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

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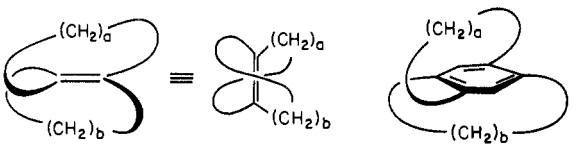
"[*a.b*]Betweenanene" is a descriptive name for a novel class of compounds in which a pair of *trans*-cycloalkenes shares a common tetrasubstituted double bond.[1] This

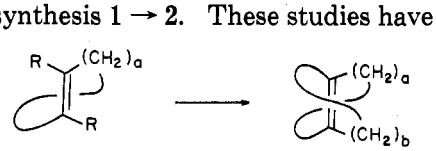


[a.b.] betweenanene [a][b] paracyclophane

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*]paracylophanes.[2]

We became interested in betweenanenes in 1966 while developing new methodology for the synthesis of *trans*-cyclodecenes.[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]betweeenanene 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



1 **2**

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]

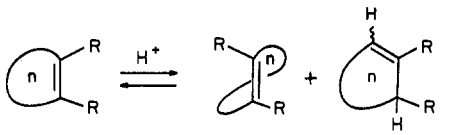
trans-Cycloalkenes

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 thereafter Ziegler and Wilms recognized that the "more reactive form" of cyclooctene must possess a trans double bond.[8] Subsequent work by Blomquist[9] and Cope[10] 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.

Table I
Acid Catalyzed Isomerization of Cycloalkenes

n	R, R	*K* cis/trans	*n*	R, R	*K* 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			

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



3 **4** **5**

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*-

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(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.

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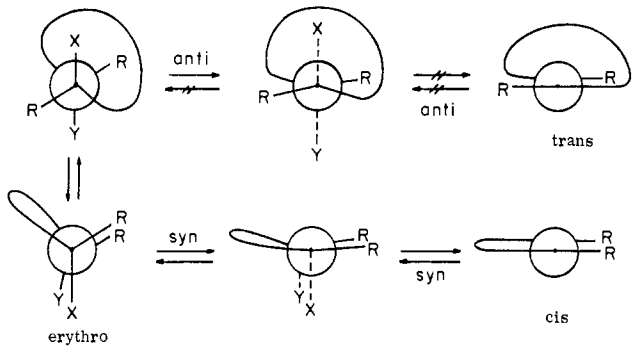


Figure 1. Elimination/additions involving *erythro*-cycloalkane systems.

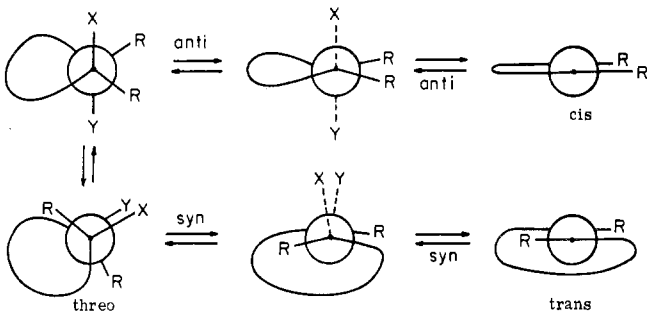


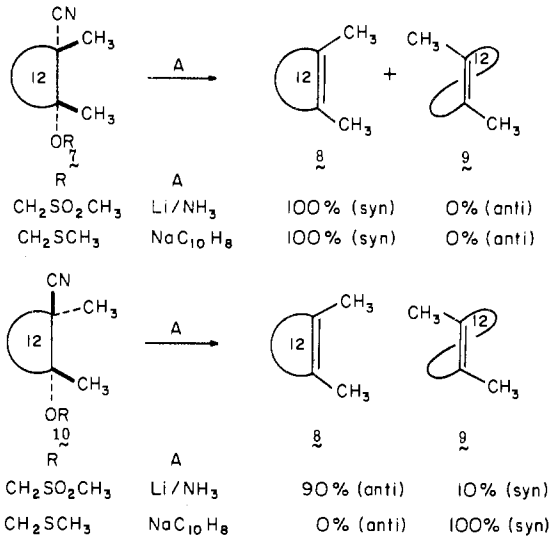
Figure 2. Elimination/additions involving *threo*-cycloalkane systems.

