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Strained Bridgehead Double Bonds

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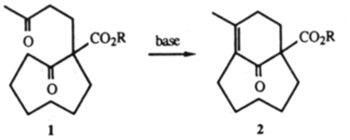
Philip M. Warner, Professor and Chair of the Chemistry Department at Northeastern University, was born in New York City in 1946. Following degrees at Columbia (B.A., 1966) and UCLA (Ph.D., 1970), he was an NSF Postdoctoral Fellow at Yale (1970–1971) and a member of the faculty at Iowa State University (1971–1988). His current research emphases are the study of strained-ring compounds, carbenes, carbenoids, and organolithium species. His hobbies include collecting, tennis, and traveling.

I. Introduction

The study of strained-ring compounds has a long and glorious history in organic chemistry. Distortions of σ bonds, as typified by cyclopropane, were of earliest concern and are discussed in a companion article in this issue of *Chemical Reviews*. It was not until the work of J. Bredt in the early part of this century that the twisting distortion of π bonds was given serious attention. Although his conclusions were aimed at bicyclic skeletons of the camphane and pinene series,[1] “Bredt’s Rules” came to imply a complete prohibition of bridgehead double bonds. To this day, bridgehead alkenes are often referred to as Bredt’s Rule violators.

Of course, bridgehead double bonds are readily accommodated in larger ring systems; many such alkenes actually have lower heats of hydrogenation than cyclohexene (they may resist hydrogenation[3]) and have been dubbed “hyperstable”.[2-4] By 1950, Prelog[5] had found that **1** could be condensed to **2**, thereby establishing the isolability of a Bredt’s Rule violator. The fact that a similar bicyclo[4.3.1] product could not be isolated led to the assumption that it and smaller ring systems could not feature a bridgehead double bond. In his 1950 review,[6] Fawcett introduced the concept of S numbers ($S = a + b + c + 1$ in **3**) and proposed that if $S \leq 8$, the bridgehead alkene would be too unstable to isolate.



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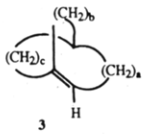

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In 1967, Wiseman[7] and Marshall[8] independently reported the preparation of **4**, a stable, albeit reactive, olefin, for which $S = 7$. The conceptual breakthrough, mainly due to Wiseman,[9] was to note that all bridgehead double bonds are endocyclic in two rings [in **3**, that containing ($a + b + 3$) carbons and ($a + c + 3$) carbons, but not that with ($b + c + 2$) carbons] and as such must be cisoid in one [the ($a + b + 3$)-membered ring of **3**] and transoid in the other [the ($a + c + 3$)-membered ring of **3**]. Wiseman noted that when the transoid (normally larger) ring had ≥8 carbons (as is the case for **4**), the bridgehead alkene should be stable and comparable in strain energy to the *trans*-cycloalkene to which the transoid ring corresponds (e.g., **5**). Wiseman’s

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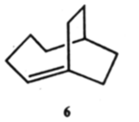

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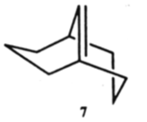

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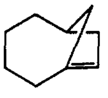
revelations, later borne out by experiments, as well as calculations,[10,11] invalidated the S number concept (**4** and **6**[12] should have similar stability, although for **4**, $S = 7$, and for **6**, $S = 8$; more importantly, S numbers do not distinguish between **4** and the much more strained **7**), but problems still remained. For example, how might one qualitatively understand the greater stability of **8** relative to **9**,[13] or **10** relative to **11**,[14] or how may one compare **4**, **6**, and **8**–**11**, all of which are *trans*-cyclooctene (**5**) derivatives? As we will see, the answer is that qualitative rules in response to these questions are unavailable.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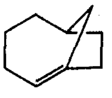
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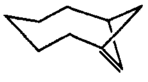
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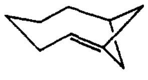
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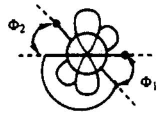
A. Structure of Bridgehead Double Bonds

Apart from conformational effects in flexible bicyclic systems which are mainly controlled by torsional strain factors, the key structural concern revolves around distortions at the π bond itself. These distortions are essentially the same as those suffered by *trans*-cycloalkenes. As recognized first by Allinger,[15] but enunciated most clearly by Mock,[16] the loss of π bonding due to twisting is partially recovered by rehybridization of the π centers, the consequence of which is pyramidalization (cf. **12** → **13**). In **12**, where only twisting has occurred, there is only one twist angle, Φ (i.e., $\Phi_1 \equiv \Phi_2$). But after possibly different degrees of rehybridization in an unsymmetrical molecule, two twist angles may emerge. Thus it may be better to discuss a twist angle, θ, between the hybrid π-bonding orbitals. Additionally, the degree of rehybridization is related to χ_1 and χ_2, the out-of-plane bending angles. Rehybridization may also be defined by a pyramidalization angle, ω (see **14**), defined as the angle between the axis of the π-bonding hybrid orbital and any of the three bonds to the carbon in question, less 90°. For an sp^3 hybrid, $\omega = 19.5°$.



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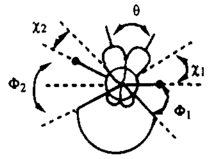

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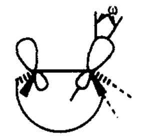

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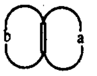
In the case of *trans*-cycloocten-3-ol 3′,5′-dinitrobenzoate, X-ray data[17] reveal $\Phi_1 = 22°$, $\Phi_2 = 15°$, $\chi_1 = 20°$, $\chi_2 = 28°$, dihedral angle $C_3C_2C_1C_8 = 137°$, and dihedral angle $H_1C_1C_2H_2 = 174°$, which demonstrates that both C_1 and C_2 are cis pyramidalized. Ermer has calculated twisting and bending distortion energies for many bridgehead alkenes using a force-field approach. This work has now appeared as a book,[18] although the utility of these partitioned distortion energies per se is unclear. It seems that the olefinic strain (OS) approach[10] is more useful, albeit not in all cases.

B. Scope of This Review

A number of reviews[19-23] of bridgehead alkene chemistry have appeared, the most recent (and broad-based) one in 1983. This review will cover the material that has appeared since then (or was not covered then) up to mid-1988, subject to the conditions given below.

1. *Definition of "Bridgehead Double Bond"*

As recognized by Szeimies,[23] a bridged bicyclic compound may contain a zero-atom bridge. Therefore, three types of bridghead alkenes may be defined: type A (**15**), type B (**16**), and type C (**17**). Type A, in which both carbons of the π bond are at bridgeheads, normally does not contain a twisted bridgehead double bond *in simple systems* (see, however, **27**). As discussed in the next section, further bridging can generate polycycles that are at once more than one type of bridgehead alkene.



15
Type A

16
Type B

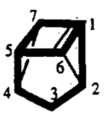
17
Type C

2. *What Is Not Included*

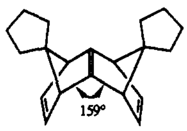
Type A bridgehead double bonds are not discussed. This omits important work on bicyclopropenes (**18**),[24,25] **19**,[23] and **20**[23] (but these are covered in another article in this issue) and Δ-1,4-bicyclo[2.2.0]hexene.[26] As shown by the heavy lines, **19** is both a type A and type B bridgehead olefin, while **20** actually qualifies as a type A, B, or C. We also omit discussion of other untwisted, but pyramidalized bridgehead olefins such as the *syn*- and *anti*-sesquinorbornenes[27] (e.g., **21**[28] and **22**, respectively), **23**[29] and **24**[30] (which are type A like, but really only type C), **25**,[31] and **26** (cubene);[32] these are discussed in a separate article in this issue.[33] Nor do we deal with betweenanenes (**27**),[34-36] doubly bridged alkenes[37] (betweenallenes[38]) (**28**), or doubly bridged cumulenes (**29**),[39] since the known cases really are not strained;[40] some of these will also be covered separately in this issue.

18
Type A

19
Type A, B



20
Type A, B, C



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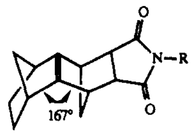
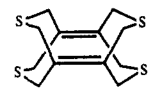
Type A



22
Type A


23
Type C



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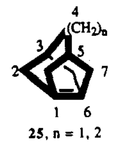
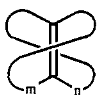
Type C

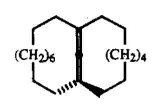


25, n = 1, 2
Type A, C

26
Type A, B, C



27
Type A



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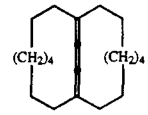
Type C



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Type C

Type B bridgehead double bonds are also not discussed. This excludes such recent cases as **30**,[41] **31**,[42] **32**,[43] **33**,[44] and **34**.[45]


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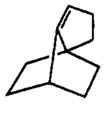
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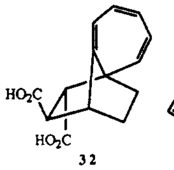

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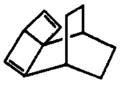
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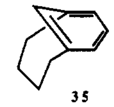
Among type C bridgehead double bonds, we omit consideration of meta- (e.g., **35**[46]) and paracyclophanes (e.g., **36**[47]); these are to be covered separately in this issue and have also been recently reviewed.[48] We also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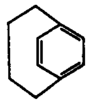
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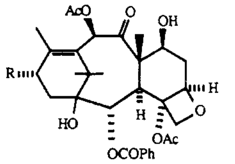
do not cover bridged double bonds that are transoid in 10-membered or larger rings. The reason is that such double bonds are not strained; indeed they tend to be hyperstable.[2,10] This excludes consideration of bridged-annulene chemistry, naturally occurring bridgehead double bonds such as found in taxol (**37**), the antitumor compound that is the object of several synthetic approaches,[48,50] or medium-ring syntheses via bridgehead alkenes (e.g., via **38**[51]).



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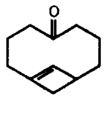
R = OCCH(OH)CH(Ph)NHCPh (with C=O on both acyl carbons)

$R = O\overset{}{\underset{\|}{\underset{O}{C}}}CH(OH)CH(Ph)NH\underset{\|}{\underset{O}{C}}Ph$



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3. What Is Included

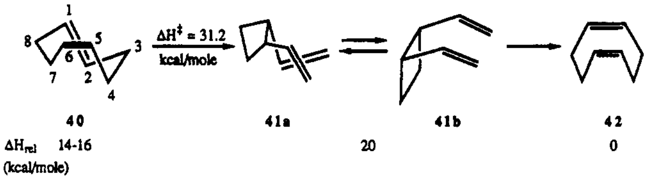
Due to the close analogy between bridgehead double bonds and *trans*-cycloalkenes, we begin with a survey of the latter class of compounds. We then discuss the post-Szeimies-review[23] material on bridgehead double bonds transoid in rings of nine or fewer atoms, including compounds with two bridgehead double bonds. Lastly, results on bridgehead imines (**39**) are also covered.

II. trans-Cycloalkenes

The concept of "strain energy"[52] (SE) has been very useful to organic chemists. For example, the statement that cyclopropane contains 28 kcal/mol in strain energy allows one's mind to focus on the energetic cost of forming a small ring and to assess how much energy the cleavage of such a ring could provide. But the concept is less useful in discussing twisted double bonds because the unstrained model that one must use to calculate the straing energy (an acyclic alkene) is normally not relevant to the chemistry of the twisted system. Thus Schleyer[10] introduced the concept of "olefinic strain" (OS), which is the *difference* in strain energy between an alkene and its corresponding alkane hydrogenation product. With this definition, the OS value gives an immediate picture of how much extra strain the introduction of a double bond induces.

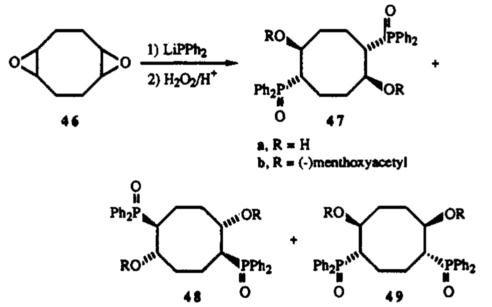
For the medium-ring *cis*-cycloalkenes of 7–10 carbons, the OS values are all negative, indicating a strain decrease upon double-bond introduction. *trans*-Cyclodecene also has a negative OS (=–2.6 kcal/mol) value, while that for *trans*-cyclononene is zero. *trans*-Cyclooctene has OS = 5.5 kcal/mol [OS(calcd) = 6.3 kcal/mol], while *trans*-cycloheptene is considerably more strained [OS(calcd) = 19.6 kcal/mol]. That extra strain shows up structurally in extra (calculated) deformation (compared to *trans*-cyclooctene: angle $H_1C_1C_2H_2$ = 166° (vs 174°) and angle $C_3C_1C_2C_7$ = 125° (vs 137°).[15b]

The cyclooctadienes provide an interesting series of compounds, and some of these have been studied. (*E*,*Z*)-1,5-Cyclooctadiene (**40**) isomerizes to (*Z*,*Z*)-1,5-cyclooctadiene (**42**) at ~150 °C via a Cope sequence.[53]

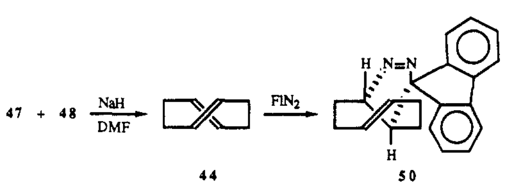


The difference in energy, and hence strain energy, between **40** and **42** was found to be 14–16 kcal/mol (force-field calculated difference = 15 kcal/mol). Since the OS value for **42** is 2 kcal/mol (1 kcal/mol per π bond), an OS value of 16–18 kcal/mol for **40** is computed. If the *Z* double bond of **40** is no more strained than the corresponding one of **42**, then the *E* double bond would have an OS value (15–17 kcal/mol) very similar to *trans*-cycloheptene's. However, the calculated $C_3C_2C_1C_8$ dihedral angle of 136° is more consistent with a *trans*-cyclooctenoid than a *trans*-cycloheptenoid double bond. Thus perhaps the cis double bond of **40** is much more strained than its counterpart in **42**.

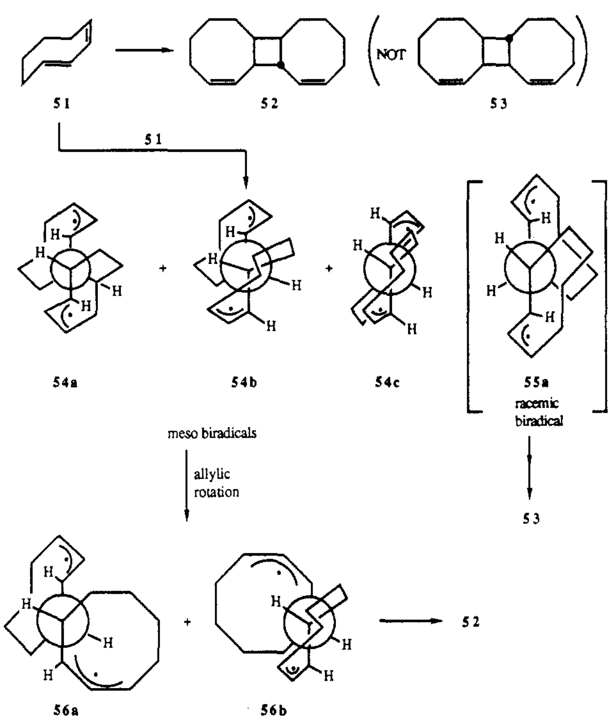
(*E*,*E*)-1,5-Cyclooctadiene has just one type of double bond but may exist in two forms: the meso conformer, **43**, or the racemic conformer, **44**; the two cannot interconvert due to the structural constraints of the system. Allinger's force-field calculations[15b] favor **44** (OS = 5.6 kcal/mol per π bond) over **43** (OS = 8.3 kcal/mol per π bond). Originally,[54] **44** was assumed to be present on the basis of the photochemical formation of **45**. Recently,[55] Huisgen systematically approached **43** and **44** from **46**. S_N2 opening/oxidation of **46** gave enantiomers **47a** and **48a** of C_2 symmetry and regio-



isomer **49a** of C_s symmetry. The mixture of **47a** and **48a** was converted to the separable esters **47b** and **48b** (both with C_2 symmetry), whereas **49a** gave only one ester, **49b**, of no symmetry. Upon base-induced cis elimination, **47** and **48** must give **44**, while **49** is predestined to give **43**. In the event, **47** and **48** gave a single diene, whereas **49** gave no volatile alkene(s). Further evidence that **44** was indeed formed came from the X-ray structure of the diazofluorene adduct, **50**, which showed the twist configurational arrangement required for **44**. However, it must be said that **43** could give **50** via cycloaddition, followed by "jump rope" rotation[56] (which, while activated, could occur within the framework of how **50** was synthesized and handled), although the totality of the work strongly implicates **44**. Compound **50**, itself a *trans*-cyclooctene, showed structural parameters very close to those of *trans*-cycloocten-3-ol 3′,5′-dinitrobenzoate.[17]

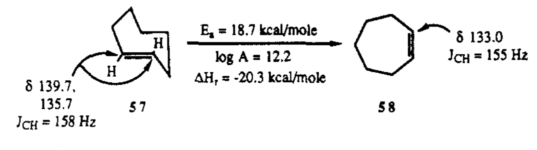


The dimerization of (*Z*,*E*)-1,3-cyclooctadiene (**51**) has been reinvestigated by Wiseman,[57] and the major dimer reassigned as **52** (not **53**). In line with some,[23,58] but not all,[59] of the observed bridgehead alkene dimerizations and several dimerizations of *trans*-cyclooctenones and -heptenones,[60] a stepwise diradical mechanism was proposed. The argument is that there are two distinctly different dimerization modes: (a) two optical antipodes of **51** may join, whereby meso biradicals **54a–c** may be formed (shown in their transoid conformations), and (b) two like enantiomers may become bonded to produce racemic biradicals such as **55a**. Clearly **54a** (and, to a lesser extent, **54b**) is the sterically least hindered biradical (and also the one expected on a least motion basis) but suffers the most in terms of having a double *trans*-allylic structure in the eight-membered rings. Thus allylic isomerization to **56a** (or **54b** to **56b**) would require considerably less activation than the 15 kcal/mol normally associated with radical conjugation. Rotation and closure of **56a** and/or **56b** would afford **52**.

