to give *o*-thioquinonemethide (**63**) which, by valence tautomerization, gives benzo[*b*]thiete (**64**). That valence tautomerization occurs much more readily with the sulfur analogue **64** than in the parent benzocyclobutene case is shown by the easy reaction of benzo[*b*]thiete (**64**) with boiling cyclohexene, presumably via **63**, to give the Diels–Alder adduct **65**. Heating **64** in the absence of a dienophile results in dimerization to **66**, in close analogy to the behavior of benzocyclobutene.[38]

When a similar gas-phase pyrolysis of *N*-phenyl-*o*-(hydroxymethyl)aniline (**67**) was carried out, the product was not the expected *N*-phenylbenzo[*b*]azetine (**69**)[57] but was, instead, acridine (**71**).[55] Apparently, the
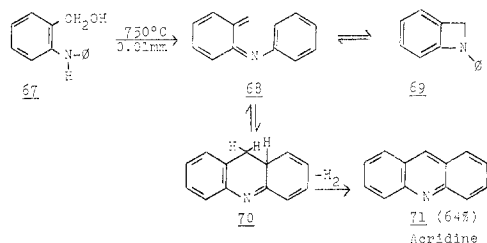
intermediate *o*-quinonemethide imine (**68**) undergoes

(55) Y.-L. Mao, Doctoral Dissertation, University of Oregon, 1979.
(56) W. J. M. van Tilborg and R. Plomp (*Recl. J. R. Netherlands Chem. Soc.*, 96, 282 (1977)) have described the preparation of benzo[*b*]thiete in 45% yield by the gas-phase pyrolysis of thianaphthene 1,1-dioxide at 1000 °C.
(57) E. M. Burgess and L. McCullagh, *J. Am. Chem. Soc.*, 88, 1580 (1966).

triene cyclization to **70**, followed by an irreversible thermal dehydrogenation to acridine.

Although the yield of acridine in this pyrolytic, one-step synthesis is good, it seemed that in terms of the proposed mechanism it would be improved if the starting material were at the right oxidation level to avoid the thermal dehydrogenation. This proved to be true. When *N*-phenylanthranilic acid (**72**) was pyrolyzed at 750 °C, acridone (**74**) was isolated in 87% yield.
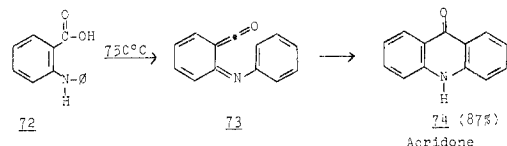
Presumably, in this case loss of water gives the ketene imine **73** which, by triene cyclization followed by tautomerization, gives acridone (**74**) directly.

The results of these preliminary studies suggest that the pyrolytic formation of hetero analogues of *o*-xylylenes and their use in synthesis has considerable potential. However, the more important conclusion is that gas-phase pyrolysis is a synthetic method of general utility. It is usually clean, convenient, and efficient, and frequently has advantages over other synthetic methods for accomplishing the same goals.

Benzocyclobutene and Related Compounds

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Received July 26, 1979

Benzocyclobutene and related compounds represent a unique compromise between the thermodynamic stability associated with a benzenoid aromatic system and the kinetic reactivity of a strained cyclobutene. In the next lower homologue, benzocyclopropene, reactivity is the dominant feature while the next higher homologue, indan, is too unreactive toward ring opening to be of much interest.

Physical and chemical studies have been directed primarily at determining how the fused benzene and cyclobutene rings interact with one another. Early efforts in this area were comprehensively reviewed by Klundt.[1] For synthetic as well as mechanistic reasons, there has recently been a new surge of interest in benzocyclobutene chemistry. This Account chronicles some of the more salient features of this resurgence.

Synthesis

The first synthesis of a benzocyclobutene derivative was reported by Finkelstein in 1910,[2] but it was not until 1956 that Cava and Napier succeeded in preparing the parent compound.[3] Since that time this once thought to be elusive molecule has been prepared by a variety of approaches. We will look at three recently developed methods which complement each other in their design. The pyrolytic approach starts with the aromatic ring intact and closes one or more fused rings. The Diels–Alder approach starts with the small ring intact and builds up the aromatic nucleus. Finally, the cooligimerization route creates both rings simultaneously.

