulfonate derivatives. Subsequent fragmentation-reduction with lithium aluminum hydride yielded the cycloalkenes 20. The absolute configuration of these cycloalkenes was determined through analysis of the ORD curve of ketone 23 (positive Cotton effect), secured from alcohol 21, a reduction product of camphorsulfonate 19²⁰ (Chart I).

In another approach we attempted to secure optically active *trans*-1,2-dimethylcyclododecene via partial hydroboration of the racemic olefin with isopinocampheylborane.²² In fact, asymmetric hydroboration did occur since the derived alcohol 24 (25% yield, $[\alpha]_D^{22}$

(18) Binsch, G.; Roberts, J. D. *J. Am. Chem. Soc.* 1965, 87, 5157-62.

(19) Cf.: Hill, R. K.; Fracheboud, M. G.; Sawada, S.; Carlson, R. M.; Yan, S. *J. Tetrahedron Lett.* 1978, 945-8. Haruhisa, S.; Osawa, E.; Matsumoto, T. *Ibid.* 1979, 2245-6.

(20) Konicek, T. R. "The Synthesis and Absolute Configuration of (*E*)-1,2-Dimethylcyclodecene"; Ph.D. Thesis, Northwestern University, 1980, pp 38-55.

(21) Flynn, K. E., unpublished results.

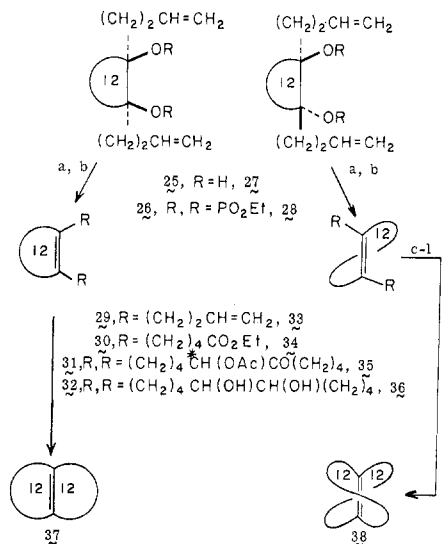
(22) Brown, H. C.; Schivier, J. R.; Singaram, B. *J. Org. Chem.* 1978, 43, 4395-97.

(15) Svoboda, M.; Sicer, J. *Collect. Czech. Chem. Commun.* 1958, 23, 1540-58. For a study of five-membered ring closure to give 2-oxazolinium methanesulfonates from *threo*- and *erythro*-2-benzamidocycloalkyl methanesulfonates, see: Sicer, J.; Svoboda, M. *Collect. Czech. Chem. Commun.* 1958, 23, 2094-2110.

(16) Cope, A. C.; Gamellin, C. R.; Johnson, H. W., Jr.; van Auken, T. *V. J. Am. Chem. Soc.* 1963, 85, 3276-79.

(17) Cope, A. C.; Metha, A. S. *J. Am. Chem. Soc.* 1964, 86, 1268-9.

Chart II
Lewellyn [10.10]Betweenanene Synthesis



(Z)-bicyclo [10.10.0] docos-1(12)-ene (E)-bicyclo [10.10.0] docos-1(12)-ene

([10.10] betweenanene)

- (a) *n*-BuLi; Cl₂PO₂Et (b) Li, NH₃ (c) Si₂BH; H₂O₂, NaOH (d) TsCl, C₅H₅N
(e) NaCN (f) KOH; HCl, EtOH (g) Na-K, xylene, Me₃SiCl (h) *n*-Bu₄NF, THF
(i) Ac₂O, C₅H₅N (j) LiAlH₄; H₂O, NaOH (k) *n*-BuLi; Cl₂PONMe₂ (l) H₂/Pt

+14.9°) was optically active.²⁰ However, the recovered dimethylcycloalkene showed no rotation. Analogous treatment of *trans*-1,2-dimethylcycloalkene afforded optically active recovered olefin **22** (*n* = 1) in 33% yield ([α]_D²² -18°).²⁰ Thus it would appear that *trans*-1,2-dimethylcycloalkene must racemize rather easily. Accordingly synthetic routes to optically active betweenanenes starting from *trans*-cycloalkenes (e.g., 1 → 2) would best be explored with rings smaller than cycloalkene (Chart IV).