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/NH_3 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 = $Me_2N\rightarrow O$).[14]

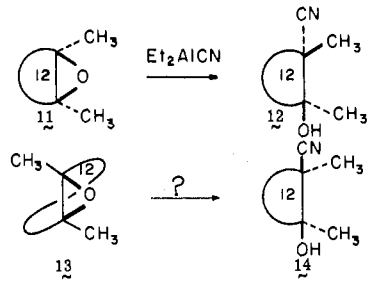
Epoxides and cyclopropanes should also be subject to ring-chain steric control since they are geometrically similar to alkenes. Thus, while the *cis*-epoxide **11** affords the *threo*-cyanohydrin **12** (cis/anti/threo) upon treatment with diethylaluminum cyanide,[13] the trans isomer **13** would be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

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

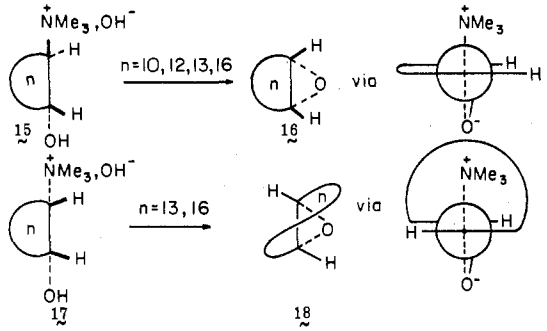
(13) Marshall, J. A.; Karas, L. J.; Royce, R. D., Jr. *J. Org. Chem.* **1979**, *44*, 2994–99. See footnote 7.

(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-cyclononenone.[9] Cope resolved *trans*-cyclooctene[16] 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*-cyclooctene[16] but falls off rapidly for

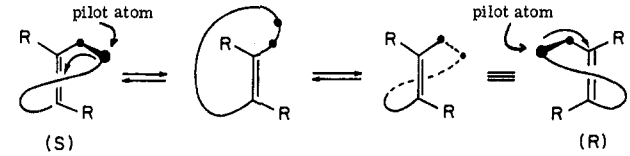
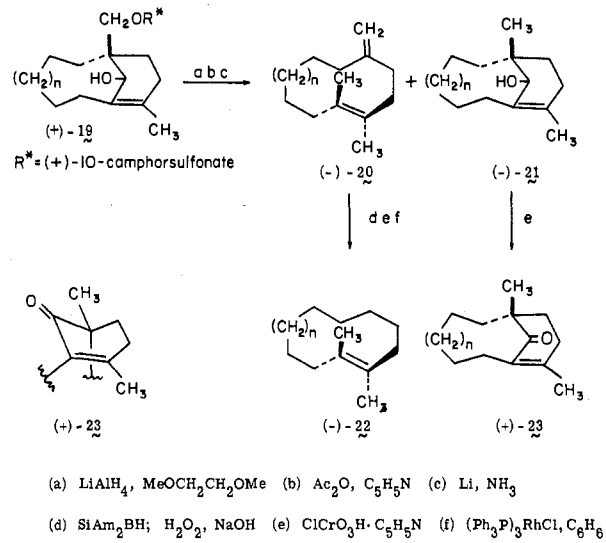


Figure 3. Chirality designation and racemization in *trans*-cycloalkenes.

Chart I
Synthesis of Optically Active *trans*-Cycloalkenes



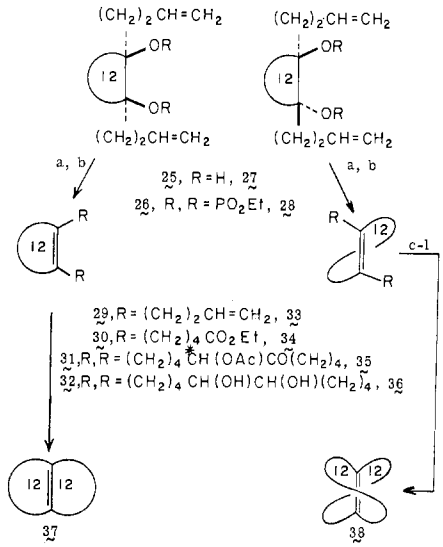
trans-cyclononene and higher homologues.[18] Efforts to isolate optically active *trans*-cyclodecenes have not succeeded.[19] The R/ring-chain interaction responsible for the aforementioned rotational barrier may also influence the ease of anti-periplanar internal reactions (double constraint processes) 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** ($n = 1, 2$; R* = 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 **19**[20] (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, $[\alpha]^{22}_D$

(15) Svoboda, M.; Sicher, 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: Sicher, 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.
(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.