Very early in the history of benzocyclobutene, it was discovered that pyrolytic methods could be employed for straightforward access to this compound from easily available starting materials. Cava and Deana showed

(1) I. Klundt, *Chem. Rev.*, 70, 471 (1970).
(2) H. Finkelstein, *Chem. Ber.*, 43, 1528 (1910).
(3) M. P. Cava and D. R. Napier, *J. Am. Chem. Soc.*, 78, 500 (1956).

that passing 1,3-dihydroisothianaphthene 2,2-dioxide (2) over a nichrome wire heated to 770 °C produced benzocyclobutene (3) in 67% yield.[4] Optimization of
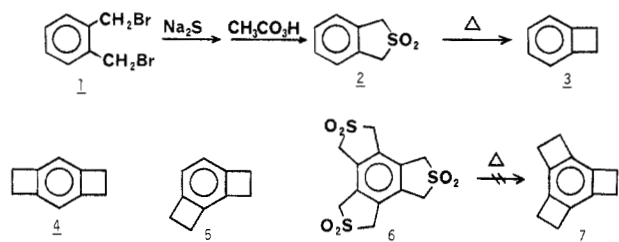
this approach has provided for the efficient and economical preparation of benzocyclobutene in an overall yield of 56% for the three steps.[5] A double-barreled version of this approach has been successful in providing the benzodicyclobutenes **4**[6] and **5**,[7] albeit in somewhat lower yields. Extension of this reaction to the preparation of tricyclobutabenzene (**7**) has so far been unsuccessful.[8] A similar extrusion reaction occurs with the tellurophene **8** at 500 °C to give a 74% yield of benzocyclobutene.[9] Naphtho[*b*]cyclobutene (**9**) may be prepared in a similar fashion by the extrusion of either SO_2 or Te.[9,10]
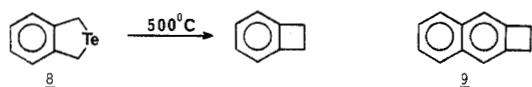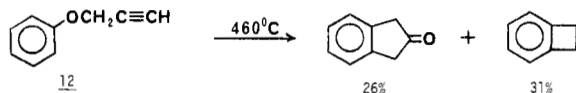

Spangler and co-workers have shown that CO can be extruded from 3-isochromanone (**11**) at 565 °C to provide up to an 85% yield of benzocyclobutene.[11] This
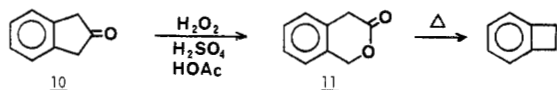
same reaction is also successful with a variety of oxygenated substituents. Since 3-isochromanone can be obtained in 68% yield by the Baeyer–Villiger oxidation of 2-indanone, this method appears comparable to the SO_2 extrusion route; moreover, it involves only two steps.
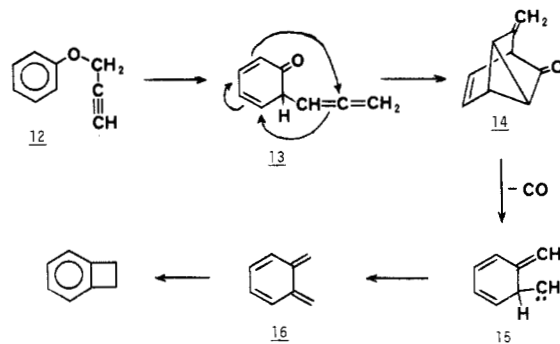
Trahanovsky and associates have reported that the pyrolysis of phenyl propargyl ether (**12**) at 460 °C produces benzocyclobutene as well as 2-indanone.[12]


The fact that 2-indanone does not extrude CO under the reaction conditions led them to propose a mecha-

nism involving initial Claisen-type rearrangement to an allene which then undergoes a thermally allowed conversion to the tricyclic ketone **14**. Loss of CO provides

a carbene which undergoes C–H insertion and ring closure to provide benzocyclobutene. Although this reaction is chiefly remarkable for its mechanistic interest, the analogous reaction for propargyl 4-pyridyl ether (**17**) does provide an extremely useful preparation for both isomers of cyclobutapyridine.[13] A mechanism similar to that set forth above is postulated for the formation of **18** and **19**.
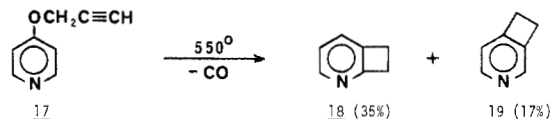
In 1960 Hart and Fish discovered that the thermal elimination of HCl from **20** gave a high yield of benzocyclobutene **21** which could then be hydrolyzed to the benzocyclobutenone **22**.[14] It appears that the but-

tressing effect of the four methyl groups is important to the success of the reaction. Very recently this process has been rediscovered by Schiess at the University of Basel and Boekelheide at the University of Oregon and their co-workers. These workers find that pyrolysis of commercially available 2,4,6-tris(chloromethyl)mesitylene (**23**) at 660–800 °C gives hexaradialene (**24**) in yields of up to 60% based on the isolation of a suitable adduct with hydrogen or bromine.[7,15] Once again no tricyclobutabenzene (**7**) is detected in this reaction. At somewhat lower temperatures, however, **25** and **26** are

formed as the result of mono- or bisdehydrochlorination and subsequent ring closure. Schiess and Heitzmann have shown this technique to be readily adaptable to the preparation of a variety of benzocyclobutenes[16] as