Betweenanene Nomenclature

As noted in the introduction, our semisystematic nomenclature system for bicyclic bridged alkenes such as **2** emphasizes the sandwich relationship between the outside bridging chains and the inside double bond. Of course, conventional IUPAC nomenclature employing the Baeyer convention for bridged ring systems²³ can also be used. Double bond isomers can be designated as *cis* (**37**) and *trans* (**38**) or *Z* (**37**) and *E* (**38**). In the case of symmetrical bicyclics such as **37** and **38**, it is possible to assign priorities to identical olefin substituents (CH₂'s) by exploration from the first (arbitrarily selected) to the second through the ring containing both (the common ring). The common ring basis for priority assignments has previously been used in cyclic structures possessing central and linear chirality.²⁴ Finally, it should be noted that the *cis* isomer **37** is not a betweenanene since the double bond is not sandwiched by crisscrossing chains.

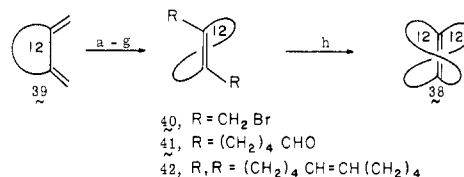
Betweenanene Synthesis

We felt that the initial synthesis of the novel betweenanene framework should be structurally definitive.

(23) Cf.: Fletcher, J. H.; Dermer, O. C.; Fox, R. B. *Adv. Chem. Ser.* 1974, No. 126, 16-7.

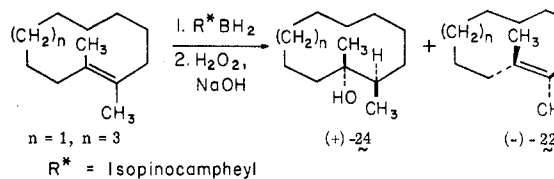
(24) We thank Dr. Kurt Loening, Director of Nomenclature, Chemical Abstracts Service, for calling this point to our attention.

Chart III
Chung [10.10]Betweenanene Synthesis



- (a) Br₂ (b) CH₂=CHCH₂MgCl (c) R₂BH; H₂O₂, NaOH (d) p-TsCl, C₅H₅N
(e) NaCN (f) (*i*-Bu)₂AlH; H₃O⁺ (g) TiCl₃/Zn(Cu) (h) H₂/Pt

Scheme IV
Kinetic Resolution of *trans*-Cycloalkenes



We therefore concentrated on methods for preparing substituted *trans*-cycloalkenes of defined structure which could be directly cyclized (1 → 2). Several variations of this general approach were eventually completed. The first of these (Chart II) utilized the cyclic phosphate derivative **28** of the 1,2-cycloalkenediol **27**. Stereoselective syn elimination to the *trans*-cycloalkene **33** was effected using Li/NH₃.^{1,23} Attempts at ring closure of the derived diester [i.e., **33**, R = (CH₂)₃CO₂Et] to a [10.8]betweenanene derivative were not successful so we extended the side chains via bis homologation (Chart II, c-f). Cyclization of diester **34** with Na/K alloy followed by acetylation yielded the [10.10] acetoxy ketone **35** as a 1:1 mixture of diastereoisomers, a consequence of *trans*-cycloalkene chirality and the asymmetric (*) α-acetoxy center. Reduction via the diol **36** yielded [10.10]betweenanene (**38**), a crystalline solid, mp 64-65 °C. An analogous series of steps converted diol **25** to the *cis* isomer **37**, mp 136-138 °C.

Our second synthesis of [10.10]betweenanene utilized *trans*-1,2-bis(bromomethyl)cycloalkene (**40**) secured through bromination of 1,2-dimethylenecycloalkene (Chart III).²⁶ Coupling with allylmagnesium chloride followed by homologation yielded the dialdehyde **41**. This was cyclized with reduced TiCl₃ by the method of McMurry.²⁷ Hydrogenation of the resulting diene **42** afforded [10.10]betweenanene (**38**).