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; Cl_2PO_2Et (b) Li, NH_3 (c) Sia_2BH; H_2O_2, NaOH (d) TsCl, C_5H_5N (e) NaCN (f) KOH; HCl, EtOH (g) Na-K, xylene, Me_3SiCl (h) n-Bu_4NF, THF (i) Ac_2O, C_5H_5N (j) $LiAlH_4$; H_2O, NaOH (k) n-BuLi; Cl_2PONMe_2 (l) H_2/Pt

+14.9°) was optically active.[20] However, the recovered dimethylcyclododecene showed no rotation. Analogous treatment of *trans*-1,2-dimethylcyclodecene afforded optically active recovered olefin **22** (n = 1) in 33% yield ($[\alpha]^{22}_D$ −18°).[20] Thus it would appear that *trans*-1,2-dimethylcyclododecene 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 cyclododecene (Chart IV).

Betweenanene Nomenclature

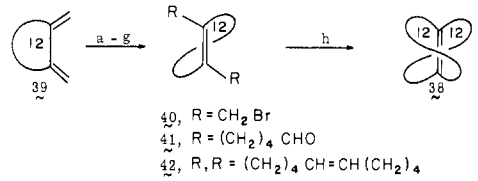
As noted in the introduction, our semisystematic nomenclature system for bicyclic bridged alkenes such as **2** emphasizes the sandwich relationship between the outside bridging chains and the inside double bond. Of course, conventional IUPAC nomenclature employing the Baeyer convention for bridged ring systems[23] 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 (CH_2'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.

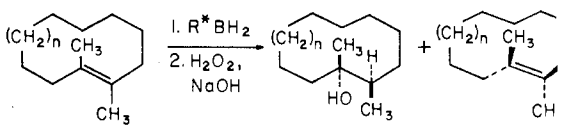
Chart III
Chung [10.10]Betweenanene Synthesis



40, R = CH_2 Br
41, R = $(CH_2)_4$ CHO
42, R, R = $(CH_2)_4$ CH=CH $(CH_2)_4$

(a) Br_2 (b) CH_2=$CHCH_2MgCl$ (c) R_2BH; H_2O_2, NaOH (d) p-TsCl, C_5H_5N (e) NaCN (f) $(i\text{-}Bu)_2AlH$; H_3O^+ (g) $TiCl_3$/Zn(Cu) (h) H_2/Pt

Scheme IV
Kinetic Resolution of *trans*-Cycloalkenes



n = 1, n = 3 (+)-24 (−)-22
R* = Isopinocampheyl

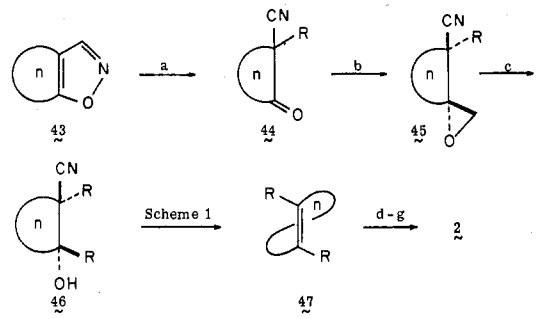
We therefore concentrated on methods for preparing substituted *trans*-cycloalkenes of defined structure which could be directly cyclized (1 → 2). Several variations of this general approach were eventually completed. The first of these (Chart II) utilized the cyclic phosphate derivative **28** of the 1,2-cyclododecanediol **27**. Stereoselective syn elimination to the *trans*-cycloalkene **33** was effected using Li/NH_3.[1,23] Attempts at ring closure of the derived diester [i.e., **33**, R = $(CH_2)_3CO_2Et$] 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-acetoxyl 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)cyclododecene (**40**) secured through bromination of 1,2-dimethylenecyclododecane (Chart III).[26] Coupling with allylmagnesium chloride followed by homologation yielded the dialdehyde **41**. This was cyclized with reduced $TiCl_3$ 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 = $(CH_2)_aCH{=}CH_2$; n = 11, 12



(a) KO-t-Bu; RBr (b) $CH_2=S(CH_3)_2$ (c) R'Li (d) Sia_2BH; H_2O_2, NaOH (e) $ClCrO_3H \cdot C_5H_5N$ (f) $TiCl_3/Zn(Cu)$ (g) H_2/Pt

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

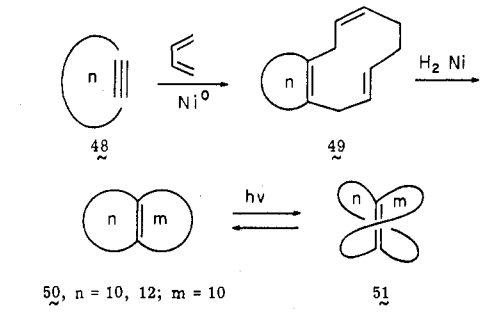


Table II
Photoisomerization of Bridged Bicycloalkenes

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]