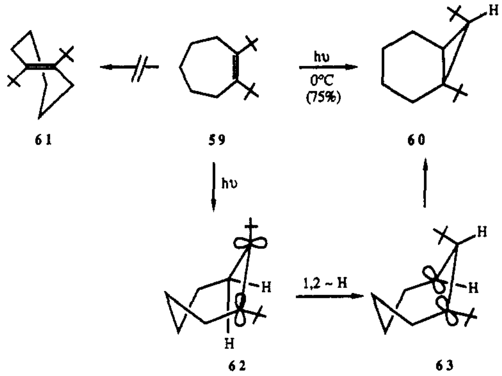


It is important to note that cleavage of **56a,b** would still re-form one molecule of **51** and is, therefore, inhibited. The more hindered racemic biradical (e.g., **55a**) would give **53** after allylic rotation, followed by ring closure. In any event, it appears that various combinations of stereoisomeric biradical processes serve better to explain dimer formation from strained alkenes, relative to postulating ${}_{\pi}2_{s} + {}_{\pi}2_{a}$ processes.

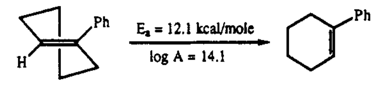
(*E*)-Cycloheptene[61] (**57**) and its 3-methoxy derivative[62] are known (as are conjugated derivatives[60]) and are stabilized by metal complexation.[63,64] The metal-catalyzed cyclotrimerization of **57** has been described by Mackor.[65] Inoue showed that (*E*)-cycloheptene alone is stable at −78 °C but isomerizes to (*Z*)-cycloheptene (**58**) around 0 °C.[66] The measured[66] activation energy, combined with the calculated heats of formation,[15b] means that the isomerization transition state is only 39 kcal/mol above **58**, which contains an ordinary π bond. Thus the transition state cannot correspond to a perpendicular (90° twisted) alkene! Recently, the ^{13}C NMR spectrum of **57** has been observed[67] to consist of seven lines, which is appropriate for the unsymmetrical chair conformation shown. The carbon–hydrogen coupling constant is not indicative of significant rehybridization, however. This suggests that said coupling is not an adequately sensitive measure for detecting small hybridization changes.



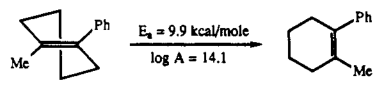
Jendralla's attempt[68] to generate a (perhaps stable) tetrasubstituted *trans*-cycloheptene (**61**) was unsuccessful when **59** photoisomerized solely to **60**. This reverse of the cyclopropane to propene rearrangement may be understood by noting that 1,2-H migration from **62** to **63** must occur on the exo face, thereby producing the less stable endo isomer, **60**.



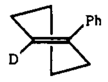
Bonneau and Dauben have generated (*E*)-1-phenylcyclohexene (**64**) from the *Z* isomer, **65**.[69] Laser flash techniques[70] have provided the activation parameters shown below.[71] The lowering of the rotational barrier on tetrasubstitution (**66** → **67**) must be a transition-state effect. More interestingly, deuterium substitution as in **68** or **69** leads to an unprecedentedly large secondary isotope effect of 2.0 at room temperature. Temperature-dependent studies on **69** led Dewar to the conclusion that tunneling was not a major factor, but rather loss of the out-of-plane bending mode at the transition state produced a "quasi-primary" isotope effect.[71]



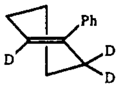
64 **65**



66 **67**

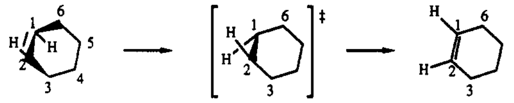


68



69

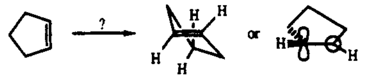
The existence of (*E*)-cyclohexene (**70**) itself has been postulated on the basis of photoadditions to (*Z*)-cyclohexene (**71**),[72] particularly ionic addition of MeOH.[73]



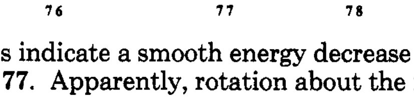
	70	**72**	**71**
∢ $C_3C_2C_1C_6$	81°	54°	1°
∢ $H_1C_1C_2H_2$	177°	135°	2°
rC_1C_2	1.421Å	1.504Å	1.343Å
E_{rel} (kcal/mole)	56	71	0
birad. char.	30%	90%	10%

But **70** has never been observed, and Schleyer's calculations indicated it was not an energy minimum.[74] Recent two-configuration GVB calculations with a 6-31G* basis set (plus CI through singles and doubles in the GVB space) by van Lenthe gave the energies and geometries shown.[75] The transition state, **72**, almost certainly lies too high in energy above **71**, but the lack of corrections for zero-point energy and the use of minimal basis set geometries may be responsible. The calculated strain energy of **70** (56 kcal/mol) is considerably above the 42 kcal/mol estimated via MM1[15b] (admittedly not optimized for geometries such as in **70**). Interestingly, the π orbitals of **72** are calculated to be orthogonal. We note that the observed E_a for the isomerization of **64** is very close to that calculated for **70**; certainly the SE's of **70** and **64** must be almost identical.

Finally, what about (*E*)-cyclopentene (**74**)? On the basis of nonionic photoadditions to (*Z*)-cyclopentene (**73**), it was concluded that either **74** was photochemically inaccessible or **74** was a biradical (**75**).[73] Wiberg[76] has reported that **76** isomerizes to cyclopentadiene (**78**) at −50 °C via a retrocarbene addition to **77** (**77** was calculated to lie 33 kcal/mol below **76**!). But as clearly shown for **76**, the hydrogens at C_1 and C_2 are trans, and concerted retrocarbene addition should produce a carbene related to **74**. Wiberg has informed us[77] that



73 **74** **75**



76 **77** **78**

calculations indicate a smooth energy decrease on going from **76** to **77**. Apparently, rotation about the incipient double bond is concomitant with bond breaking, and the trans carbene isomer of **77** may, at best, correspond to a point on the energy surface, perhaps a transition state (TS).

III. Bridgehead Double Bonds

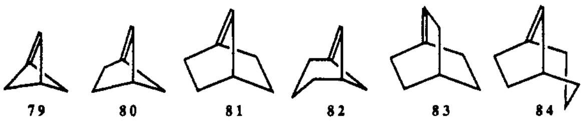
A. General

In this section are found some brief comments on theoretical developments, followed by a section summarizing the synthetic approaches that have been used to make bridgehead double bonds. The subsequent sections on specific compounds are organized according to ring size in which the bridgehead double bond is transoid.

1. Theory

Two papers devoted to bridgehead monoenes,[10,11] one to bridgehead dienes,[78] and a book[18] that covers a large variety of species have been published in the 1980s. All report the results of force-field calculations[79] (additional like calculations are occasionally found in experimental papers); ab initio calculations do not yet appear to have been carried out on these systems.

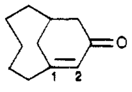
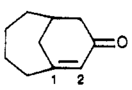
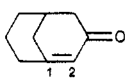
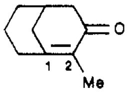
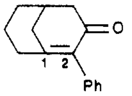
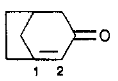
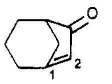
For the most part, ab initio results are unnecessary. But for some cases, they are clearly desirable. For instance, Schleyer[10] has calculated an OS = 21 kcal/mol for **79**, a compound that is *trans*-cyclobutenoid. This implies low-temperature stability for **79** (OS ≤ 17 kcal/mol means isolable at ambient temperature; 17 < OS < 21 kcal/mol means observable at ≥−78 °C; OS > 21 kcal/mol means too unstable to observe except perhaps in a matrix), which is surprising in that *trans*-cyclobutene is certainly not an energy minimum. But admittedly[10] the MM1 force field was not parametrized to handle **79**, so the result may be unreliable. This is made more likely by the OS values calculated for *trans*-cyclopentenoids **80** and **81** and *trans*-cyclohexenoids **82**–**84**. Of **79**–**84**, experimental evidence is available only for **83** and a derivative of **81** (vide infra); but since they have not been *observed*, detailed ab initio calculations would be valuable.



	79	**80**	**81**	**82**	**83**	**84**
OS (calc) kcal/mole	21	33	39	39	40	37

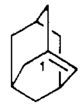
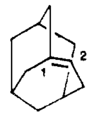
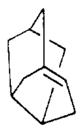
Besides strain energies, structural deformations have been studied theoretically. House has included MMP1-generated values of Φ_{av}, χ_1, and χ_2 (see **13**) for some enones as part of his experimental (vide infra) papers.[80–82] As shown in Table I, the twisting and pyramidalization angles increase inversely with ring size, as expected. Note that despite the greater deformation at the bridgehead double bond, each [3.3.1] system studied (**87**–**89**) is predicted to prefer the chair geometry (of course, the calculations do not take into account any conjugative substituent effects; these, however, apparently influence the observed chemistry; vide infra). While the calculated pyramidalizations, in these cases, are greater at the bridgehead carbon (C_1) than the attached olefinic carbon (C_2), it is the (unsymmetrical) bending of the nonring substituent at C_2 that does the most to restore π bonding lost from twisting.

TABLE I. Calculated (MMP1) Deformations for Some Enones[80,81]

compd	av twisting about C=C (Φ_{av}), deg	pyramidalization, deg	
		at C_2 (χ_2)	at C_1 (χ_1)
 **85**	4	1	9
 **86**	14	14	21
 **87**			
twist boat	21	19	37
chair[a]	25	25	42
 **88**			
twist boat	22	18	34
chair[a]	27	23	40
 **89**			
twist boat	21	13	38
chair[a]	27	17	44
 **90**	36	29	60
 **91**	36	36	62

[a] The more stable conformation overall.

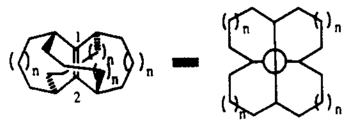
TABLE II. Calculated (MNDO) Deformations for Some Bridgehead Alkenes[83a]

compd	twist angle (θ), deg	pyramidalization, deg	
		at C_1 (ω)	at C_2 (ω')
 **92**	64	13	8
 **93**	44	9	6
 **94**	44	11	6

Michl[83a] has explicitly recognized this point for adamantene (**92**) and related cases (Table II). MNDO calculations give a θ of only 64° for **92**, despite the 80° twist angle of the heavy-atom skeleton: the difference is due to bending of the hydrogen at C_2. It is thus clear that no trisubstituted bridgehead double bond can have an orthogonal twist angle. Further structural restrictions would be required.

Along the same lines, Ermer[18] has calculated (force field) the inversion barrier for a series of bridgehead alkenes (Table III), where the presumed transition state[84] is the orthogonal alkene. Even the *trans*-cyclopentenoid **81** is calculated to have a substantial barrier to orthogonalization, an inescapable conclusion irrespective of the shortcomings of the force-field approach.

A serious candidate for an orthogonal double bond is the "fixed-betweenanene" **96**,[18] dubbed an "orthogonene" by Maier.[85] For **96a**, MNDO with 2 × 2 or 3 × 3 CI predicts a lower energy for the orthogonal than any twisted form of the alkene.[85b] Some preliminary efforts toward orthogonene synthesis have appeared.[85a]



96 a, n = 0
b, n = 1

2. Synthetic Approaches

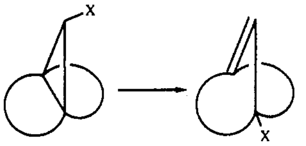
There have been some six widely used methodologies applied to the synthesis of bridgehead double bonds; all have been mentioned in previous reviews, or are detailed later:

(*a*) *1,2-Eliminations*

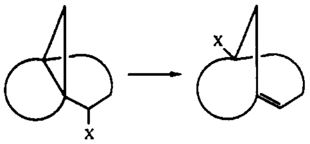
97 98 (1)

e.g.: X = OAc, Hal, $\overset{+}{N}Me_3$, Y = H
X = Hal, Y = Hal; X = $SiMe_2H$, Y = OH
X,Y = $-\underset{\underset{XN}{\|}}{N}-\underset{\underset{O}{\|}}{C}-O-$ (cycloelimination)

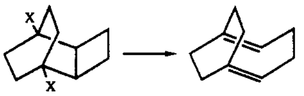
(*b*) *Ring Openings*



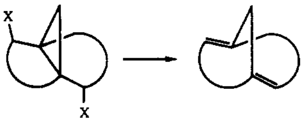
99 100 (2)



101 102 (3)



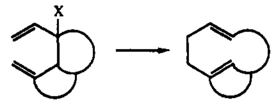
103 104 (4)



105 106 (5)

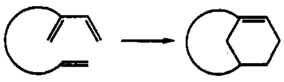
(c) *Ring Closings (Cyclizations)*

107 **108** (6)



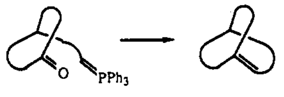
109 **110** (7)

X = H, OR



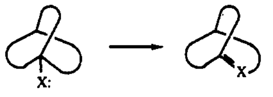
111 **112** (8)

113 **114** (9)



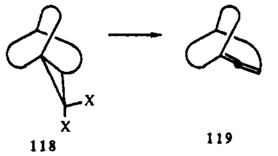
115 **98** (10)

(d) *Ring Expansions*



116 **117** (11)

X = C, N

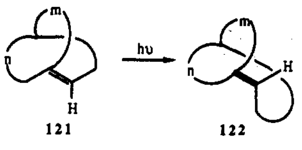


118 **119** (12)

(e) *Ring Contractions*

120 **98** (13)

(f) *Photoisomerization*



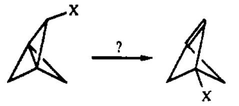
121 **122** (14)

TABLE III. Calculated[a] Barriers to Orthogonality for Some Bridgehead Alkenes[18]

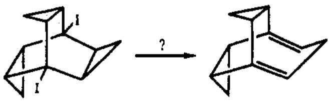
compd	parameters for the ground state,[b] deg			parameters for the orthogonal TS,[b] deg			$\Delta H^{\ddagger}$,[c] kcal/mol
	θ	χ_1	χ_2	θ	χ_1[c]	χ_2	
 **95**	27	26	41	90	22 ± 5	0	32 ± 2
93	26	34	38	90	32 ± 6	0	31 ± 2
83	34	54	48	90	54 ± 4	0	19 ± 5
7	38	42	50	90	42 ± 5	0	17 ± 5
92	41	50	49	90	52 ± 5	0	13 ± 6
81	43	62	60	90	66 ± 4	0	11 ± 7

[a] Force-field calculations. [b] See 13 for definition of these parameters. [c] Two different force fields were used for the TS calculations; the data given are averages.

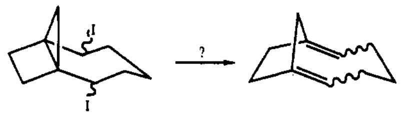
It is clear that many extensions and variations on the above themes are possible. For example, Szeimies'[86] synthesis of [1.1.1]propellane might be extendable to **123**; would **124**, a derivative of **79**, be accessible from **123**? Would the methodology of eq 4 be useful for generating **126** from **125**? Might any of the three stereoisomers of **128** be available from **127**? It seems that more use could be made of carbene ring expansion strategies, for example in the production of bridgehead dienes. Also ring contraction procedures employing the Favorskii rearrangement, episulfides, or carbenes might work well.



123 **124**

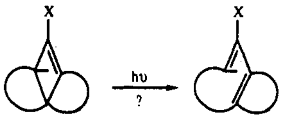


125 **126**

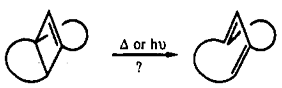


127 **128**

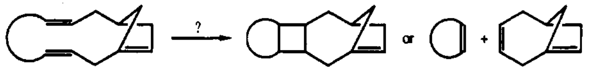
Among processes that appear not to have been tested, we mention cyclobutene ring opening of **129** to **130** (but see **460** for a possible example), of **131** (already a bridgehead alkene) to **132** (two stereoisomers of **132** might be available depending upon whether heat or light was used to initiate the ring opening), photoclosure of **133** to **134** (or other metathesis of **133** to give **135**), and intramolecular 1,4-carbene addition[88] of **136** and **137**. Lastly, we point out that allenes should be more easily accommodated at bridgeheads. For example, given the ready accessibility of 1,2-cyclohexadiene (**138**),[89] **139** ought to be a serviceable source of **140**, and **141** of **142**.[90]



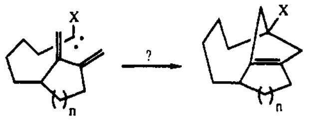
129 **130**



131 **132**

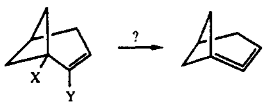


133 **134** **135**

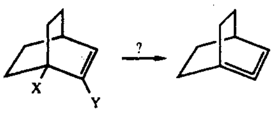


136 **137**

138



139 **140**



141 **142**

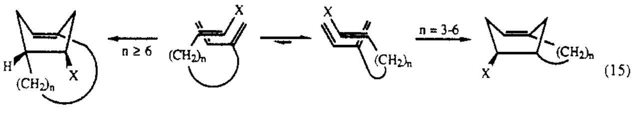
B. Systems with One C═C Bridgehead Double Bond

This section is organized according to the ring size in which the bridgehead double bond is transoid (*E*), in order of increasing strain.