The cyanohydrin chemistry outlined in Scheme I suggests a third stereocontrolled route to *trans*-1,2-disubstituted cycloalkenes and hence betweenanenes. Our work here is still in progress, but we have found that cyano ketone **44** available from the corresponding isoxazole **43** affords the epoxide **45** stereoselectively.^{28,29} Reduction elimination of the cyanohydrin derivative **46** should give triene **47**. Since triene **47** (*n* = 11) should be amenable to asymmetric hydroboration (Scheme IV), the approach is capable of yielding optically active

(25) Marshall, J. A.; Lewellyn, M. E. *J. Org. Chem.* 1977, 42, 1211-5.

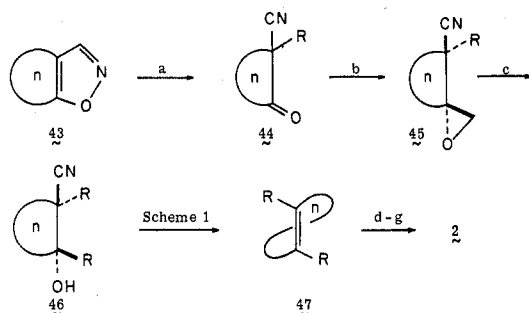
(26) Marshall, J. A.; Chung, K.-H. *J. Org. Chem.* 1979, 44, 1566-7.

(27) McMurry, J. E.; Fleming, M. P.; Kees, K. L.; Krepski, L. R. *J. Org. Chem.* 1978, 43, 3255-66.

(28) Bierenbaum, R. "Stereoselective Synthesis of Olefins via Reduction-Decyanation"; Ph.D. Thesis, Northwestern University, 1979, p 107.

(29) Peterson, J., unpublished results.

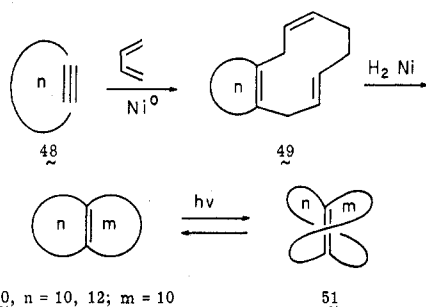
Chart IV
R = (CH₂)_nCH=CH₂; n = 11, 12



(a) KO-t-Bu; RBr (b) CH₂=S(CH₃)₂ (c) R'Li (d) Si₂BH; H₂O₂; NaOH

(e) ClC(O)₃H; C₅H₅N (f) TiCl₃/Zn(Cu) (g) H₂/Pt

Chart V
Nakazaki [8.8]- and
[10.8]Betweenanene Synthesis (n = 10, 12)



50, n = 10, 12; m = 10

51

Table II
Photoisomerization of Bridged Bicycloalkenes

n, m	conditions	cis/trans
10, 10	direct (185 nm)	9 ⁵
12, 10		0.5 ⁵
10, 10	sensitized (xylene)	very large ⁵
12, 10		2.4 ⁵
12, 12		1 ²⁸
24, 12		0.5 ³⁰

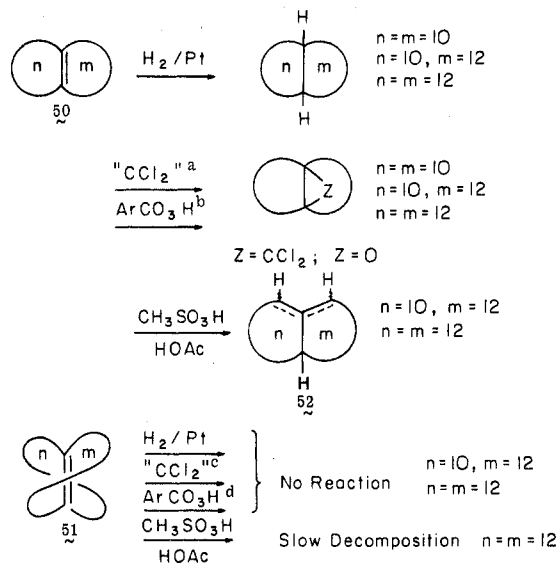
betweenanenes (Chart IV).