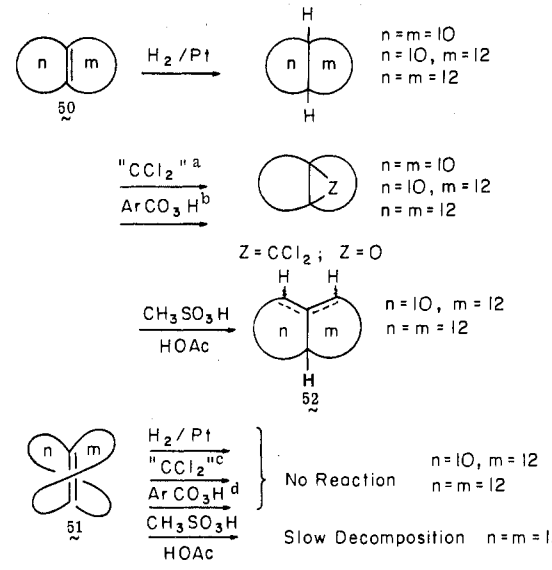
betweenanenes (Chart IV).

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 similarities in spectral properties and chromatographic behavior led us to initially conclude[32] 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-dimethylcyclododecene (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]

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

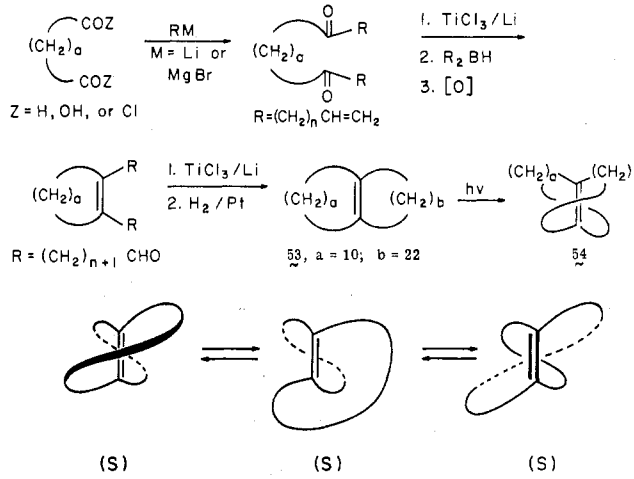


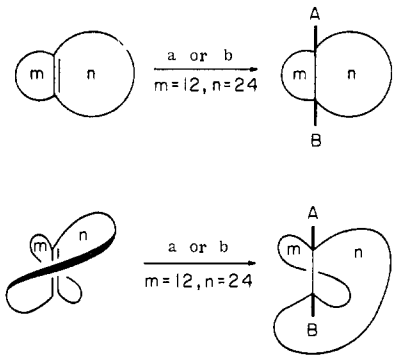
Figure 4. Conformational flexibility in jump rope betweenanenes.

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-$ClC_6H_4CO_3H$ (b) $BH_3 \cdot THF$; H_2O_2, 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**, $a \sim 20$–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 examined 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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(35) E.g., Macrolides: Masamune, S.; Bates, G. S.; Corcoran, J. W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 585–90. Cembranolides: Weinheimer, A. J.; Chang, C. W. J.; Matson, J. A. *Fortschr. Chem. Org. Naturst.* **1979**, *36*, 286–387. Germacranolides: Yoshioka, H.; Mabry, T. J.; Timmerman, B. N. "Sesquiterpene Lactones"; University of Tokyo Press: Tokyo, 1973; pp 7–22. Ansamycin antibiotics: Kupchan, S. M.; et al. *J. Am. Chem. Soc.* **1972**, *94*, 1354–5. Rinehart, K. L., Jr.; et al. *Ibid.* **1971**, *93*, 6273–4.

Allylic and Propargylic Imidic Esters in Organic Synthesis

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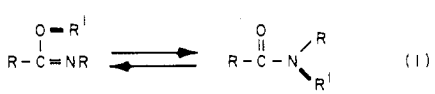
The imidic acid–amide interconversion (eq 1, R^1 = H) played an important role in the evolution of modern



(1)

concepts of molecular structure and tautomerization. Baeyer in 1882,[1] as part of his classic investigations of indigo, was the first[2] to correctly formulate the concept

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

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