1. *trans*-Cyclononenoid Systems

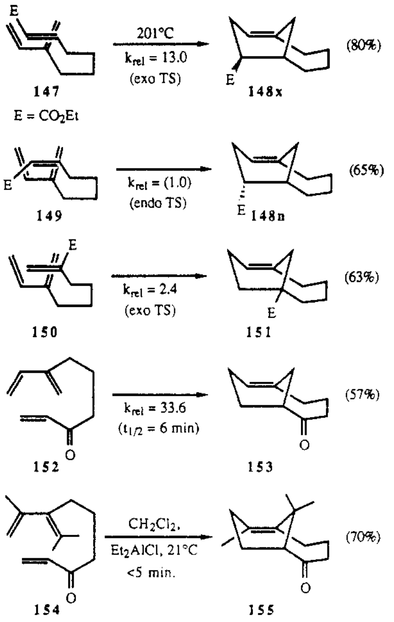
Since *trans*-cyclononenoids are not particularly strained, they have not received much attention, except in the course of work aimed at smaller ring systems or as demonstrations of synthetic methodology.

In the latter area, Shea has published a full paper[91] on his Diels–Alder route to bridgehead alkenes; a summary of this work has also appeared.[92] Since Shea's review[22] detailed most of this material (prior to publication), we only briefly summarize it here. The general concept is shown in eq 15: a 1,3-diene linked to an alkene at the 2-position can undergo an intramolecular Diels–Alder reaction via two regioisomeric transition states, each of which is sterically constrained to one stereochemistry (exo for the case shown, but see below). Obviously the "para" arrangement of 144 is less stable, due to the linkage, than the "meta" arrangement, 143. It is, therefore, not surprising that 145 was the exclusive thermal product for n = 3–5; for n = 6, a mixture dominated by 145 was found.



146 144 (exo) 143 (exo) 145

The stereoselectivity of the reaction was studied kinetically. The greater reactivity of 147 over 149 suggested that secondary orbital interactions were unimportant in the (relatively late) cyclization transition state.



147 E = CO_2Et → 148x

149 → 148n

150 → 151

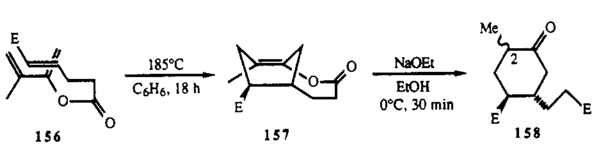
152 → 153

154 → 155

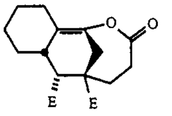
The usual efficacy of electron-withdrawing groups in enhancing dienophilicity was immediately obvious from the greater cyclization rate of 152 over 147, and both over 143 (X = H, n = 4). These rate differences were apparent in both solution and gas-phase thermolyses.

Another strategy for increasing Diels–Alder reactivity is to employ Lewis acid catalysis. In the event,[93] 154 was rapidly converted to 155; other, less strained, bridgehead alkenes were also so synthesized, and the percentage of the "para" transition state (in one appropriate instance) also increased, as predicted by FMO theory.

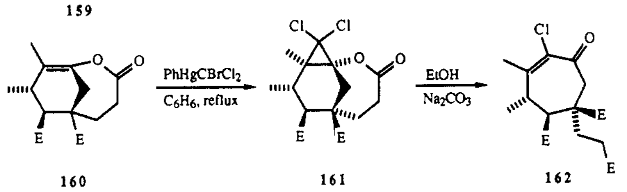
Substitution at the diene side allowed the production of an enol lactone (157),[94] which was cleaved stereoselectively to 158, with the major isomer having the Me group up (equatorial) at C_2. Application of this methodology also afforded 159[95] and 160,[96] the latter of which was converted to 162 via dichlorocyclopropanation, followed by ring cleavage.[97] It would certainly be interesting to know more about the conversion of 161 to 162. In particular, one might expect that the tetrahedral intermediate 163 would cleave according to path a, with direct formation of 162. However, dihalonorcaranes do not always follow the "normal" reactivity pattern; we showed[98] that a process analogous to pathway b (to give 164) obtained in a dihalonorcarane solvolysis.[99] Certainly, if formed, 164 would isomerize to 162;[60] the distinction could be made by studying the bromo chloro analogues of 161, or possibly by trapping 164. The question becomes more intriguing when the cleavages of 165a and 165b are considered.[97] We recognize that possible intermediates 166a and 166b are type B bridgehead alkenes, as well as *trans*-cycloheptenones.



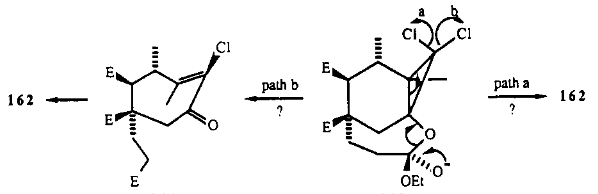
156 E = CO_2Et 157 158 85 : 15



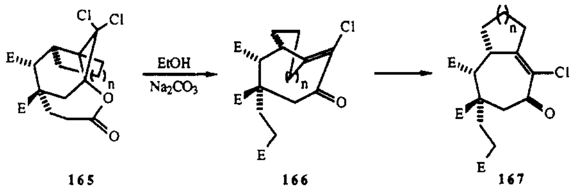
159



160 161 162



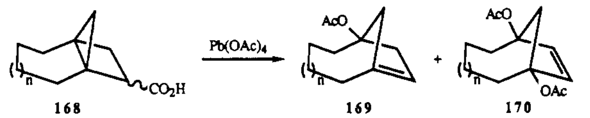
164 163



165 a, n = 2 b, n = 1 166 E = CO_2Et 167 (a, 55%) (b, 65%)

A scattered variety of other *trans*-cyclononenoids have appeared. Tobe showed that oxidative decarboxylation of 168a gave 169, along with some 170.[100]

Strain was clearly a factor, since the one-carbon-larger case (**168b**) gave no **170b**, while the one-carbon-smaller case (**168c**) gave no bridgehead olefin (**169c**) product.

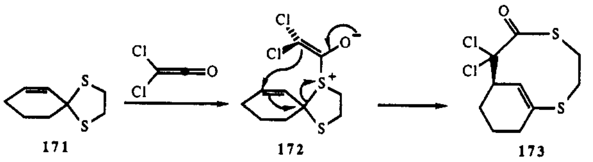


168
a, n = 2
b, n = 3
c, n = 1

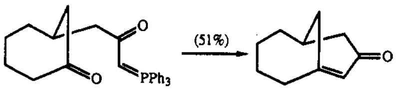
169
a: 30%
b: 58%
c: --

170
8%
--
33%

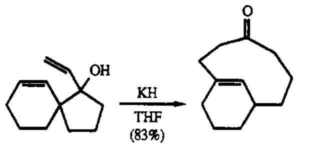
The addition of dichloroketene to **171** produced the unusual dithia-bridgehead alkene **173**.[101] Wittig cyclization of **174**[102] gave the previously known[103] enone **175**. Application of the oxy-Cope rearrangement gave **177** from **176**.[104] Lastly, the production of allene **180** from **178**[12] was reported.[105]



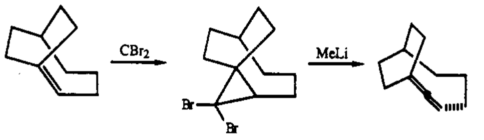
171 **172** **173**



174 **175**



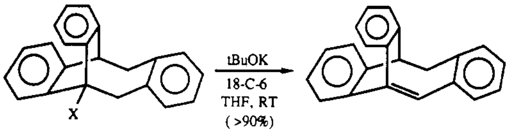
176 **177**



178 **179** **180**

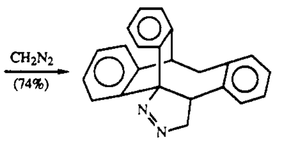
2. trans-Cyclooctenoid Systems

Most of the general synthetic approaches outlined earlier herein were applied to this group of compounds. Most recently, the elimination approach was used by Oda to make **182**,[106] a more strained analogue of **178**.[12]



181
X = Cl, Br, or I

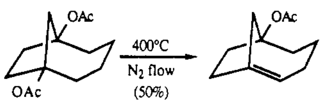
182



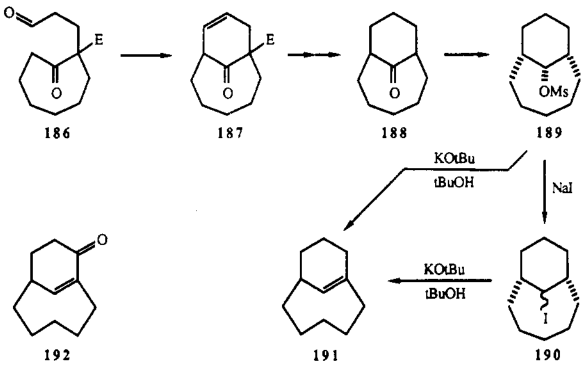
183

Compound **182** slowly air oxidized to the keto aldehyde derived from the 2 + 2 dioxetane intermediate. While **182** underwent normal addition of trifluoroacetic acid to the bridgehead trifluoroacetate, it added CH_2N_2 to give the adduct **183**, where the *positive* end of the 1,3-dipole attached itself to the bridgehead position.[107]

Flow pyrolysis of **184** gave **185**,[100] a derivative of the well-known parent bicyclo[4.2.1]non-1-ene.[108] Bicyclo[5.3.1]undeca-1(11)-ene (**191**), the parent of the known enone **192**,[109] was synthesized by Reese from **186** as shown.[105] The closely related **194** arose via the oxy-Cope rearrangement of **193**.[104] Shea's full report[91,92] also included Diels–Alder syntheses of **196**. The apparently more rapid conversion of **195b** relative to **195c** is reversed from the *trans*-cyclononenoid series (**152** vs **147**) and is thought to reflect poor enone overlap in the TS leading to **196c**. Also, 2 + 2 cycloadduct **197** became an important byproduct from **195d**.

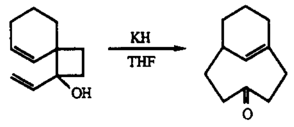


184 **185**

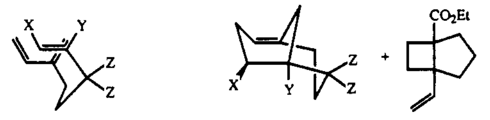


186 **187** **188** **189**

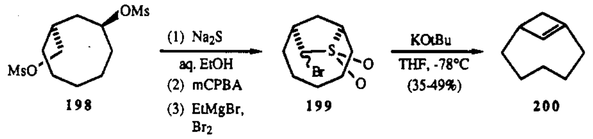
192 **191** **190**
(tr/cis = 2.3)



193 **194**



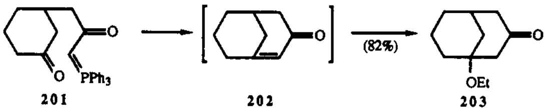
195		**196**	**197**
a, X = Y = Z = H	420°C, 23s	32% conversion	
b, X = CO_2Me Y = Z = H	318°C, 18s	76% conversion	
c, X = Y = H Z, Z = (=O)	395°C, 18s	72% conversion	
d, Y = CO_2Et X = Z = H	390°C, 12s	30% conversion	20% conversion



198 **199** **200**

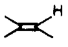
The Ramberg–Bäcklund contractive route to **200** was conveniently employed by Becker, beginning with **198**.[109] The alkene **200** reacted rapidly with O_2 (to give unspecified products), acids, and reactive dienes such as diphenylisobenzofuran (DPIBF).

The formation of **202** from cyclization of **201** was inferred by Bestmann from the production of **203**;[102] as before,[110] **202** was too reactive to isolate. While **202** readily underwent Michael-type additions,[110] Diels–Alder adducts were not readily formed or required large excesses of dienes.[111] Recently, Kraus has been ap-



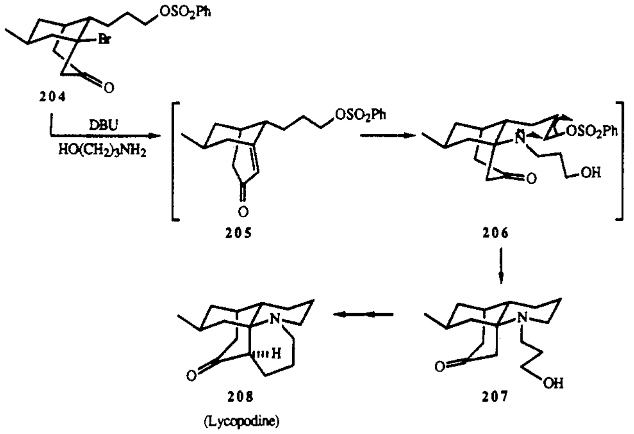
201 **202** **203**

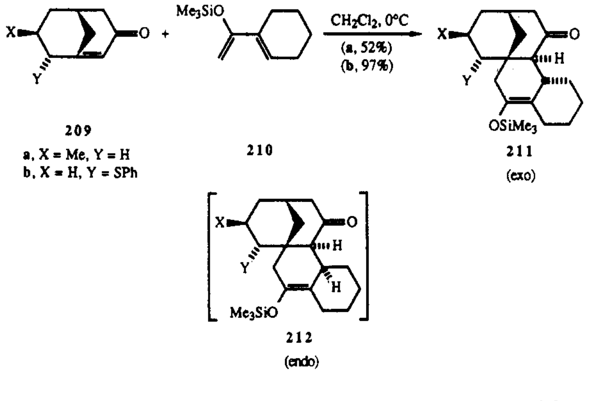
TABLE IV. Some Bridgehead Alkene Stretching Frequencies[83]

compd	C=C stretch, cm^{-1}		transoid ring size
	exptl	calcd[a]	
 **341**	1675[b]	1689	
homoadamantene (**93**)	1610[c]	1616	7
protoadamant-3-ene (**94**)	1587[b]	1607	7
adamantene (**92**)	1481[b]	1523	6

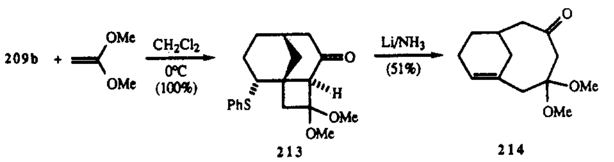
[a] MNDO. [b] Measured in an Ar matrix. [c] Measured on neat material.

plying reactions of **202** derivatives to total synthesis. First,[112] lycopodine (**208**) was efficiently synthesized via enone **205**. Then Diels–Alder reactions of in situ generated enones **209a** and **209b** with a variety of unsymmetrical, activated dienes were studied,[113] a representative example of which is shown. It was emphasized that in this case, as well as several other cases, only exo adduct (**211**) was formed. This surprising result was rationalized in terms of a stepwise, ionic cycloaddition process. Support for this idea came from the fact that several dienes that cannot easily achieve the s-cis conformation and that are generally unreactive toward cycloaddition nevertheless reacted rapidly with **209**. Thus these "cycloadditions" may really just be more instances of nucleophilic capture of the bridgehead enone at the bridgehead carbon.