A most straightforward betweenanene synthesis was described by Nakazaki and co-workers at virtually the same time as our own initial work appeared.⁵ This completely independent effort (Chart V) employed Ni-template chemistry to prepare a cyclodecatriene-fused cycloalkene, 49. Partial hydrogenation afforded the cis bicyclic alkene 50 which could be photoisomerized to the trans isomer 51. The conversion (see Table II) was found to depend upon ring size and wavelength of light.^{5,28,30}

Chemical Probes for Betweenanenes

Studies on reactions of [10.10]- and [10.8]betweenanenes and the corresponding cis isomers have confirmed the anticipated contrast in cis/trans double bond reactivity. Scheme V summarizes the major findings to date.^{5,30-33} The acid-catalyzed isomerization of 50 to trisubstituted isomers 52 is noteworthy. Close sim-

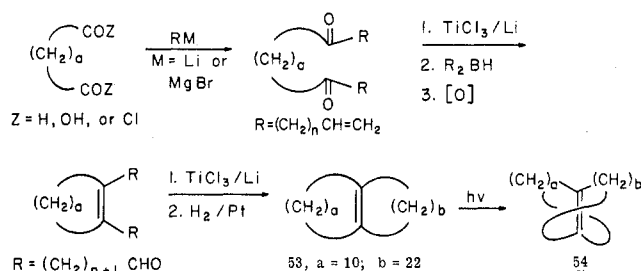
Scheme V
Reactions of Bicyclic Alkenes



(a) 1.5 hr at 25°C (b) 30 sec at 25°C

(c) no reaction after 1.5 hr (d) no reaction after 3 weeks

Chart VI
Black Synthesis of [22.10]Betweenanene



R = (CH₂)_{n+1}CHO

53, a = 10; b = 22

54

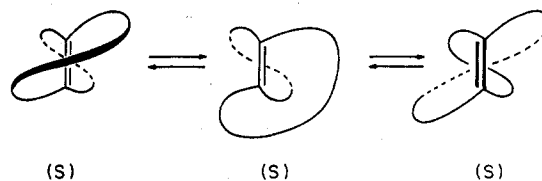


Figure 4. Conformational flexibility in jump rope betweenanenes.

ilarities in spectral properties and chromatographic behavior led us to initially conclude³² that the products of this isomerization were betweenanenes, but a more critical examination clarified the outcome as indicated.³¹ The preferred formation of trisubstituted olefins 52 is consistent with the behavior of 1,2-dimethylcyclo-dodecene (Table I). One additional reaction which distinguishes the cis and trans bicyclic alkenes 50 and 51 is the formation of wine-red tetracyanoethylene charge-transfer complexes with the former but not the latter.³⁴ The trisubstituted olefins form a weakly colored charge-transfer complex.³⁰

Betweenanene Jump Ropes

We have recently developed a highly flexible, efficient synthesis of betweenanenes and their cis isomers (Chart VI) which we have used to prepare a prototype "jump

(30) Black, T. H., unpublished results.

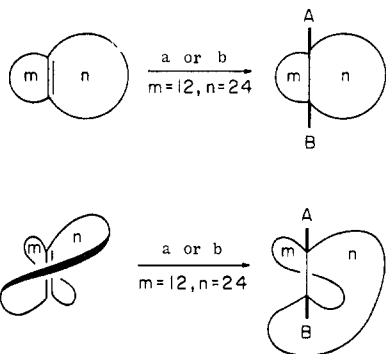
(31) Marshall, J. A.; Black, T. H.; Shone, R. L. *Tetrahedron Lett.* 1979, 4737-40.

(32) Marshall, J. A.; Bierenbaum, R. E.; Chung, K.-H. *Tetrahedron Lett.* 1979, 2081-4.

(33) Chung, K.-H. "Studies on the Synthesis and Chemistry of Betweenanenes"; Ph.D. Thesis, Northwestern University, 1979, pp 75-78.