(4) M. P. Cava and A. A. Deana, *J. Am. Chem. Soc.*, **81**, 4266 (1959).
(5) J. A. Oliver and P. A. Ongley, *Chem. Ind. (London)*, 1024 (1965).
(6) M. P. Cava, A. A. Deana, and K. Muth, *J. Am. Chem. Soc.*, **82**, 2524 (1960).
(7) E. Giovannini and H. Vuilleumier, *Helv. Chim. Acta*, **60**, 1452 (1977).
(8) L. G. Harruff, M. Brown, and V. Boekelheide, *J. Am. Chem. Soc.*, **100**, 2893 (1978).
(9) E. Cuthbertson and D. D. MacNicol, *Tetrahedron Lett.*, 1893 (1975).
(10) M. P. Cava and R. L. Shirley, *J. Am. Chem. Soc.*, **82**, 654 (1960).
(11) (a) R. J. Spangler and J. H. Kim, *Synthesis*, 107 (1973); (b) R. J. Spangler, B. G. Beckmann, and J. H. Kim, *J. Org. Chem.*, **42**, 2989 (1977); (c) R. J. Spangler and B. G. Beckmann, *Tetrahedron Lett.*, 2517 (1976).
(12) (a) W. S. Trahanovsky and P. W. Mullen, *J. Am. Chem. Soc.*, **94**, 5911 (1972); (b) J. M. Riemann and W. S. Trahanovsky, *Tetrahedron Lett.*, 1863 (1977).
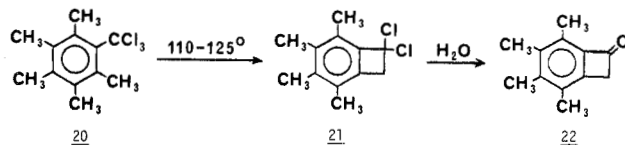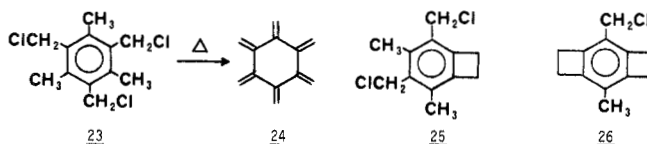
(13) (a) J. M. Riemann and W. S. Trahanovsky, *Tetrahedron Lett.*, 1867 (1977); (b) R. P. Thummel and D. K. Kohli, *J. Org. Chem.*, **43**, 4882 (1978).
(14) (a) H. Hart and R. W. Fish, *J. Am. Chem. Soc.*, **82**, 749 (1960); (b) H. Hart, J. A. Hartlage, R. W. Fish, and R. R. Rafos, *J. Org. Chem.*, **31**, 2244 (1966).
(15) P. Schiess and M. Heitzmann, *Helv. Chim. Acta*, **61**, 844 (1978).

well as of benzocyclobutenones when the chloromethyl substituent is replaced by a chloroacyl group.[17]

This facile entry into synthetically useful quantities of unusual benzocyclobutenes has already led to some fascinating fused aromatic systems. Starting with the bromo analogue of **26**, Boekelheide et al. have employed his well-established dithiacyclophane methodology to prepare [2.2](3,6)benzo[1,2:4,5]dicyclobutenophane (**27**).[18] Pyrolysis of this material at 900 °C was hoped
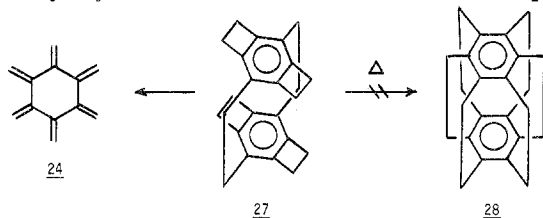

to lead to the "superphane" **28** but instead gave only hexaradialene.