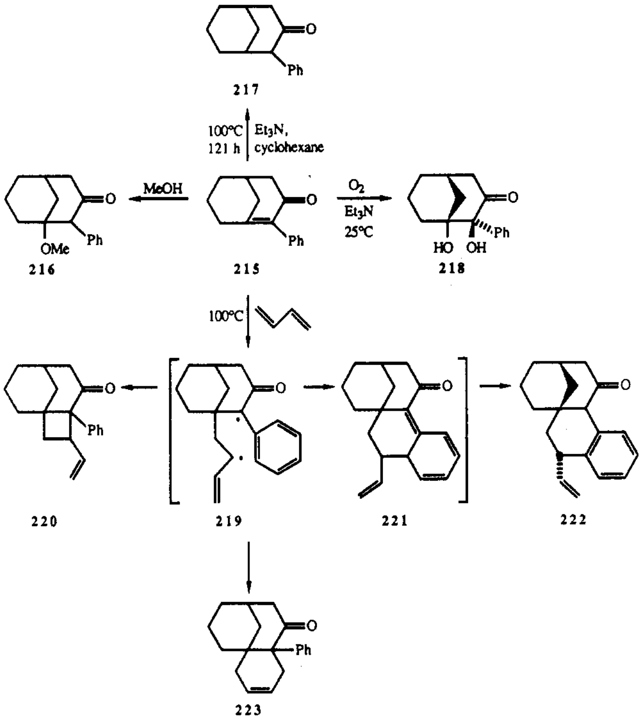




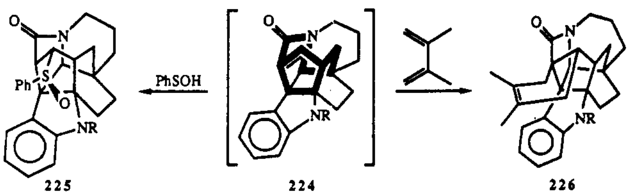
Another unusual cycloaddition was achieved with 1,1-dimethoxyethylene and **209b**; cyclobutane **213** was the product.[114a] This compound was then reductively converted to bridgehead alkene **214**, which contains the bridgehead double-bond subunit of the taxanes. The initial cycloaddition, which did not occur in a synthetically useful manner with other electron-rich alkenes, could involve electron transfer, nucleophilic addition, or ordinary (biradical) 2 + 2 cycloaddition of **202** derivatives. Similarly useful, if mechanistically unresolved, chemistry of **209b** involved conjugate addition of organocuprates.[114b]



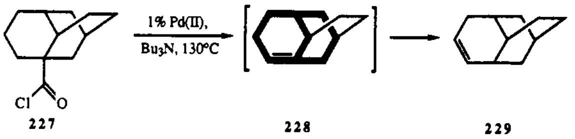
House[81a] found that the 2-phenyl derivative of **202** (**215**) was isolable, but quite reactive; however, it did not self-dimerize. MeOH addition to give **216** was normal, and diol (**218**) formation was thought to proceed via an observable dioxetane. More interesting, however, were the reactions with butadiene and Et$_3$N/cyclohexane. In the former case, formal Diels–Alder adduct **223** was accompanied by 2 + 2 adduct **220** and the aromatic substitution product, **222**. These were rationalized as products of biradical **219**. Reduction product **217** also looks like the product of radical abstraction. The authors speculated that **215** might first be thermally converted to a biradical species, possibly a triplet biradical, but they admittedly could not make a substantive case for this proposal. The parent **202**, generated by FVP,[81b] dimerized above −40 °C but did not react with added O$_2$.

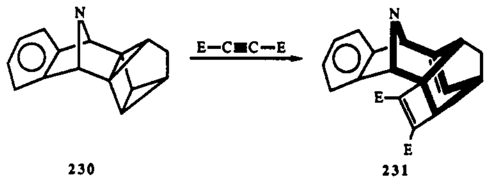


In another, possibly the first, use of bridgehead double bonds in total synthesis, Magnus[115] generated **224** by thermal elimination of benzenesulfenic acid from the bridgehead-substituted precursor. At 215 °C, **224** was trapped to give **225** (an overall 1,2-rearrangement reminiscent of benzyne chemistry), whereas thermolysis in 2,3-dimethylbutadiene at 230 °C gave cycloadduct **226**.

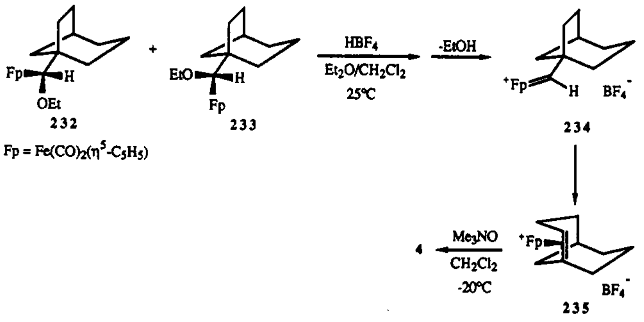


Other polycyclic bridgehead alkenes in this group are **228**, thought by Takaishi to be an intermediate in the conversion of **227** to **229**,[116] and **231**, isolated by Szeimies from a 2 + 2 + 2 reaction of acetylenedicarboxylic ester and **230**[117] (itself a Diels–Alder adduct from **20** and isoindole).



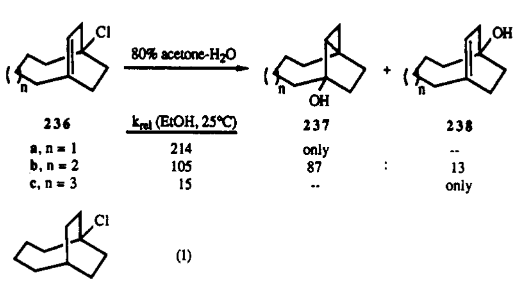


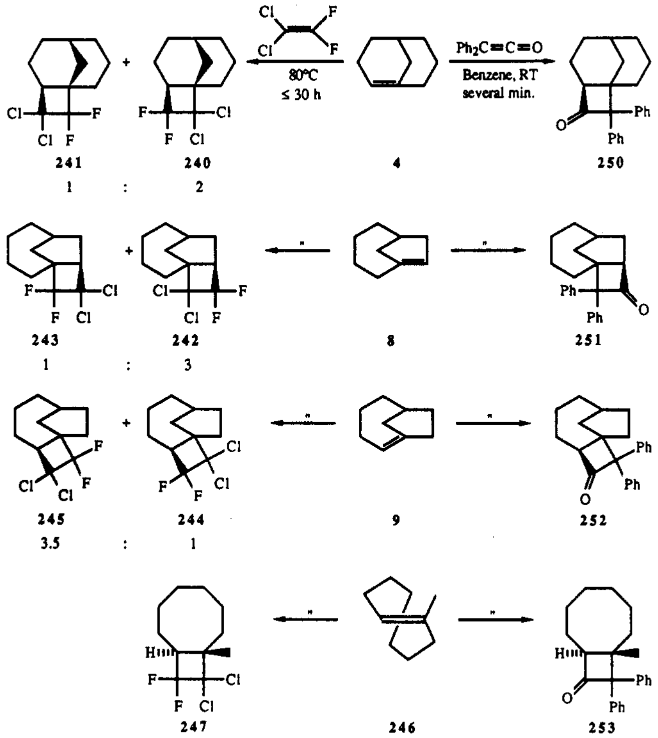
Several bridgehead alkenes have been reacted with (Ph$_3$P)$_2$Pt^0 or Cl$_2$(C$_5$H$_5$N)Pt^{II} to give platinum complexes, including **4**,[118] **8**,[119] and **9**.[119] Another approach by Bly[120,132] involves the generation of the bridgehead olefin complex in one step. Indeed, when a 1:1 mixture of diastereomers **232** and **233** was treated with HBF$_4$, a single complex (**235**), from which **4** could be liberated via Me$_3$NO/CH$_2$Cl$_2$/−20 °C treatment, was produced.



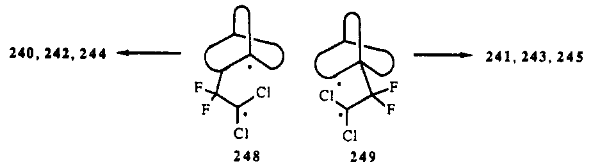
The reaction was proposed to involve the iron alkylidene **234** and the expansion mode (six ring-expanded alkene complexes are possible from **234**) possibly controlled by the stability of the corresponding bridgehead carbocation (i.e., the transition state for ring expansion should resemble the ring-enlarged bridgehead carbocation more than the resultant bridgehead alkene); this favored the formation of **235**. A key assumption was that all the rotamers of **234** interconverted faster than the rearrangement to **235**.

Reaction studies of bridgehead alkenes include a kinetic examination by Sakai et al. of neighboring group participation in **236**[121] and Becker's work on cycloadditions to **4**, **8**, and **9**.[122,123] In the former case, the rates clearly show a direct dependence of the degree of double-bond participation on the ring strain. But the activation parameters show the effect is entropic; the more tightly held π bond of **236a** is in better position to participate (an entropy effect).



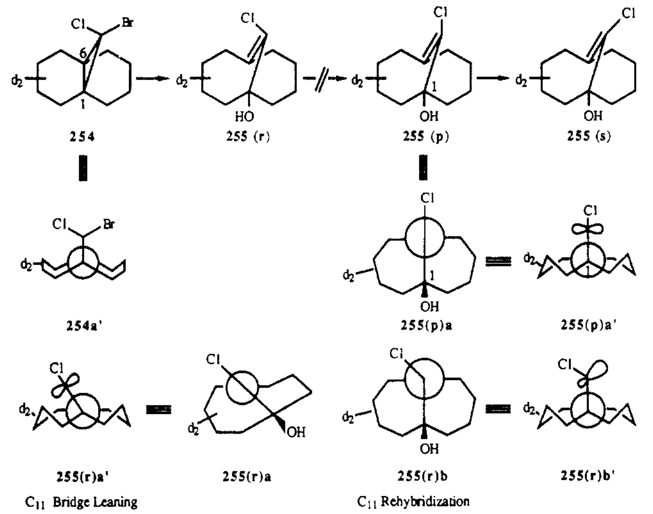


The cycloadditions of **4**, **8**, **9**, and **246** with diphenylketene each gave a single, expected compound (**250**–**253**, respectively). This was explained in terms of a concerted "${}_\pi 2_s + {}_\pi 2_a$" transition state.[123] The reactions with 1,1-dichloro-2,2-difluoroethylene were accounted for in the usual fashion, i.e., as proceeding via diradicals. On the basis of the product distribution, it was concluded that biradicals **248** and **249** are of similar stability. If so, some rather subtle effects are involved in reversing the major orientation in the addition to **9** vs **8** and **4**.



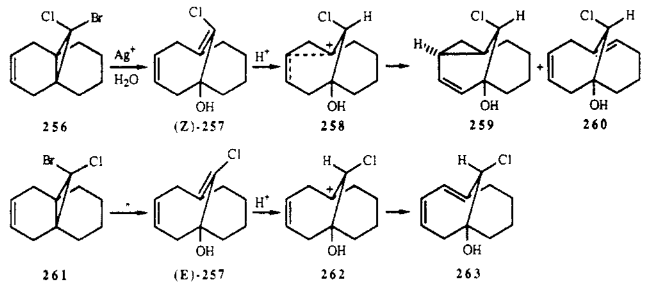
3. *trans*-Cycloheptenoid Systems

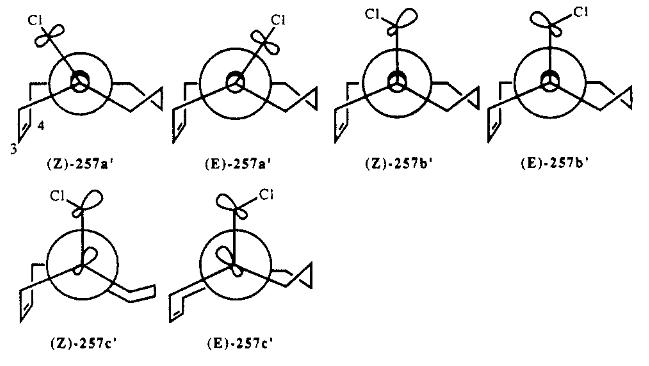
The cyclopropyl to allyl ring-opening route was extended to probe the question of bridgehead double-bond rehybridization in more detail.[124] Earlier,[125] we had shown that **255** maintained its configuration throughout its lifetime (i.e., prior to protonation). But although rehybridization at least at C$_{11}$ seemed most reasonable, the results could not exclude purely "bridge leaning". These points are illustrated in the various **255** structures. In the top line, **255(r)** and **255(s)** are enantiomers of a chiral olefin, irrespective of exact structure; **255(p)** represents the orthogonal alkene



which *might* connect the enantiomers. Structure **255(p)a** shows a Newman projection down the "double bond", with C_{11} in front, while **255(p)a′** shows a Newman-type projection between the bridgehead carbons (C_1 and C_6), C_1 in front (OH omitted for clarity). For **254a′**, this is a real Newman projection, for C_1 and C_6 are still bonded. The other **255** projections are as above, with **255(r)a** illustrating purely C_{11} "leaning" (to regain π bonding) and **255(r)b** purely C_{11} rehybridization. While it is certainly true that **254** begins with essentially the rehybridized geometry, it is obvious that **255(r)a** contains the requisite asymmetry.

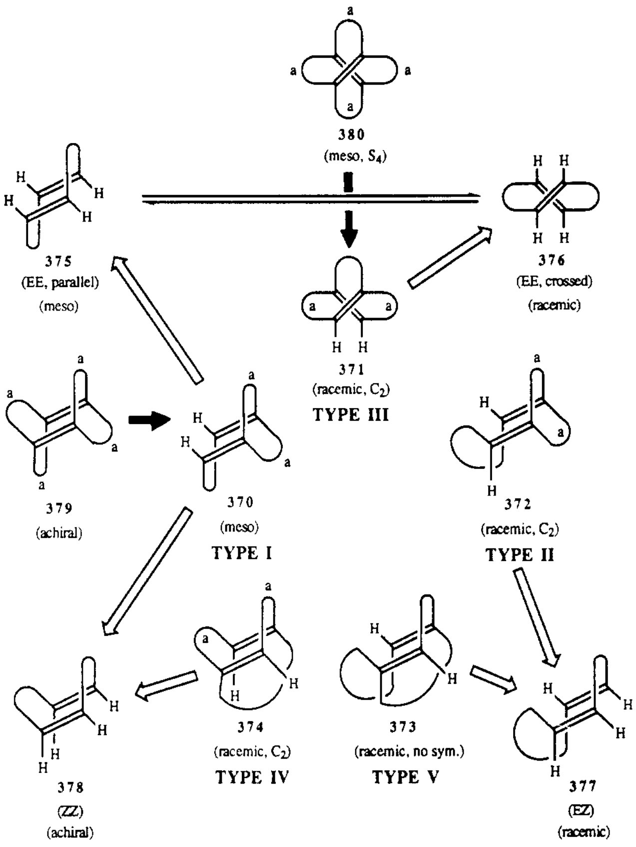
The newer experiments[124] involved the solvolyses of **256** and **261**; the pertinent results are shown below. Since **256** and **261** are diastereomers, so are their daughter bridgehead alkenes, (*Z*)-**257** and (*E*)-**257**. The former gives a major product (a rearrangement product of **259**) that reveals participation by the 3,4-double bond in **258**; no analogous participation occurs in the epimeric ion **262**. This difference must be explained by structural features of the bridgehead alkenes, (*Z*)- and (*E*)-**257**. The **257a′** drawings show, as before, C_{11} bridge leaning, while **257b′** drawings show C_{11} rehybridization.

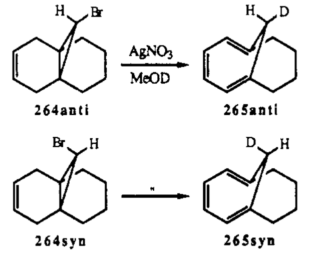


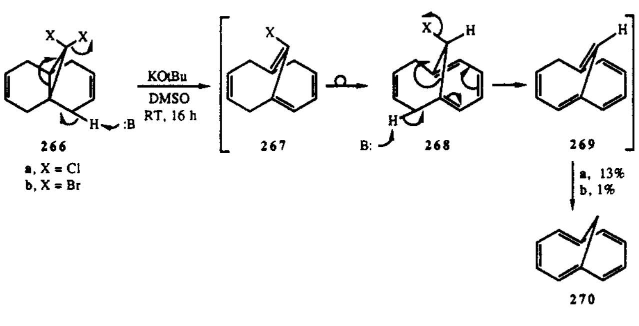


Clearly, neither of these distortions differentiates the orientation of the 3,4-double bond with respect to the π orbital at the C_6 bridgehead position on going from (*Z*)-**257** to (*E*)-**257**. Another distortion, namely rehybridization at C_6, is necessary, as shown by (*Z*)-**257c′** and (*E*)-**257c′** (where rehybridization at C_{11}, not technically required, is also shown). Now the 3,4-double bond can "see" the C_6 p-type orbital (and participate) in (*Z*)-**257c′**, but not in (*E*)-**257c′**. Similar considerations served to explain the stereochemical outcome of the solvolyses of *anti*-**264** and *syn*-**264**.[124] A conversion similar to **264** → **265** involved the base-catalyzed reaction of **266**.[126] 1,6-Methano[10]annulene (**270**) was produced, albeit inefficiently; presumably bridgehead alkenes like **267** and **269** were involved.

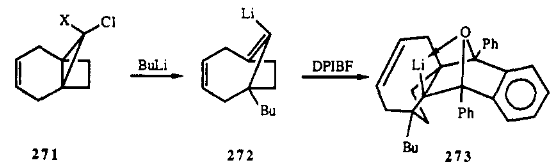
CHART I. Architectural and Genetic Relationships among Cycloalkadienes and Bridgehead Dienes







Another example of the cyclopropyl ring-opening route to bridgehead alkenes led to the first bridgehead vinyllithium (**272**),[127] which was trapped with DPIBF (37% as protonated or deuterated derivative of **273**; i.e., H replaces Li (structure determined by X-ray crystallography)) to give **273**. The stereochemistry of **273** was explained on the basis of oxygen–lithium interaction.

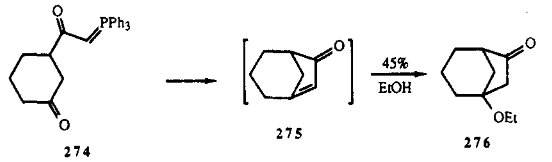


271
a, X = Cl
b, X = Li

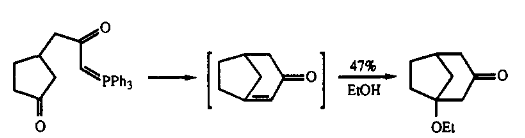
272

273

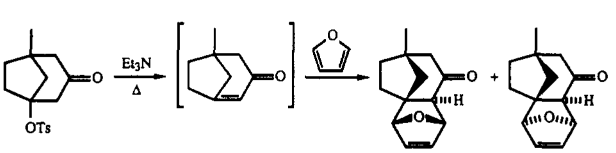
Enones that have been studied in this group include **275**,[102] **278**,[80,102] and **281**. The furan adducts **282x** and **282n** again demonstrated a preference for exo cycloaddition (this time to **281**, previously to **202**).