(34) We are indebted to Professor T. G. Traylor for his enthusiastic recommendation of this aesthetically appealing color test.

Scheme VI
Reactions of Large Ring Bicyclic Alkenes



(a) $m\text{-ClC}_6\text{H}_4\text{CO}_3\text{H}$ (b) $\text{BH}_3\cdot\text{THF}; \text{H}_2\text{O}_2, \text{NaOH}$

rope" betweenanene, the [22.10] system **54**.³⁰ In jump rope systems one of the bridging chains is long enough to swing around the smaller second chain, thus exposing the double bond and making it accessible to external reagents (Figure 4). Since the inner ring cannot pass through the outer chain, the process would not cause racemization of an optically active betweenanene as it does with *trans*-cycloalkenes (Figure 3). We hope to bracket the jump rope phenomenon by examining a series of [a.10]betweenanenes (**54**, $a \sim 20\text{--}30$).

Our initial studies on [22.10]betweenanene (**54**) and its *cis* isomer **53** indicate that both undergo slow epoxidation (Scheme VI, A, B = O) and hydroboration-oxidation (Scheme VI, A, B = H, OH).³⁰ However, reaction of **54** with isopinocampheylborane could not be effected even with a large excess of the reagent and prolonged reaction times. Furthermore, only the *cis* isomer **53** afforded a colored charge-transfer complex with TCNE.³⁰ Thus, the double bond of **54** appears to be shielded from sterically demanding reagents.

Conclusions

In this Account we have described some fundamental characteristics of mono- and bicyclic *trans*-cycloalkenes. We have pointed out the profound influence of bridging chains on reactions leading to and from these cycloalkenes and the resultant special considerations which must be accorded to their synthesis. The bicyclics ex-

amined to date show no unusual behavior save for the unreactivity of the encapsulated betweenanene double bond. This is in keeping with expectations based on molecular models and known cycloalkene chemistry. In that context, we might expect betweenanenes with rings of eight or fewer members to be fairly strained and to act accordingly.

The synthetic challenges of betweenanenes largely stem from the tetrasubstituted double bond. As noted above, the bridging chains limit the choice of synthetic approach that can be employed. While photoisomerization has proven extremely valuable for generating the betweenanene system from accessible bicyclic olefin precursors, some of the more interesting betweenanenes will require the development of additional new synthetic approaches to tetrasubstituted cycloalkenes. Targets of immediate interest include (1) optically active betweenanenes, (2) ring-chain functionalized betweenanenes, and (3) polycyclic (stacked) betweenanenes.

Finally, it should be noted that a number of biologically interesting natural products contain *trans*-cycloalkene rings.³⁵ The biological activity of such substances is undoubtedly influenced by ring-bridging effects of the type discussed in this Account. In fact, it is possible that *in vivo* transformations of these natural products may proceed via betweenanene-like intermediates. In this way the double bond would be shielded from external influences and could become more vulnerable to internal attack from groups on the bridging chains or from bridging enzyme functionality.

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Allylic and Propargylic Imidic Esters in Organic Synthesis

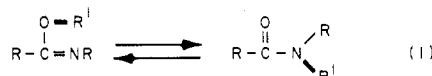
LARRY E. OVERMAN

Department of Chemistry, University of California, Irvine, California 92717

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The imidic acid-amide interconversion (eq 1, $\text{R}^1 = \text{H}$) played an important role in the evolution of modern

Larry E. Overman was born in Chicago, IL, in 1943. He earned a B.A. degree from Earlham College and completed his doctoral study in 1969 with Howard W. Whitlock, Jr., at the University of Wisconsin. After an NIH post-doctoral fellowship with Ronald Breslow at Columbia University, he joined the faculty at the University of California, Irvine, in 1971, where he is now Professor of Chemistry. He has been a Fellow of the A. P. Sloan Foundation and a recipient of a Camille and Henry Dreyfus Teacher-Scholar award.



concepts of molecular structure and tautomerization. Baeyer in 1882,¹ as part of his classic investigations of indigo, was the first² to correctly formulate the concept

(1) Baeyer, A.; Oekonomides, S. *Chem. Ber.* 1882, 15, 2093.