These studies have been extended to the corresponding naphthalenes by Hart and co-workers.[19] They find that pyrolysis of either **29** or **30** at 620–640 °C gives a 15% yield of **33** as a yellow crystalline com-

X = CH₃

Z = CH₂Cl
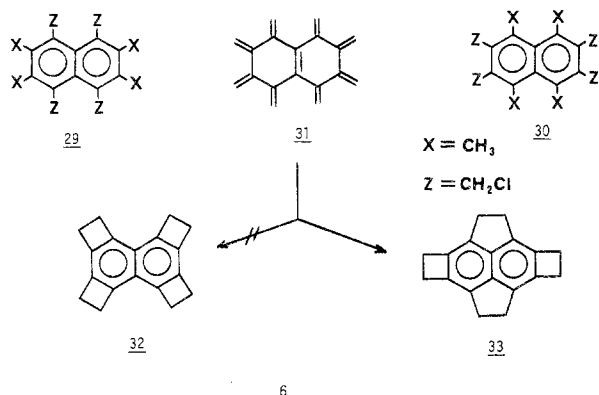
pound, mp 175–176 °C. The final distinction between structures **32** and **33** required an X-ray crystal analysis. There is some evidence for the intermediacy of naphtharadialene **31**, but further support for this species must be awaited.

This approach has also been applied to a heteroaromatic system with the preparation of [2,3:5,6]dicyclobutapyridine (**35**).[20] It is most likely that the ring closures involved in this process occur in a stepwise fashion since no convenient radialene-type intermediate can be drawn.
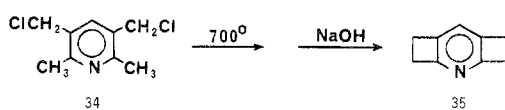
Although pyrolytic eliminations have certainly facilitated the preparation of a number of unusual molecules, shortcomings are apparent in the attempted preparation of molecules such as **7** and **28** which may be unstable at high temperature. Furthermore the direction of ring closures is not always predictable, as

demonstrated by the failure of **32** to be formed.

The development of a Diels–Alder approach to benzocyclobutenes has provided a useful route to many annelated derivatives under much milder conditions. The key starting material for these syntheses is dimethyl cyclobutene-1,2-dicarboxylate (**36**) which can be readily prepared from adipic acid.[21] The general scheme for this approach is illustrated below for the preparation of benzocyclobutene. Cycloaddition of butadiene to **36** occurs smoothly at 100 °C to give an 80% yield of adduct **37**.[22] Although both ester func-

tions in **37** are sterically hindered, they may be readily hydrolyzed by refluxing with KOH in aqueous methanol followed by acidification. Treatment of **38** with 1 equiv of lead tetraacetate in Me₂SO gives mainly bicyclo-[4.2.0]octa-1(6),3-diene (**39**). If the amount of lead tetraacetate is doubled, a 57% yield of benzocyclobutene may be obtained directly.[23]

If the appropriate 1,2-dimethylenecycloalkane or 1-vinylcycloalkene is substituted into the above sequence, a variety of bisannelated benzenes such as 4, 5,[24] and **40–42** can be prepared.[25] The cycloaddition
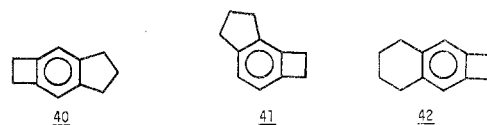
reaction works equally well with 1,2-dicyanocyclobutene, but the hydrolysis step requires more severe conditions. The ring strain inherent in **36** is critical to its reactivity, so that the corresponding cyclopentene diester is by comparison far less reactive. By employing bicyclic dienes, trisannelated benzenes may be prepared.

The ultimate application of this approach is the synthesis of tricyclobutabenzene (**7**), mp 141–142 °C,

from the reaction of **36** with 1,1′-dicyclobutenyl (**43**).[26] In this sequence substantial ring strain is incorporated

(16) P. Schiess, M. Heitzmann, S. Rutschmann, and R. Stäheli, *Tetrahedron Lett.*, 4569 (1978).

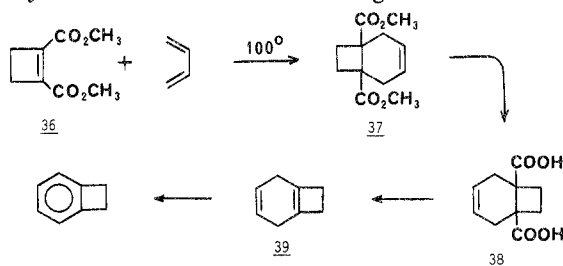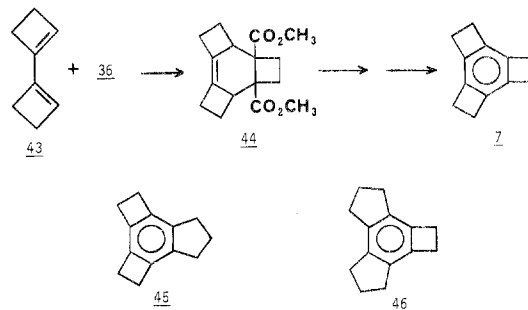(17) P. Schiess and M. Heitzmann, *Angew. Chem., Int. Ed. Engl.*, 16, 469 (1977).