274 **275** **276**

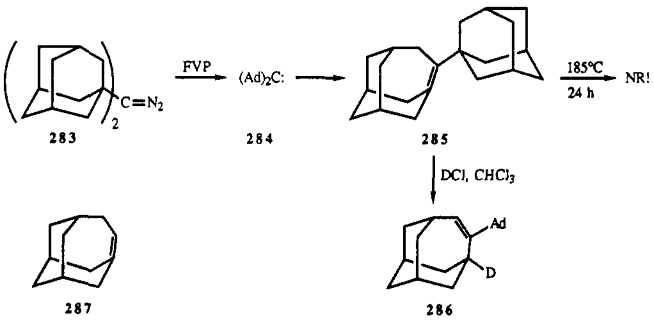


277 **278** **279**

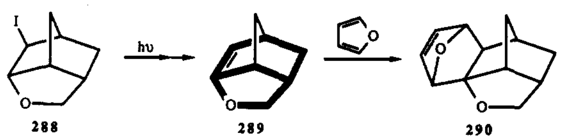


280 **281** **282x** 46% **282n** 12%

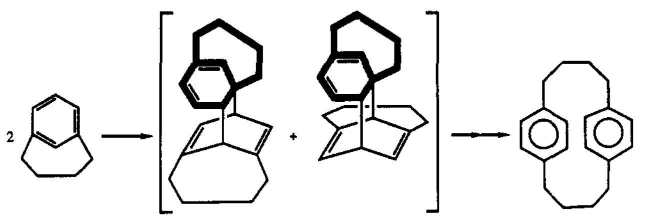
A number of polycyclic *trans*-cycloheptenoids have appeared, including the extraordinarily stable, tetrasubstituted homoadamantene, **285**.[128] The Princeton group also confirmed that homoadamantene from adamantylcarbene gave the same pyrolysis products as 3-homoadamantyl acetate, an alternate source of homoadamantene (**287**).[129] Photolysis of iodide **288** gave some **289**, partly trapped as **290**.[130] Bridgehead alkenes **291** and **292** were proposed as intermediates in the dimerization of [4]metacyclophane (**35**)[46] to **293**. Another interesting observation involves the reaction of **294** with PTAD, which leads to the isolation of **296**; **295** was proposed as the intermediate.[131] Interestingly, the rates of reaction of **294** and **297** with PTAD are essentially the same, and analysis of the strain energies indicates that both reactions have about the same exothermicity. Other chemistry of **294** includes protonative ring opening to bridgehead alkene **299**, which itself suffers protonation (but in the opposite direction from related systems[23,124,125]) to finally give **301** and **302**.



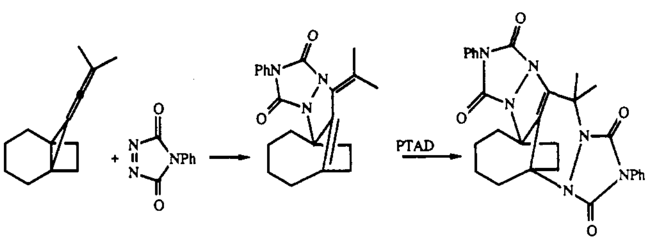
283 **284** **285** **287** **286**



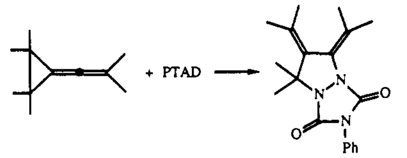
288 **289** **290**



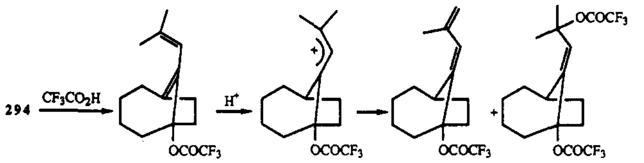
35 **291** **292** **293**



294 PTAD **295** **296**

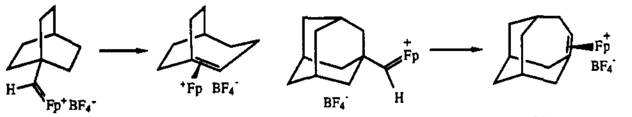


297 **298**



299 **300** **301** **302**

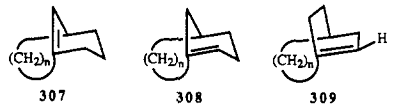
Lastly, the iron alkylidene methodology was extended to the production of **304** and **306**.[132]



303 **304** **305** **306**

4. *trans*-Cyclohexenoid Systems

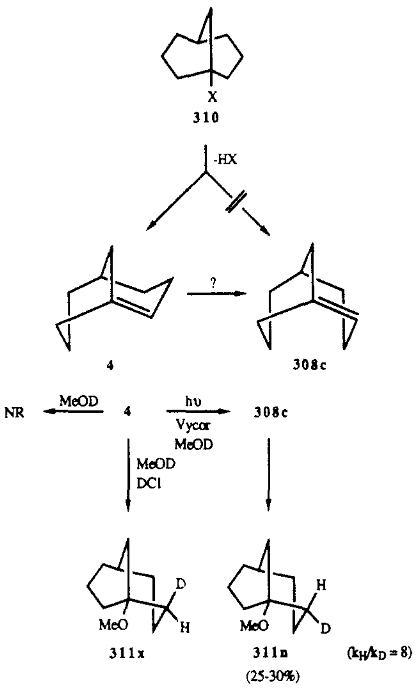
There are only three different ways to bridge a *trans*-cyclohexene to produce a type C bridgehead olefin, namely as in **307**, **308**, and **309**. As shown, all of these have a very high calculated[10] OS value (despite some apparent unreliability in the numbers) and are expected to be quite reactive. Experimental examples are known only for those starred, and they are discussed next.



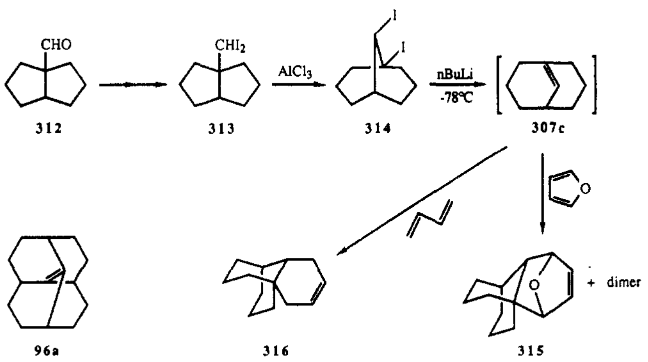
	307	**308**	**309**	
a, n = 1	39.1	28.9	34.9*	OS_{calc},[10] kcal/mole
b, n = 2	36.7*	42.2	40.4*	
c, n = 3	48.2*	44.2*	35.1	
d, n = 4	-	44.9	-	

*Experimental examples given below

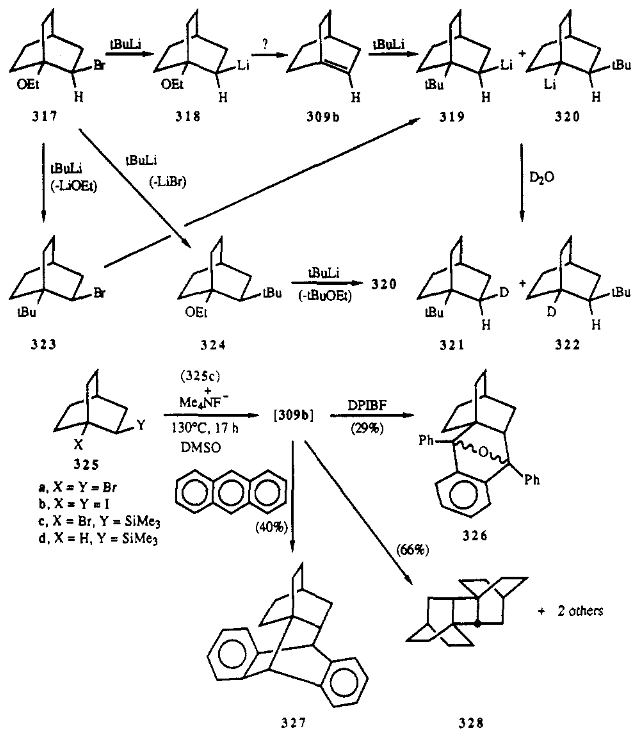
Inspection of the known cases reveals that all *must* be *trans*-cyclohexenoid (or even more strained), except for **308c**. Here, generation of the skeleton of **308c** would normally produce **4**; an attempt at a stereocontrolled elimination from a 1,2-disubstituted bicyclo[3.3.1]nonane failed to give **308c**.[133] What worked[134] was Wiseman's photoisomerization of **4**, which was possible due to the tailing beyond 230 nm of the UV absorption maximum of **4**. The photochemistry was best carried out unsensitized, although photosensitized methanolysis of **4** did produce some **311n**. The endo stereochemistry observed from MeOD addition to **308c** was convincing evidence for its structure being stereoisomeric with that of **4**, which itself produced exo adduct with MeOD (**311x**).



Compound **307c** has been made by the route shown below.[105] Elimination of iodine from **314** produced the transient **307c**, which was Diels–Alder trapped with either furan or 1,3-butadiene. In the absence of trapping agents, dimer and some trimer and tetramer were observed. It should be noted that the hypothetical orthogonene **96a**[85] is a "double" derivative of **307c**.

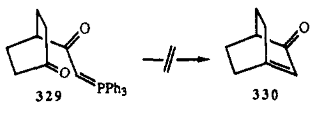


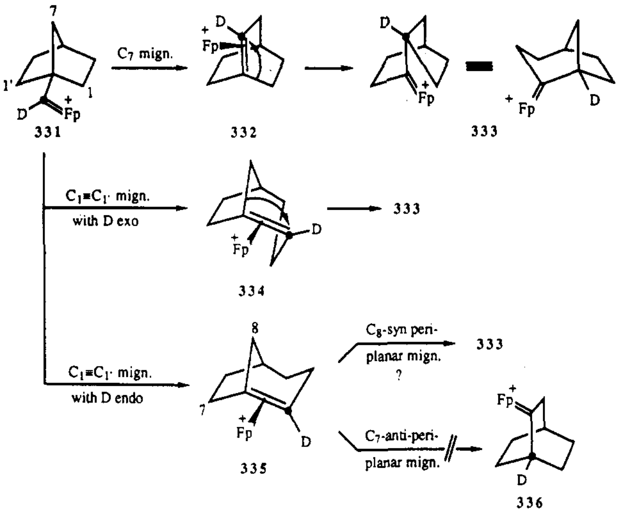
The experimental evidence regarding **309b** presents a somewhat confusing picture. Bickelhaupt[135] proposed **309b** as the intermediate in the room-temperature conversion of **317** to **321** + **322**. However, alternate routes involving ether cleavage (e.g., **317** to **323**, and **324** to **320**), which we have observed to be competitive with carbon–bromine exchange in even 1,1-dibromocyclopropanes, could account for the production of **321** and **322**. If so, this would obviate the need to explain the apparent lack of regioselectivity in addition of *t*-BuLi to **309b**. This notion gained support from Wiseman's brief report[105] that **325a** reacted with *n*-BuLi to give butylated products via non-**309b** pathways; he said, however, that **325b** did give **309b**, which did not add BuLi.



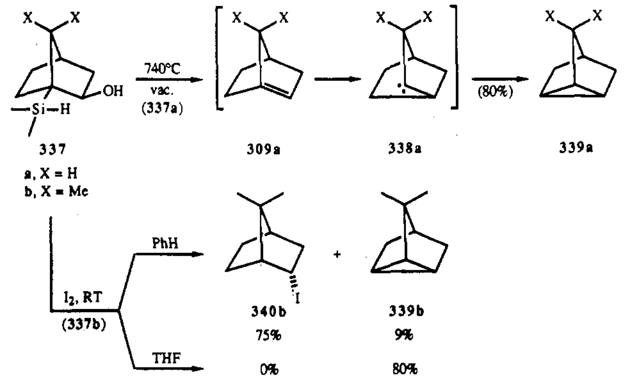
Thus Jones'[136] 330 °C carbene route to **309b**, where only the retro-Diels–Alder product from **309b** could be observed, was the best (if sketchy) evidence for **309b**. Recently,[137] however, **325c** was found to smoothly produce **309b** upon treatment with $Me_4N^+F^-$. Transient **309b** was trapped with either DPIBF or anthracene or dimerized in the absence of traps to give mainly **328** (X-ray analysis). The elimination of Me_3SiBr from **325c** is thought to involve an E2 process, since **325d** was inert to the desilylation conditions after even 22 h.

Among failed attempts to generate **309b**, or a derivative, one should note the inability of **329** to cyclize to **330**,[102] as well as the recently reported chemistry of **331**.[138] Unlike the previous cases (cf. **304** and **306**), a stable bridgehead olefin–metal complex was not obtained from **331**, but rather the rearranged alkylidene complex, **333**. Consideration was given to the three migration channels available to **331**; these would produce **332**, **334**, or **335**. The labeling results showed that subsequent rearrangement involved a carbon shift. While **335** is clearly the most stable of the possible bridgehead olefin complexes, it is sterically least able to give **333** and should give (the unobserved) **336**. Thus **332** and/or **334** (the complex of **308b**) remain as possible intermediates.





1-Norbornene (**309a**) was the earliest, most convincingly documented member of this group.[139,140] Recently, Barton[141] has found that pyrolysis of **337a** gives **339a** ("nortricyclene") and has proposed **309a**, which gives way to 2-norbornanylidene (**338a**) via a 1,2-alkyl shift, as the alkene intermediate. In other work,[137] it was discovered that **339b** and **340b** (both very likely the products from reactions of 7,7-dimethyl-1-norbornene, **309a**, X = Me) are formed in solution at room temperature.

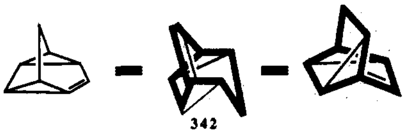


There are several polycyclic derivatives of **307–309**, the best known of which is adamantene (**92**),[83,142] which

92

is at once an example of **307c** and **308c**. Table IV gives Michl's measured and calculated vibrational stretching frequencies[83] for **92–94** and model **341** (trimethylethylene). The values indicate a frequency loss (π-bond energy decrease) of ca. 100 cm^{-1} for a *trans*-cycloheptenoid and ca. 200 cm^{-1} for a *trans*-cyclohexenoid. This is similar to what is found for bridgehead imines, but for different reasons (vide infra). Also, the vinylic C–H stretching (~2970 cm^{-1}) and bending (~900 cm^{-1}) frequencies found for **92** were indicative of *rehybridization* at the olefinic carbon.[83b]

Three derivatives of **307b**, namely **342**,[143] **343**,[144] and **344**,[145] have been reported. As shown, both **342** and **343** are also derivatives of **309b**.



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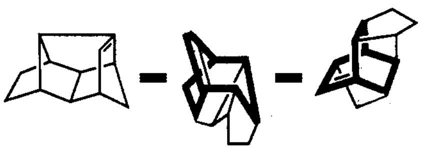

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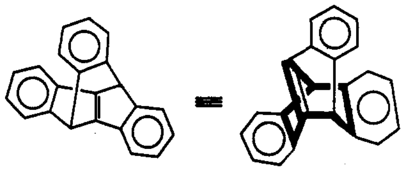
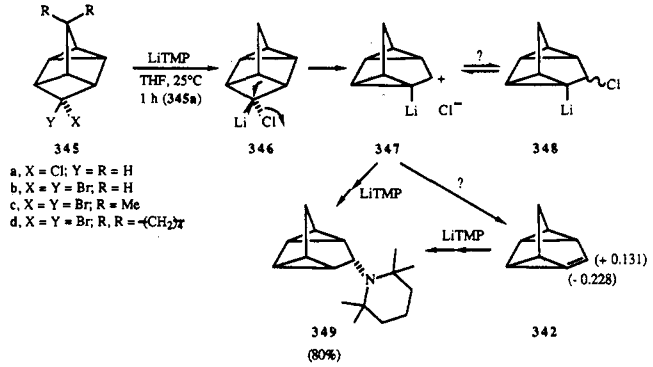
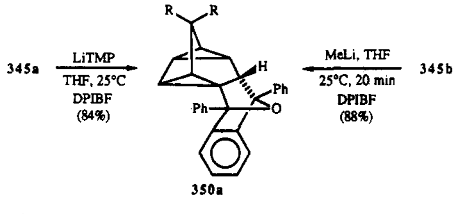
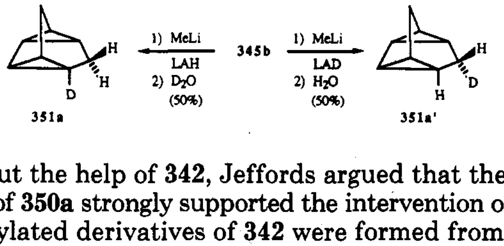


344

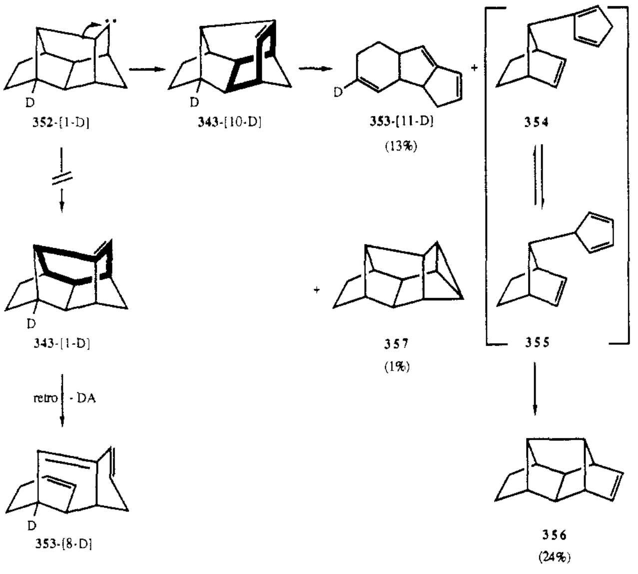
The chemistry surrounding **342** is particularly intriguing because it suggests a substantial polar character for the double bond. Calculated net charges (MINDO/3) are also in accord with this idea. It is to be noted that the direction of polarization (and addition) is opposite to what has been found for simple bridgehead alkenes,[23] as evidenced by, among others, the formation of 1-methylbicyclo[3.3.1]nonane from bicyclo[3.3.1]non-1-ene and MeLi.[143] This is likely due, of course, to the cyclopropylcarbinyl nature of any addition TS. Although **349** could have formed from **347** or **348** without the help of **342**, Jeffords argued that the high yield of **350a** strongly supported the intervention of **342**. 8-Alkylated derivatives of **342** were formed from **345c** and **345d**. They were trapped by DPIBF to give mainly **350c** and **350d** (formed via endo TS's on the exo face of **342** analogues), along with minor amounts of the exo,exo adducts, too.