(18) R. Gray, L. G. Harruff, J. Krymowski, J. Peterson, and V. Boekelheide, *J. Am. Chem. Soc.*, 100, 2892 (1978).

(19) H. Hart, M. Jeffares, A. Teuerstein, and D. L. Ward, *J. Am. Chem. Soc.*, 100, 8012 (1978).

(20) R. P. Thummel and D. K. Kohli, *Tetrahedron Lett.*, 143 (1979).

(21) R. N. McDonald and R. R. Reitz, *J. Org. Chem.*, 37, 2418 (1972).

(22) E. Vogel, O. Roos, and K. H. Disch, *Justus Liebigs Ann. Chem.*, 653, 55 (1962).

(23) R. P. Thummel, *J. Chem. Soc., Chem. Commun.*, 899 (1974).
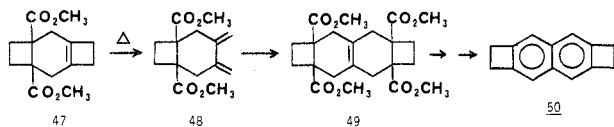
(24) R. P. Thummel, *J. Am. Chem. Soc.*, 98, 628 (1976).

(25) R. P. Thummel and W. Nutakul, *J. Org. Chem.*, 42, 300 (1977).

(26) W. Nutakul, R. P. Thummel, and A. D. Taggart, *J. Am. Chem. Soc.*, 101, 770 (1979).

into the reacting partners of the initial cycloaddition reaction which is then accompanied by some relief of strain while establishing the tetracyclic framework of the molecule in a single step. The final aromatization profits from the resonance energy gained by the system and, most importantly, this final step can be carried out under relatively mild conditions (<40 °C). The higher homologues 45[27] and 46[28] have been prepared by the use of 1-(1-cyclobutenyl)cyclopentene and 1,1'-dicyclopentenyl instead of 43 in the same sequence.

It was discovered that 47, which is the cycloadduct precursor to 4, underwent thermal opening of the cyclobutene ring to provide 48 which could then add a second molecule of 36 to provide the tetracyclic tetraester 49. Hydrolysis to the tetraacid followed by ox-

idative decarboxylation and aromatization gave naphtho[b,e]dicyclobutene (50).[29] A similar route which combines the Diels–Alder benzocyclobutene synthesis and the Billups benzocyclopropene synthesis has been employed by Garratt and Davalian to prepare the next lower homologue 51.[30]
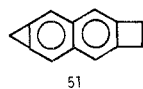
A third route to benzocyclobutene derivatives which has received some recent attention involves the cooligomerization of 1,5-hexadiynes and substituted acetylenes by (η^5-cyclopentadienyl)cobalt dicarbonyl.[31] For most substituents, R_1 and R_2, yields were only moderate, but when R_1, R_2 = SiMe$_3$, a 44% yield of 54
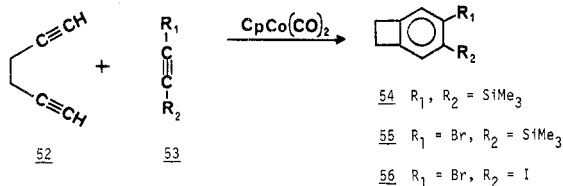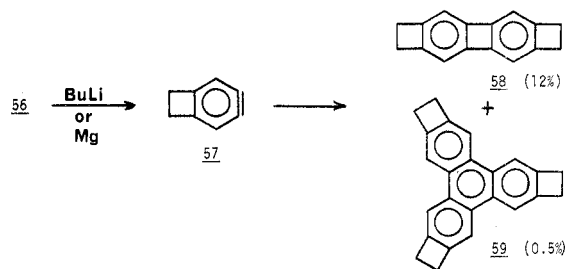

could be obtained.[32] The reaction appears to be quite sensitive to the scale on which it is run as well as the conditions employed, requiring syringe pump high-dilution techniques and air-free conditions. Nevertheless, bis(trimethylsilyl)acetylene is now commercially available, and various 3-alkyl-1,5-hexadiynes are also accessible by alkylation of 1,5-hexadiyne trianion. Appropriately substituted benzocyclobutenes available by this method can serve as important intermediates in the preparation of various interesting polycyclic systems.[33]