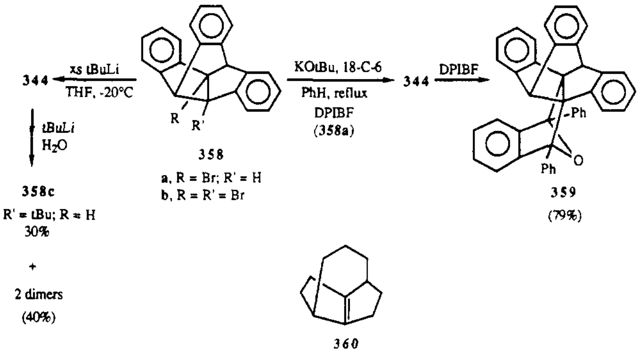




Kirmse's production of **343** utilized the carbene route from pyrolysis of the tosylhydrazone sodium salt (285–300 °C, 10^{-3} Torr). The major products (**353**, **356**) came from retro-Diels–Alder reactions of **343**; insertion product **357** constituted only 5% of the product mixture. That alkyl, not hydrogen, migration gave **343**, was demonstrated through labeling. The unsymmetrical product from **352**-[1-D] was **353**-[11-D], *not* **353**-[8-D].

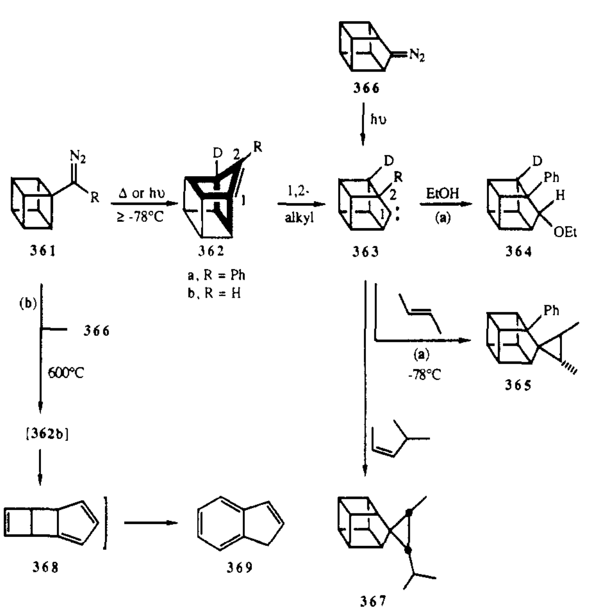


Lastly, **344** was transiently generated from **358** by either of the two routes shown.[145] Since **344** lacked the ene dimerization pathway accessed by **360**,[146] it was readily trapped in Diels–Alder fashion to give **359**.



5. *trans-Cyclopentenoid Systems*

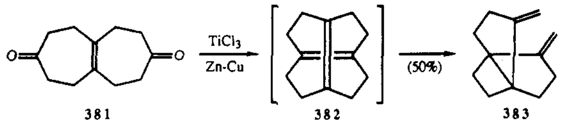
Although no *trans*-cyclopentenoids have yet been trapped via cycloaddition, two reports of the generation of such a system (**362**) have appeared.[147,148] In the first, phenylcubyldiazomethane was the starting material. Even at −78 °C, only **363a** could be trapped (e.g., as **365**). Labeling experiments[149] established that the rearrangement of **362** to **363** must have transpired via an alkyl (rather than phenyl) shift. It is still unknown whether **363** reverts to **362**, despite the fact that Jones[148] used **366** as a possible source of **362b** (**362b** was trapped with MeOD to give a D at the bridgehead of the homocubyl ether product, but **362** could have arisen via Wolff-type rearrangement of **366**). At high temperatures, either **361b** or **366** unraveled to give indene (**369**), possibly via **362** and **368**.



C. Systems with Two C=C Bridgehead Double Bonds

1. *Structural and Theoretical Aspects*

Although there is only fundamentally one type C bridgehead monoene, the structural complexities added when two bridgehead double bonds coexist in a bicyclic system lead to *five* different type C bridgehead dienes, which we call types I–V (see Chart I). That there are five is readily seen when one remembers that each bridgehead double bond must be *E* on one ring, *Z* in a second ring, and exocyclic to the third ring of the bicyclic system. Thus both double bonds may be *E* and *Z* in the same ring (*E*,*E*, *Z*,*Z*, exo,exo (type I)), in the opposite ring (*E*,*Z*, *Z*,*E*, exo,exo (type II), or in different rings altogether (*E*,*E*, *Z*,exo, exo,*Z* (type III)); *Z*,*Z*, *E*,exo, exo,*E* (type IV)); *E*,*Z*, *Z*,exo, exo,*E* (type V)). Two of these, namely types I and III, may be further bridged to yield tricyclic compounds of general structure **379** (cf. **23** and **24**) and **380** (**382** is an example that appears to have been transiently generated[150]), both of which are pyramidalized, but not twisted (and hence not covered herein).

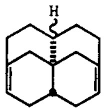


As shown in Chart I, there is a familial relationship between the various type C dienes and the three possible cycloalkadienes (*E*,*E*, *E*,*Z*, *Z*,*Z*). Type I (**370**) is unique in that it is related to both *E*,*E* (**375**) and *Z*,*Z* (**378**) progenitors; type III emanates from the (*E*,*E*)-cycloalkadiene in its other conformational extreme (**376**). The type II (**374**) and type V (**373**) bridgehead dienes are both derived from the corresponding (*E*,-*Z*)-cycloalkadiene (**377**) by bridging proximal (**372**) or distal (**373**) olefinic carbons; the type II diene appears to be the least studied kind. Lastly, the type IV diene (**374**) comes from distal bridging of the (*Z*,*Z*)-cycloalkadiene (**378**).

It is worth noting that the cycloalkadienes are both conformationally and configurationally mobile (cf. **375** ↔ **376**), whereas the bridgehead dienes are configurationally fixed, but still conformationally mobile (e.g., most examples of **371** do not have their double bonds lying directly across from each other). The tricyclic **379** and **380** are totally fixed (at least for small bridges).

As detailed in Chart I, different stereochemical properties accrue to the different bridged dienes. With two equal bridges (designated a in Chart I), **370** is meso (if the two bridges are unequal, there are *E,E* and *Z,Z* isomers, both of which are meso), **371**, **372**, and **374** are racemic with a C_2 axis (if the two bridges are unequal, these are still racemic, but sans the C_2 axis), and **373** is racemic without any symmetry. The fourth bridge produces achiral **379** and meso (S_4 axis) **380** (all bridges equal). If appropriate unsymmetrical bridges are used (e.g., by incorporating a heteroatom), diastereomers can be produced that are not interconvertible without bond breaking and that lack any stereogenic centers.

Of course, other kinds of "bridgehead dienes" are possible if one allows polycyclic structures. Some examples include (unknown) **384**–**386** (**386** is related to the mostly hypothetical beltenes ≡ columnenes, such as **387**[151,152]) and (known) **388**.[153]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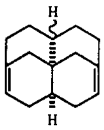
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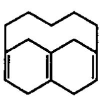
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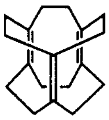
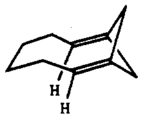
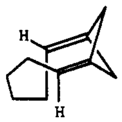
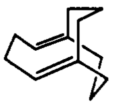

387


388

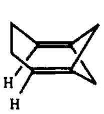
To this point, theoretical investigations of bridgehead dienes seem to have been restricted to force-field calculations.[2,78] The quantity DS [diene strain = (strain energy of the bridgehead diene) − (strain energy of the corresponding saturated bicyclic parent compound)] was suggested[78] to extend the OS concept. While the expected pattern of greater DS for dienes transoid in smaller rings was partially satisfied, the concurrence was nowhere near what was found for bridgehead monoenes. For example, **389** and **390** have DS's over 30 kcal/mol greater than that of **391**, but all are *trans,trans*-cyclononenoids; **389** and **390** are more strained than several *trans,trans*-cyclooctenoids. Predictably, those dienes with both double bonds transoid in seven-membered rings were the most strained (of those studied); no bridgehead dienes of this type have been made to date. The pairs represented by **393**/**394** and **395**/**396** are quite interesting, since in each case the type I diene (**393**, **395**) was not found as a minimum by MM2. Rather, those geometries were transformed into the type II structures (**394**, **396**) by the energy minimization routine (normally, type II structures are less stable than their type I counterparts). This may have implications

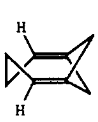


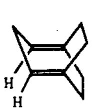


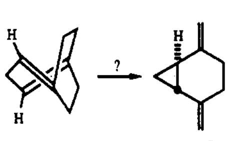


	389	**390**	**391**	**392**
DS (kcal/mole)	26.4	32.8	-8.2	60.7
	(Type I)	(Type II)	(Type I)	(Type I)



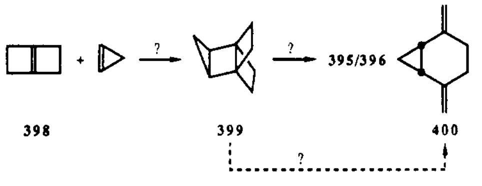






	393	**394**	**395**	**396**	**397**
DS	?	60.7	?	64.0	
	(Type I)	(Type II)	(Type I)	(Type II)	

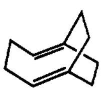
for experimental work. Thus were **395**/**396** to be synthesized, Cope rearrangement to a bicyclo[4.1.0]heptane system might be quite rapid. But **396** would give trans-fused **397**, itself quite strained. So this might protect **396**, or at least be a telltale sign of its having been present. An approach to **396** might involve **398**[26] plus cyclopropene to give **399**, which should open up (but could give **400** directly).



398 **399** **400**

2. Type I Dienes (Meso)

Most of the dienes made to date fall into this group, including the ones published before the last review[23] (**104**,[154] **401**,[155] **402**,[156] and most of the annulenes), of which **104** remains the most strained diene isolated or observed. Apart from the recent occasional, mostly serendipitous successes represented by the production of **405**,[157] **407** (along with **408**, a type III diene),[158] **411** and **412**,[159] and **414**[160] (which is a "perpendicular triene" with no UV maximum above 200 nm, whereas (*Z,Z,Z*)-1,3,5-cyclononatriene (**415**) has λ_{max} = 296 nm), or the intermediacy of **291**, **292**,[46] and **417**[117] (from **416**,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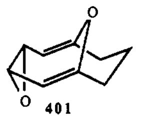

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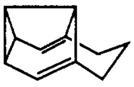
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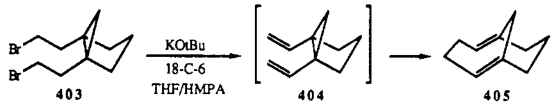
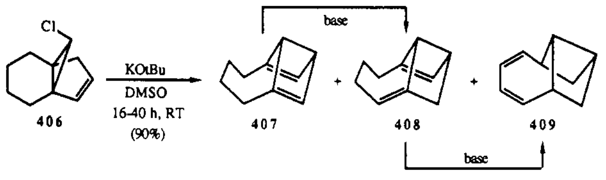
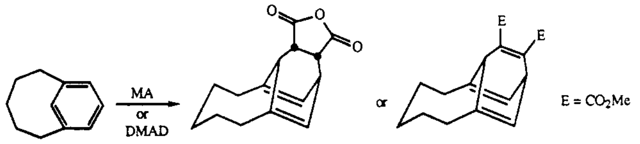


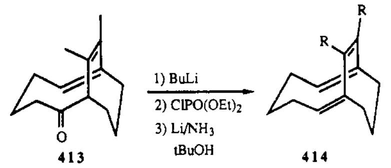
403 **404** **405**



406 **407** **408** **409**



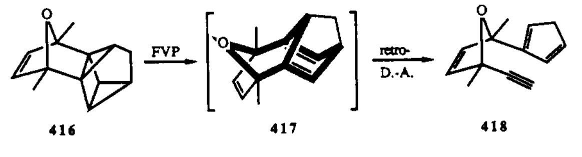
410 **411** **412**



413 **414**

a, R = Me (78%)
b, R = H

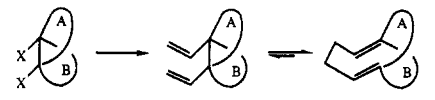

415



416 **417** **418**

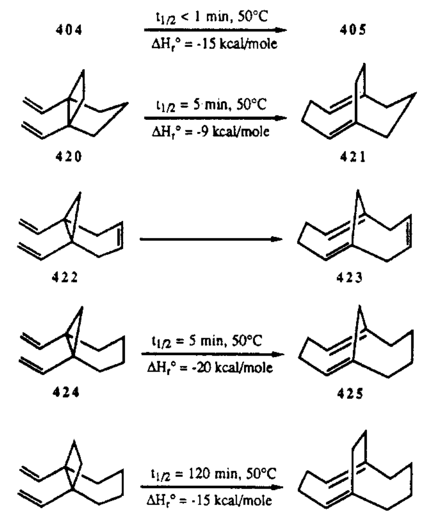
itself an adduct of **20** and 2,5-dimethylfuran), the efforts of the Shea group seem to be the only systematic attempts to explore this class of compounds. Shea has utilized pericyclic methodology[161] in his work, including Cope rearrangements (eq 6) and Diels–Alder reactions (eq 9).

The Cope rearrangement approach,[162] of which **404** was the first example, has had its limits revealed as follows.

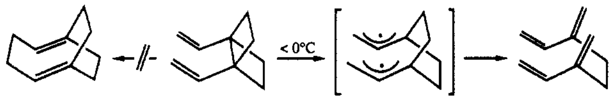


419 **107** **108**

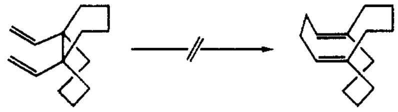
a, X = CO_2R
b, X = CH_2OH
c, X = CHO



	IP's (eV)	
	π_A	π_S
404 → 405	7.92	9.05
420 → 421	8.14	8.83
424 → 425	8.03	8.96
426 → 427	8.35	8.68



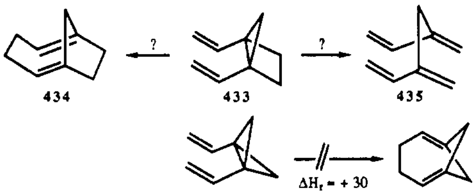
104 **428** **429** **430**



431 **432**

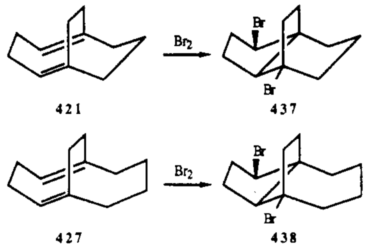
Thus each of **404**, **420**, **422**, **424**, and **426** underwent smooth rearrangement to their respective bridgehead dienes, albeit at rates that did not reflect the relative exothermicities of the reactions (a possible FMO explanation for the rates was advanced). The degree of transannular interaction, already evident in the λ_{max} = 252 nm for **405**, was assessed via the π-orbital splittings gleaned from PE spectroscopy.

The apparent limits were reached, on the "unstrained" side, with **431**, which did not rearrange to **432**; energetic estimates placed **431** some 5 kcal/mol below **432**. On the "strained" side, **428**, generated in situ, chose to open to **430**, a process that must be related to the relative ease of formation of **429**, relative to concerted Cope rearrangement to **104**. It should be pointed out that **428** → **104** may be slightly exothermic. In terms of further prospects, it seems likely that **433** would also divert from the sigmatropic rearrangement (approximately thermoneutral to **434**) in favor of cleavage to **435**, while **436** has no chance to give **393**/**394** (the reaction is ca. 30 kcal/mol *endothermic*).

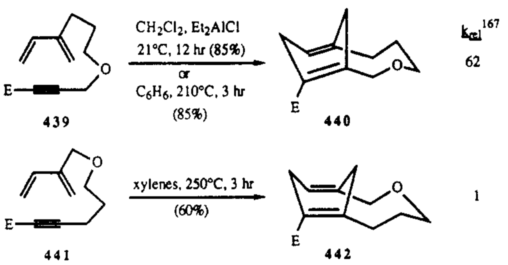


434 **433** **435**
436 **393**/**394**

The general tendency of (*Z*,*Z*)-1,5-cyclooctadienes to give bicyclo[3.3.0] systems via transannular reactions was seen in the bromination of **421** to give only **437**. Similarly, **427** gave **438**.

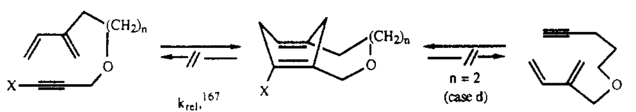


The Diels–Alder route to bridgehead dienes was first reported by Shea in 1983,[92] initially as a Lewis acid catalyzed process.[93] It was found that **440** was catalytically produced at ambient temperature, a process that otherwise required 200 °C.[163] That this general approach to bridgehead dienes would work was not too surprising, since the Diels–Alder reaction of an acetylene with a diene is about 14 kcal/mol more exothermic than is that of an alkene, and the Diels–Alder bridgehead monoene synthesis had already succeeded,[91] with exothermicities in the neighborhood of 19–25 kcal/mol. So, on the basis of the MM2 results,[78] one could expect a slightly greater exothermicity for formation of a bicyclo[4.3.1]deca-1(9),6-diene (ca. 26 kcal/mol) and an exothermicity of 12–13 kcal/mol for formation of a bicyclo[3.3.1]nona-1,4-diene. However, the analogous formation of **392** is predicted to be *endothermic* by at least 14 kcal/mol.



E = CO_2Me

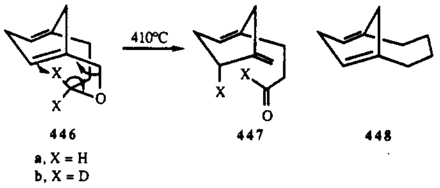
In practice, the following dienes were synthesized thermally:

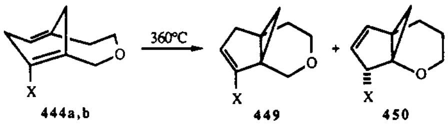


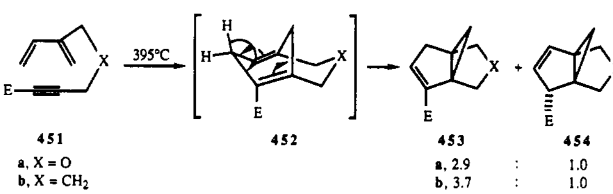
k_{rel},[167] 210°C	
-	a, n = 1, X = H[163,164]
-	b, n = 1, X = CO_2Me[163,164]
5.4	c, n = 2, X = CO_2Me (≡ **440**)[163]
-	d, n = 2, X = H
5.5	e, n = 3, X = CO_2Me[163,165]
(1.0)	f, n = 4, X = CO_2Me[163,165]

The acids from **444e** and **444f** were each analyzed crystallographically.[165] The double-bond distortions were almost none (4.5° average total deviation from planarity) for **444f**, but modest (14° average deviation from planarity) in **444e**. For comparison, the total average deviation from planarity in **401** is 25°. Both **444e** and **444f** were readily aromatized either thermally or with DDQ.[166]

The thermochemistry of the lower homologues was also interesting. The [5.3.1] system (**446** = **44d**) underwent a retroene reaction to give **447**. A large rate decrease for this reaction was observed when D (**446b**) was substituted for H (**446a**), consistent with an anticipated primary isotope effect.

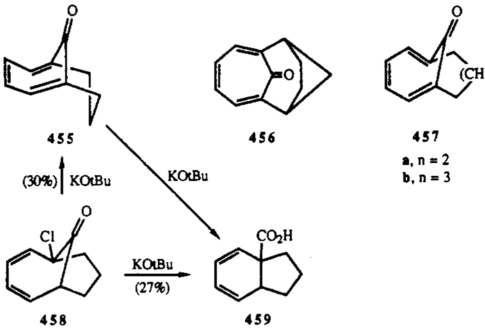






The chemistry of the isolated **444a,b** matched that previously reported for **448** (which had not been isolated).[168] And **452**, the unisolable intermediate from **451**, suffered the same fate, namely a 1,2-H_{exo} shift (really a 1,5-homodienyl H shift) to **453** + **454**.[169]

Although directed differently, the work of Itô and co-workers on bridged tropones must be mentioned in this section. Not only do the bridgehead double bonds become pyramidalized in **455**[170] and **456**,[171] but the carbonyl group becomes distorted, too. The result is a higher carbonyl stretching frequency for **455** (1746 cm^{-1}) relative to **457a** (1718 cm^{-1})[172] and **457b** (1675 cm^{-1}).[173] Trienone **455** was made from base treatment of **458** (whereby **459** was also produced) and instantly rearranged to **459** on contact with base.



Finally, a remarkable bridged cyclophane, **461**, has recently been generated from photolysis of **460**.[174] Evidence for its formulation as the cyclophane (**461**) rather than the alternate **462** came from its UV spectrum, which resembled that of [4]paracyclophane,[47] and its trapping with cyclopentadiene to give the bisadduct, **463**, obviously derived from **461**, not **462**.

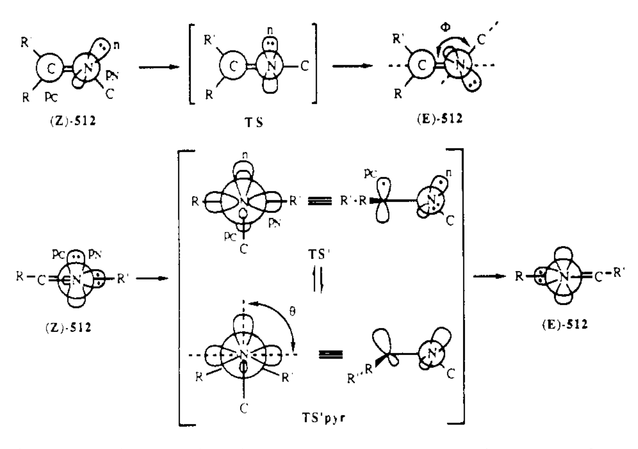
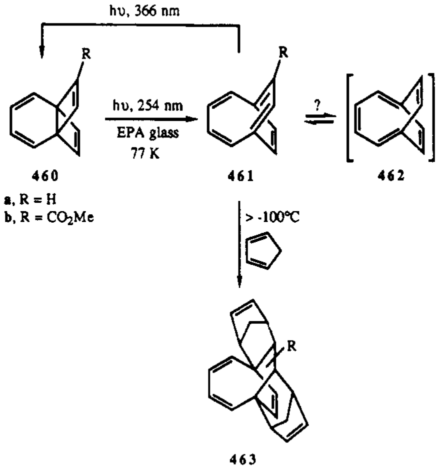
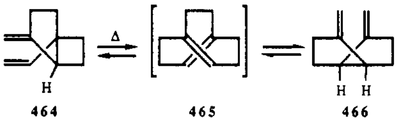


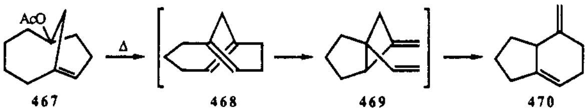
Figure 1. Top: The *Z* to *E* isomerization pathway involving inversion at N; the valence angle, Φ, goes from ~120° to 180° at TS, and back, while θ remains at 0° throughout. Bottom: The twisting pathway for *Z* to *E* isomerization at constant Φ; at TS′, the lone pair on N resides in the p_N orbital, while the p_C and the n orbitals form a "double bond". TS′pyr shows carbon pyramidalization at orthogonality.



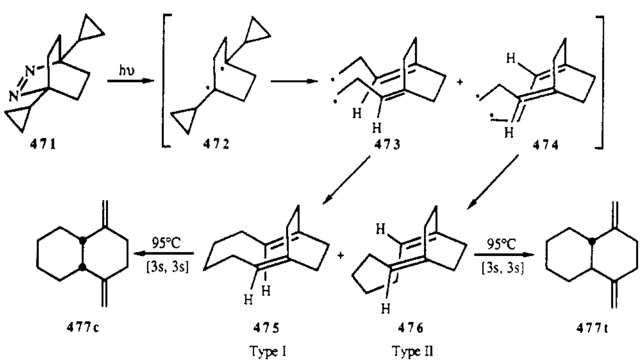
3. Type II–V Dienes (Racemic)

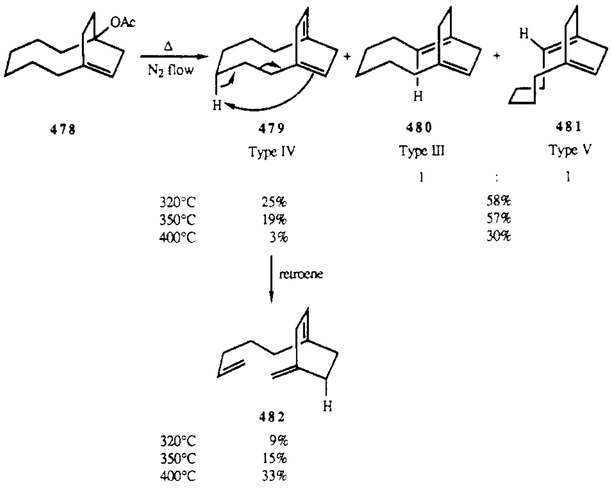
The first non-annulenic, non type I diene to be isolated was the aforementioned **408** (a type III). Prior to that, **465**[175] and **468**[168] had been proposed as reactive intermediates.



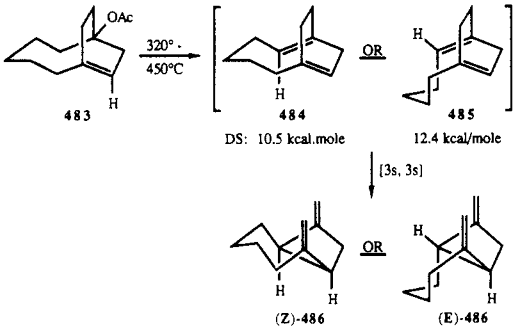


In the recent period, bridgehead dienes **475**,[176] **476**,[176] **479**,[177] **480**,[177] and **481**[177] have all been isolated. These represent a complete set of all five diene types within one skeletal framework. Though they are not expected to be very strained, they are the only such group presently known. The first two were generated in equal amounts via the ring opening of biradical **472**. It is also seen that **479**–**481** were each formed in essentially equal amounts via elimination of HOAc from **478**.

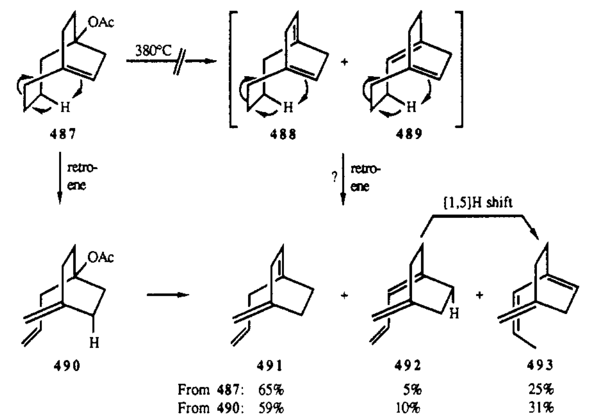




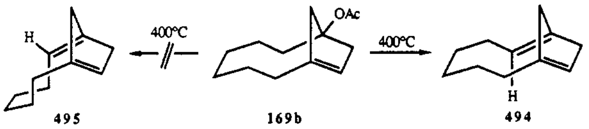
Pyrolysis of the lower homologues of **478**, namely **483** and **487**, was also studied.[177] From **483** there arose a single product, identified as either (*Z*)-**486** or (*E*)-**486**.



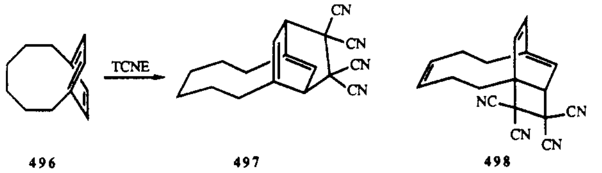
Whichever it is, it clearly arises from a Cope rearrangement (of either **484** or **485**) which is analogous to the formation of **466** from **465**. On the basis of DS values,[78] one would guess that **484**, a type III diene, was present. The lowest homologue studied, **487**, gave three ring-opened products (**491**–**493**) which could have arisen from retroene reactions of bridgehead dienes **488** and **489**, plus a [1,5]H shift from one of the products. Although the latter (**492** → **493**) undoubtedly occurred, further experiments pointed to a retroene reaction of the bridgehead alkene precursor, **487**, to give **490** (**238a** thermally gave the alcohol related to **490** under conditions where **487** gave **491**–**493**, and at about the same rate), which then eliminated HOAc to give **491** and **492**. The apparent failure to generate (or certainly instability of) **488** and **489** is consistent with their high calculated SE's. For instance, **489** is calculated to be about 4 kcal/mol less stable than **104**.[78]



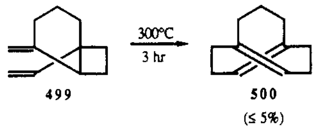
The related pyrolysis of **169b**[100] also gives only one bridgehead diene, namely the type III **494**. Remember that the closely analogous **478** gave a 1:1 mixture of the analogues of **494** and **495**. Clearly some very subtle effects are at work here. It would be interesting to know the DS values for **475**, **476**, **479**–**481**, **494**, and **495**.



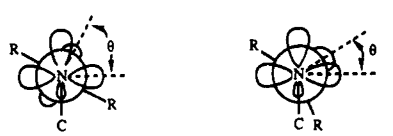
Tobe formed a bridged analogue of **479**, **497**, from the Diels–Alder reaction of [6]paracyclophane (**496**) with TCNE.[178] But the reaction resisted generalization, since (*Z*)-[6]paracycloph-3-ene gave [2 + 2] cycloadduct **498**.



In characteristic systematic fashion, Shea tried to extend the Cope rearrangement route to type III dienes.[92] But as with **465**, further rearrangement to a bis-methylenebicyclo[*m*.*n*.0] system thwarted isolation of the bridgehead diene. When the Cope process was not possible, a major alternative fragmentation channel (the retro [2 + 2]) was chosen by **499**, but a small amount of material with properties consistent with **500** was isolated.



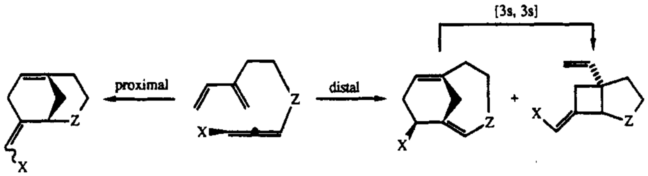
A more efficacious procedure was recently employed in the Shea group,[179] namely distal intramolecular Diels–Alder reaction of an allene (**501**) to give mainly **502** and its Cope rearrangement product, **504**; proximal adduct **503** was, at best, a minor product. In addition to the [4.3.1] systems, two [5.3.1] systems (**505** and **506**) and a [7.3.1] system (**507**) were made. Interestingly, the UV maximum decreased as ring size increased—a sure sign of decreased transannular interaction with decreasing strain. Since the details of this approach are not widely known yet, there remains the intriguing possibility that when the TS is approached from an alignment as in **509**, either **505** or **508** may be accessible



513 514

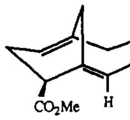
Figure 2. Left: Partially twisted, unrehybridized at C, imine. Right: Partially twisted, carbon-rehybridized imine. Note that both **513** and **514** are *chiral.*

as a function of which way the terminal allenic carbon rotates.

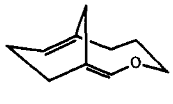


503 501 502 504

		502	504
160°C, 2 h:	a, $Z = CH_2$; $X = CO_2Me$	40%	26%
220°C, 1.5 h:	b, $Z = CH_2$; $X = H$	75% (λ_{max} = 247 nm)	
160°C, 2 h:	c, $Z = O$; $X = H$	42%	~40%

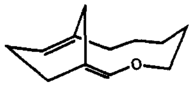


505



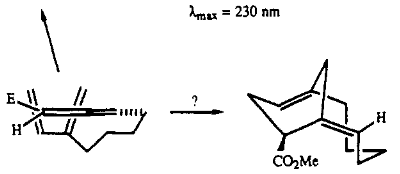
506

λ_{max} = 230 nm



507

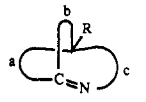
λ_{max} = 220 nm



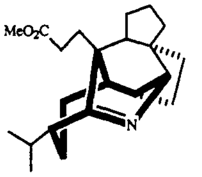
509 508

D. Systems with C=N Bridgehead Double Bonds

In order to incorporate a carbon–nitrogen double bond at a bridgehead, the carbon must be placed at the bridgehead, thereby producing the imine represented by **510**. The chemistry of such species dates from only 1970, when **511** was prepared from methyl homosecodaphnyphyllate;[180] **511** is obviously an analogue of bicyclo[3.3.1]non-1-ene (**4**). As with the all-carbon systems, work in this area initially focused mainly on trapping experiments, followed by direct observational studies more recently. Aspects of these various studies have been recently reviewed,[83a,181] so the discussion here has been abbreviated, although the coverage is complete.