One of the greatest advantages of the cooligomerization approach is the susceptibility of the

trimethylsilyl groups to displacement by electrophiles in a selective and stepwise fashion. Careful treatment of 54 with 2 equiv of bromine gives the monobromo derivative 55, and subsequent treatment of this material with ICl gives 56.[34] When compound 56 is treated with butyllithium or Mg, the corresponding benzyne 57 can be generated, as evidenced by its dimerization to dicyclobutabiphenylene 58[35] and trimerization to tricyclobutatriphenylene 59.[36] If 1,5-hexadiyne is co-
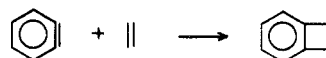

oligomerized with 53 where R_1 = CH$_2$OCH$_3$ and R_2 = SiMe$_3$, adduct 60 is obtained. The trimethylsilyl group can be replaced with bromine. Metalation with butyllithium and displacement of methoxide then lead to 1,2-cyclopropa-4,5-cyclobutabezene (61).[37] Garratt has
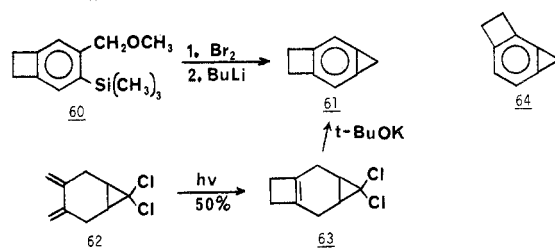
applied the Billups benzocyclopropene synthesis to compound 63 in an alternate preparation of 61.[38] This same approach works equally well for the 1,2:3,4-bisannelated isomer 64.[39]

Another direct entry to benzocyclobutenes which, however, suffers from relatively low yields is the [2 + 2] cycloaddition of o-benzyne to alkenes.[40] This ap-

proach is generally limited to o-benzyne without aromatic ring substituents. However, a variety of functionalized alkenes have been employed with moderate success. In particular, the adduct with vinyl acetate, available in 45% yield, has been shown to undergo dissolving metal reduction to benzocyclobutene in 42% yield.[41] Benzyne is more amenable to [4 + 2] cyclo-

(27) R. P. Thummel and A. D. Taggart, unpublished results.
(28) J. D. Korp, R. P. Thummel and I. Bernal, *Tetrahedron*, 33, 3069 (1977).
(29) R. P. Thummel and W. Nutakul, *J. Am. Chem. Soc.*, 100, 6171 (1978).
(30) D. Davalian and P. J. Garratt, *Tetrahedron Lett.*, 2815 (1976).
(31) K. P. C. Vollhardt, *Acc. Chem. Res.*, 10, 1 (1977).
(32) (a) K. P. C. Vollhardt and R. G. Bergman, *J. Am. Chem. Soc.*, 96, 4996 (1974); (b) W. G. L. Aalbersberg, A. J. Barkovich, R. L. Funk, R. L. Hillard III, and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, 97, 5600 (1975).
(33) R. L. Funk and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, 98, 6755 (1976).

(34) R. L. Hillard III and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, 99, 4058 (1977).
(35) R. L. Hillard III and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, 98, 3579 (1976).
(36) R. L. Funk and K. P. C. Vollhardt, *Angew. Chem., Int. Ed. Engl.*, 15, 53 (1976).
(37) C. J. Saward and K. P. C. Vollhardt, *Tetrahedron Lett.*, 4539 (1975).
(38) D. Davalian and P. J. Garratt, *J. Am. Chem. Soc.*, 97, 6883 (1975).
(39) D. Davalian, P. J. Garratt, and M. M. Mansuri, *J. Am. Chem. Soc.*, 100, 980 (1978).
(40) Early efforts in this area are reviewed by Klundt.[1] See also: (a) E. E. Waali, *J. Org. Chem.*, 40, 1355 (1975); (b) A. T. Browne, T. A. Christopher, and R. H. Levin, *Tetrahedron Lett.*, 4111 (1976); (c) M. A. O'Leary, M. B. Stringer, and D. Wege, *Aust. J. Chem.*, 31, 2003 (1978); (d) H. H. Wasserman and J. Solodar, *J. Am. Chem. Soc.*, 87, 4002 (1965).