510



511

1. Structural Considerations

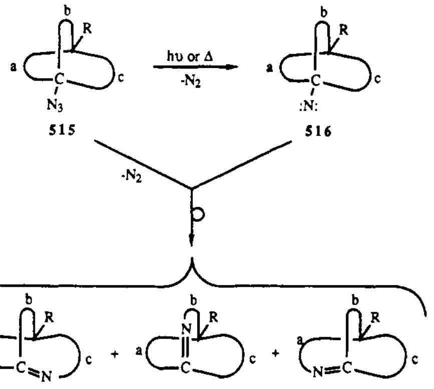
As with the all-carbon compounds, the bridgehead sp^2 carbon of **510** may rehybridize, but this concept has no meaning for the nitrogen, since it is only dicoordinate. Rather one can define the angle of twisting between the nitrogen and carbon orbitals (θ, Figure 1, bottom), and the C–N–C valence angle (Φ, Figure 1, top). As shown in Figure 1, there are two possible $Z \rightarrow E$ isomerization processes. The first is an inversion, where the valence angle, θ, increases to 180° and then decreases again to the normal value. But θ remains at 0° throughout, meaning that π bonding is not interrupted. This process is expected to have the lower barrier. In the purely rotational isomerization, θ goes from 0° to 90° and back to 0°. At 90°, there is π bonding between the p_C and n orbitals (so long as $\Phi > 90°$), while the lone pair on N is in the p_N orbital. This situation is quite different from the all-carbon system, where no nonbonding orbital is available. As is shown in Figure 1, rehybridization at C_1 is possible and will affect the equilibrium structure of twisted imines (see Figure 2). Since both θ and Φ may vary independently, an infinite number of combinations of the two isomerization paths are possible. The strength of the p_C–n interaction is a function of the degree of p character of the n orbital, wherefore this interaction obviously increases as Φ increases. In bicyclic systems, one can expect a compromise between the positive bonding effect of increasing Φ and the deleterious effect such an increase has on the overall molecular architecture; in fact, the calculated Φ's for bridgehead imines are all *smaller* than for acyclic imines.[83a]

Michl has noted[83a,182] that the S_1 (nπ*) excited state of imines *decreases* in energy as θ goes from 0° to 90°. This means that the nπ* excitation energy should (and does) decrease on going to increasingly twisted bridgehead imines.

As far as strain energy is concerned, the assumption has been that the imine values mimic the alkene values. In a qualitative sense, at least, the experimental evidence supports this assumption, in terms of both apparent stability (reactivity) and effect on bond energy (as judged by IR stretching frequencies[83a]).

2. Experimental Studies

With a few exceptions (vide infra), bridgehead imines have been generated via photolysis or thermolysis of bridgehead azides (**515**). While nitrenes are intermediates in these reactions[183] and have been observed in matrix isolation experiments,[184–186] it is possible that concerted rearrangement/N_2 evolution might occur in some cases or that concerted rearrangement and nitrene rearrangement may occur in parallel. The picture is also cloudy with respect to migratory selectivity. Some systems appear to be highly selective,[187] while others give statistical product ratios,[188,189] while still others



515 516

510 510a 510b

CHART II. Imines Generated in Solution or Gas-Phase Experiments

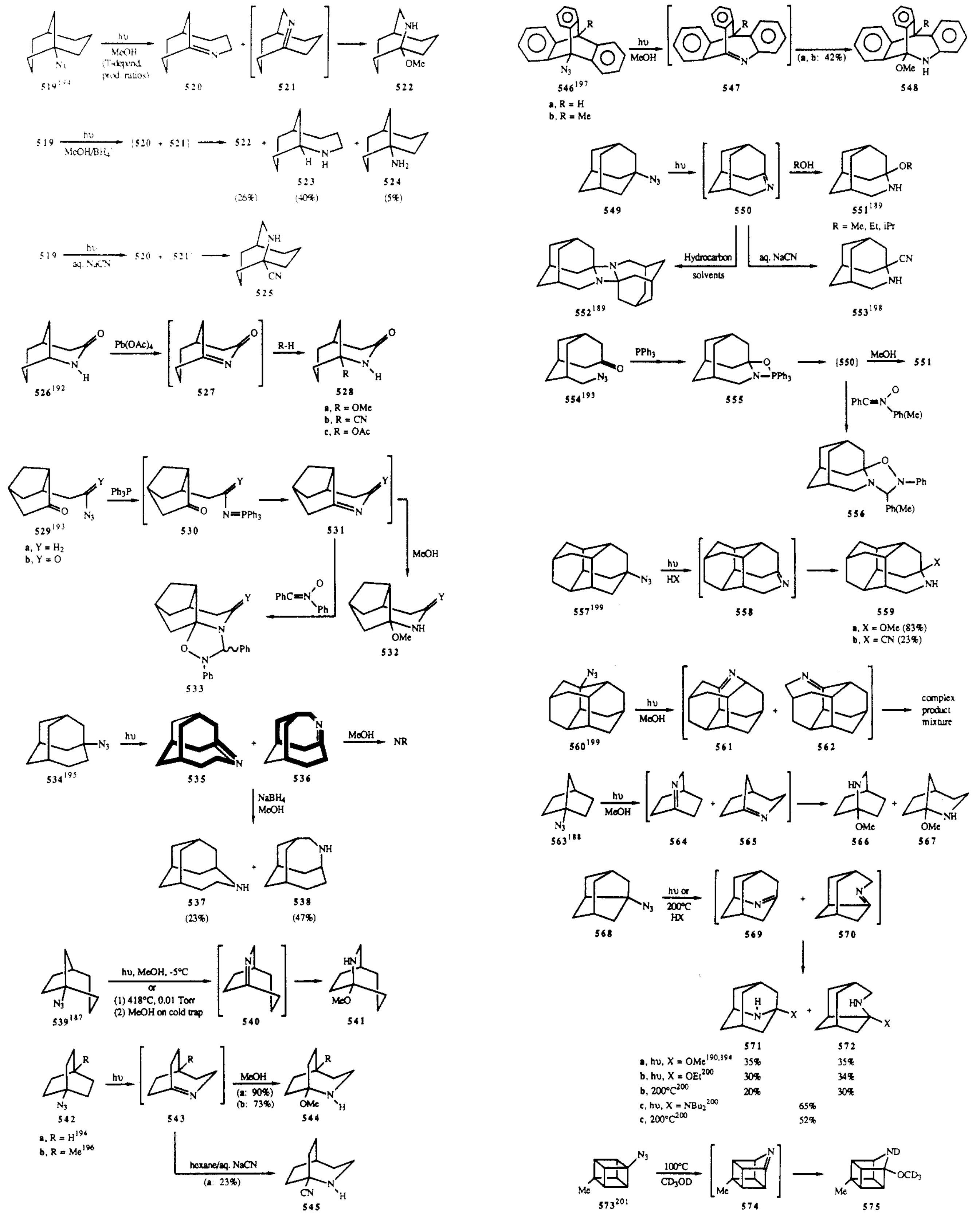
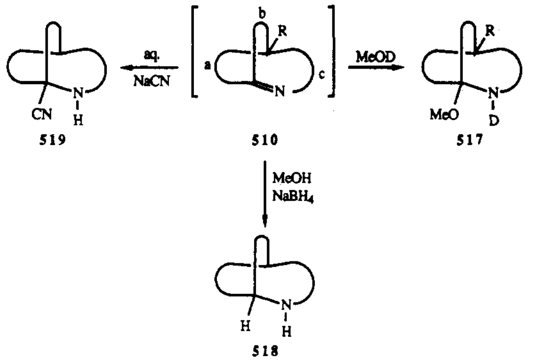


exhibit partial selectivity.[186,190] The selectivities, or lack thereof, do not separate according to the thermal vs photochemical nature of the reaction, nor do they appear to follow the Abramovitch–Kyba model[191] for azide rearrangements.

Two other synthetic procedures have been utilized. These are (a) $Pb(OAc)_4$ oxidation of an appropriate lactam[192] and (b) an intramolecular aza-Wittig reaction.[193]

In the nonmatrix isolation experiments, the general strategy has been to carry out the reactions in methanol, methanol/$NaBH_4$, or aqueous NaCN, to give **517**, **518**, or **519**, respectively. Some of the imines dimerize or have been trapped as cycloadducts. Some, relatively



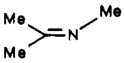
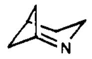
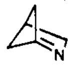
stable ones can be observed or isolated and may react with some, but not all, of the added reagents. Chart II gives a complete listing of the systems studied in the above fashion. Inspection of the structures contained therein reveals that bridgehead imines with double bonds transoid in nine- (**520**), eight- (**521**, **527**, **531**, **535**, and **536**), seven- (**540**, **543**, **547**, **550**, **558**, **561**, **562**, **565**, and **570**), six- (**564** and **569**), and even five-membered (**574**) rings have been generated.

Since one may write a mechanism for the formation of addition products that does not involve bridgehead imines (i.e., a nitrene, **516**, may be protonated, followed by a 1,2-C shift to a bridgehead cation), recent emphasis has been placed on direct observation of those bridgehead imines that are too unstable to isolate.[83,184-186,201-203] The experiments involved photolysis of the precursor azides, **515**, in Ar, N_2, and/or polyethylene matrixes at 10–15 K or in a 3-methylpentane glass at 77 K. The resulting imines (and other species, such as nitrenes) were then spectroscopically probed in the IR and UV and sometimes via ESR and CD measurements. Annealing of the matrixes usually led to reactions, the products of which were analyzed. The specific systems so far studied in this fashion are **542b**,[202] **549**,[83,185,202] **563**,[186,203] **568**,[184] and **573**.[201]

4-Azahomoadamant-3-ene (**550**), the major product from **549**, was thoroughly studied. In addition to IR, Raman, and UV absorption spectra of both normal and ^{15}N-labeled **550**, **550** was photoresolved to 2% optical purity by irradiation with circularly polarized light.[185] This result could be achieved at 12 K or at ≥160 K in a polyethylene matrix. But CD measurements, which verified the chirality, were necessary at 160–200 K. The reason is that at those temperatures rotational motion of **550** is rapid, thereby relieving problems associated with lasting linear dichroism, whereas translational motion is still prohibited, thereby preventing dimerization (which was otherwise rapid below 60 K). Since racemization of **550** prior to dimerization (to **552**) could not be observed, the minimum activation energy for racemization is 17 kcal/mol (simple imines have a 25–30 kcal/mol $Z \rightarrow E$ isomerization barrier). Additionally, the adamantylnitrene was observed as a minor byproduct via ESR. The triplet signal was destroyed upon prolonged irradiation, whereas the **550** signals (IR, UV) persisted. This demonstrated that the ESR spectrum was not due to the imine. The nitrene was also chemically trapped by CO via irradiation at 34 K (where **550** was *stable*) to give the isocyanate.

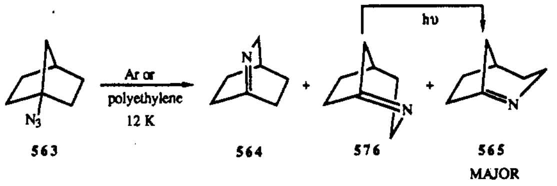
The photochemistry of **563** was also very revealing. Initial studies[203] allowed the observation of only the C=N absorption of **565** (Ar, 10 K), but warming a matrix doped with MeOH (or irradiating a so-doped

TABLE V. Some Data for Bridgehead Imines[83a]

	calcd[a] geometry,[b] deg			C=N stretching freq, cm^{-1}		transoid double-bond ring size
compd	θ	Φ	ω	calcd[a]	exptl[c]	
 **579**	0	126	0	(1669)[d]	1669	
565	39	114	13	1591	1586	7
543a	48	117	9	1595	1597	7
570	51	115	11	1585	1591	7
550	52	118	8	1594	1600	7
 **580**	54	102	17	1489	?	6
 **581**	61	108	18	1530	?	6
564	69	108	12	1493	1480	6
576	74	112	13	1523	1475	6
569	77	110	12	1472	1451	6
 **582**	84	96	23	1396	?	5
574	85					5

[a] MNDO. [b] θ = double-bond twist angle, Φ = N valence angle, ω = bridgehead carbon pyramidalization angle. [c] In Ar matrixes. [d] Calculated values for the bridgehead imines were scaled to the correction necessary for the acyclic case (a factor of 0.854).

3-methylpentane glass at 65 K) produced a 13:1 mixture of **567** and **566**. But later work[186] showed that three bridgehead imines were formed: (a) **565**, the major product; (b) **576**, the (orange) geometrical isomer of **565**, which was isomerized to **565** upon further irradiation with visible or UV light; and (c) the orange [2.2.2] product, **564**, which was also destroyed by visible light. The highest observed **576**:**565** ratio was about 1:20; this ratio was dependent upon the irradiation conditions.



When **568** was irradiated in an Ar or polyethylene matrix at 12 K, a red and a colorless product were formed. The red one was photosensitive (488 nm) and reacted with MeOH (MeOH-doped Ar matrix) at 36 K to give **571a**, whereas the colorless species gave **572a**, but not until a temperature of 90 K. Thus the red species is clearly 2-azaadamant-1-ene (**569**), while the colorless one is 4-azaprotoadamant-3-ene (**570**). The significantly greater stability of **570** indicated that it was formed as a *trans*-cycloheptenoid (not *trans*-cyclohexenoid) species. This was also borne out by the different IR C=N stretching frequencies observed for **569** (1451 cm^{-1}) and **570** (1591 cm^{-1}).

The matrix photochemistry of **573** was not supportive of the formation of **574**. Although minor bands that may yet prove to be due to **574** were observed, the only identifiable product was **578**, formed either directly from **577** or possibly from **574** (perhaps photochemically).

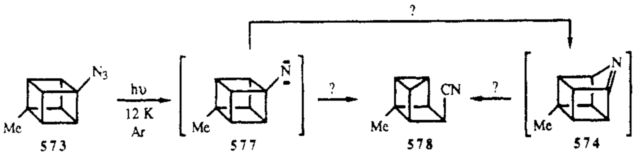
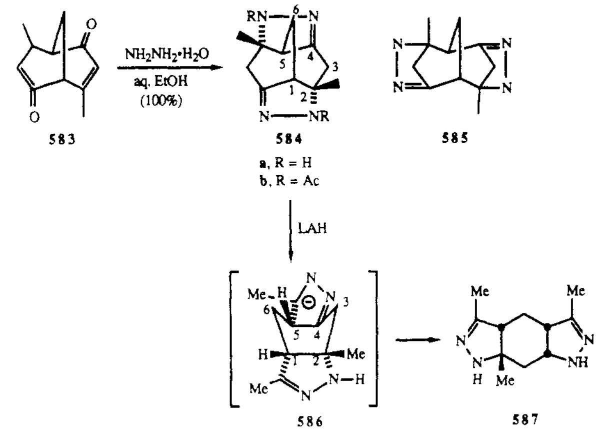
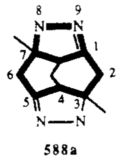


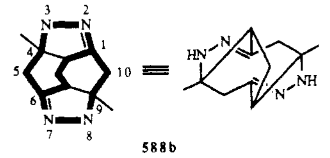
Table V gives a summation of some geometrical (calculated) and vibrational data for a series of bridgehead imines.[83a] In general, there is an excellent linear correlation between $\nu_{C=N}$ and cos θ, although **580** appears to be an exception. A rough rule of thumb is that a *trans*-cycloheptenoid bridgehead imine will have its $\nu_{C=N}$ decreased by 100 cm^{-1}, while a *trans*-cyclohexenoid will show a 200-cm^{-1} decrease. The ultimate, orthogonal case, where (as discussed in the structural section) π bonding is still present, should show about a 300-cm^{-1} C=N stretching frequency decrease, which would still be considerably higher than the C–N stretching frequency.

A correlation of cos θ with electronic excitation energies (nπ* and ππ*) has also been noted.[83a]

Lastly, one case of a double bridgehead imine is known.[204] Thus reaction of **583** with hydrazine hydrate gave bishydrazone **584a** quantitatively; **584a** was air sensitive, but otherwise stable. Acetylation product **584b** was stable to air and at room temperature for months, thereby eliminating alternative structure **585** (which is *trans*-cycloheptenoid). The stereochemistry of **584** was demonstrated via its reductive ring opening to **587**. Diimine **584** has a dual persona. As shown by **588a**, it is a *trans*-cyclononenoid bridgehead imine—twice. But as illustrated by **588b**, it is a type III *trans,trans*-cyclodecadienoid bridgehead diimine. In any case, it is not strained. As indicated by its difficult-to-hydrogenate character, it is actually hyperstable.




588a


588b

IV. Conclusion

Considerable progress in the synthesis of bridgehead alkenes, dienes, and imines has been made throughout the 1980s. One can now point to an experimental and theoretical relationship between twist angle and C=N stretching frequency or electronic excitation energy for a fairly complete series of bridgehead imines. The expected analogous relationship for the bridgehead alkenes has only been partially demonstrated. The concept of rehybridization has been demonstrated via spectroscopy (X-ray, IR) for several of these compounds and is now taken for granted.

Much work remains. The reaction chemistry of many of these species has not been explored; synthetic applications have only recently begun to be taken seriously. There is no direct observational evidence for any of the *trans*-cyclopentenoids and no evidence of any kind for *trans*-cyclobutenoids. Also, no really strained bridgehead dienes have been generated. Lastly, very close to orthogonal bridgehead double bonds, particularly C=C, have not been synthesized.

Thus major synthetic and physical organic challenges remain and will undoubtedly be addressed as chemists continue to push back the frontiers of structural possibilities.

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