additions and thus will add to 1,2-dimethylenecyclo-butane (65) or 1-vinylcyclobutene (67) to give adducts
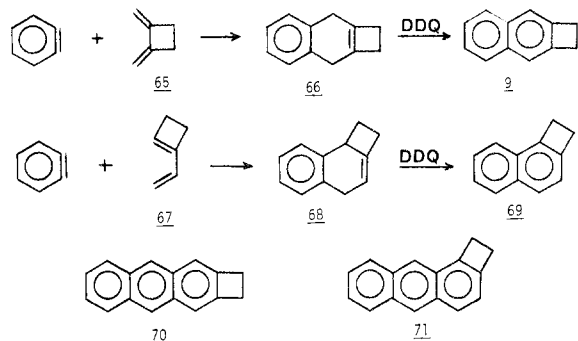
which can be oxidized to the isomeric naphthocyclo-butenes 9 and 69. Utilization of 2,3-dehydro-naphthalene in this same scheme provides the anthro-cyclobutenes 70 and 71, the smallest ring-fused anthracenes known to date.[42]

The rate of DDQ oxidation of 66 has been measured and is found to be about eight times faster than that of 68. Although a variety of factors may be involved, it appears attractive to invoke the steric relief of cyclobutene character in forming of 9 while the opposite might be true for 69.[43]

A benzyne-mediated intramolecular cyclization developed by Bunnett and Skorcz may be the most convenient nonpyrolytic route to 1-substituted benzocyclobutenes.[44] Treatment of the easily prepared *o*-chlorohydrocinnamonitrile (72) with sodamide presumably effects dehydrochlorination and proton loss to generate species 74 which then cyclizes to 75. Radlick
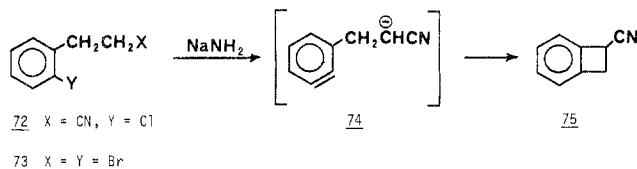
and Brown have found that lithium in liquid ammonia will reduce 75 to benzocyclobutene in 83% yield.[45] A somewhat related intramolecular cyclization involving aromatic metalation of 73 with *n*-butyllithium followed by attack at the β-bromomethyl group shows promise for preparation of various 1-substituted derivatives.[46]

Properties

From a physical organic point of view, the study of benzocyclobutene chemistry is particularly attractive in that one can examine the interaction of two distinct yet highly dependent substructures: the benzene ring and the cyclobutene ring. The chemical and physical properties of either portion are influenced to varying degrees by the other portion. We will examine some spectroscopic, structural, and chemical relationships

(41) J. H. Markgraf, S. J. Basta, and P. M. Wedge, *J. Org. Chem.*, **37**, 2361 (1972).
(42) R. P. Thummel, W. E. Cravey, and W. Nutakul, *J. Org. Chem.*, **43**, 2473 (1978).
(43) R. P. Thummel, and W. E. Cravey, and D. B. Cantu, submitted for publication.
(44) (a) J. F. Bunnett and J. A. Skorcz, *J. Org. Chem.*, **27**, 3836 (1962); (b) J. A. Skorcz, J. T. Shu, C. I. Judd, M. Finkelstein, and A. C. Conway, *J. Med. Chem.*, **9**, 656 (1966).
(45) P. Radlick and L. R. Brown, *J. Org. Chem.*, **38**, 3412 (1973).
(46) (a) P. D. Brewer, J. Tagat, C. A. Hergrueter, and P. Helquist, *Tetrahedron Lett.*, 4573 (1977); (b) W. E. Parham, L. D. Jones, and Y. A. Sayed, *J. Org. Chem.*, **41**, 1184 (1976).

Table I
Carbon-13 and Proton NMR Data for the
Aromatic C-H of Benzo[1,2:4,5]dicycloalkenes[49]

76, *m,n*	C-3[a]	H-3[a]	J_{C-H}[b]
a, 2,2	117.3	6.64	160.2
b, 2,3	118.9	6.91	158.7
c, 2,4	122.9	6.68	157.3
d, 3,3	120.0	7.08	155.1
e, 4,3	124.8	6.91	153.8
f, 4,4	134.1	6.74	152.3

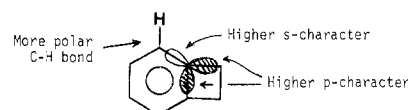[a] In ppm downfield from Me₄Si. [b] In Hz ± 0.4.

Figure 1.

and attempt to rationalize behavior in terms of the bonding properties of the system.

After some initial controversy, the ¹H and ¹³C chemical shifts of the benzocycloalkenes were assigned and several general trends were pointed out.[47] It is noted that benzocyclopropene does not correlate well with its higher homologues, and this behavior is attributed to the substantial shielding effect of the cyclopropene ring system.[48] One is therefore limited to comparison of only three systems, benzocyclobutene, indan, and tetralin, to establish trends in the NMR data. This situation has been improved, however, with the preparation and study of 1,2:4,5-bisannelated benzenes 76 where accurate assignments can be made with facility and the annelation can be varied in "half-steps" to provide a wider base for comparison.[49]

Table I summarizes some of the pertinent NMR data for this series of compounds. It may be seen that the unsubstituted aromatic carbon moves upfield with increasing strain from a value of 134.1 ppm for 76f to 117.3 ppm for 76a. Compound 76c, in which the annelated rings differ by two methylene units, is consistent in both the series f > e > c and c > b > a where one ring is held constant and the other is varied. The aromatic C-H coupling constant increases consistently from a low value of 152.3 Hz for 76f to 160.2 Hz for 76a.

Both of these trends can be adequately explained by a rehybridization theory set forth by Streitwieser[50] and by Finnegan;[51] it asserts that for small-ring fused benzocycloalkenes the bridgehead carbon rehybridizes to use orbitals of higher p character in bonding to the small ring. This leaves an orbital of higher s character to bond to the ortho carbon, which results in an inductive polarization of the ortho aromatic C-H bond (see Figure 1). This theory adequately explains the

(47) (a) E. L. Motell, D. Lauer, and G. E. Maciel, *J. Phys. Chem.*, **77**, 1865 (1973); (b) H. Günther, G. Jikeli, H. Schmickler, and J. Prestien, *Angew. Chem., Int. Ed. Engl.*, **12**, 762 (1973); (c) W. Adcock, B. D. Gupta, T. C. Khor, D. Doddrell, D. Jordan, and W. Kitching, *J. Am. Chem. Soc.*, **96**, 1595 (1974).
(48) W. Adcock, B. D. Gupta, T. C. Khor, D. Doddrell, and W. Kitching, *J. Org. Chem.*, **41**, 751 (1976).
(49) R. P. Thummel and W. Nutakul, *J. Org. Chem.*, **43**, 3170 (1978).
(50) A. Streitwieser, Jr., G. Ziegler, P. Mowery, A. Lewis, and R. Lawler, *J. Am. Chem. Soc.*, **90**, 1357 (1968).
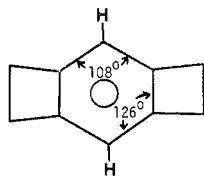(51) R. A. Finnegan, *J. Org. Chem.*, **30**, 1333 (1965).

Figure 2.

upfield shift of C-3 as well as the increase in the aromatic C–H coupling constant as the size of the annelated rings is decreased. As the aromatic C–H bond becomes polarized toward carbon, one would expect the hydrogen to become more acidic, which should result in lesser shielding and a shift to lower field in the NMR. This tendency is observed along the series **76f,e,d**, but the fusion of a cyclobutene ring onto benzene reverses the trend so that the aromatic proton of **76a** absorbs at unusually high field (6.64 ppm).

Aside from the rehybridization effect discussed above, a variety of other factors could be invoked to explain the trends observed in Table I. Geometric distortions of the benzene ring involving changes in bond lengths and bond angles might be important. An X-ray crystal study of **76a** has shown a severe pinching effect manifested by an opening of the interior bridgehead angle to 126° and a closing down of the interior angle at the unsubstituted carbon to 108°[52] (see Figure 2). The net result of this distortion is to move carbons 3 and 6 and their attached hydrogens away from the geometric center of the molecule. Such a move should decrease the paramagnetic deshielding effect experienced by this proton and perhaps account for its upfield chemical shift.

Anisotropy effects might also play an important role in establishing the trends of Table I. Such effects could result either from factors involving the local environment of the C–H bond or from perturbations of the aromatic ring current. To the extent that double bond fixation[53] might be found to occur in a benzenoid compound, a proton attached to the ring should appear to be more olefinic in nature and thus resonate at higher field in the NMR. Although this argument might at first seem appealing for a compound such as **76a**, it must be ruled out due to the high symmetry of the system where both Kekulé forms (**4a** and **4b**) are
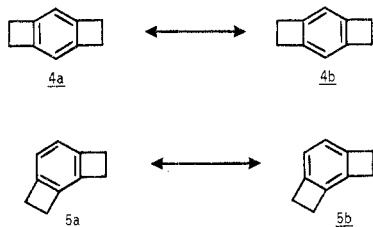

identical and must make equal contributions to the resonance hybrid. Although perturbation of the ring current is not necessarily ruled out, simple bond alternation does not appear possible.

If, however, the cyclobutene rings are fused in the 1,2:3,4 fashion, the valence bond isomers (**5a** and **5b**) are no longer equivalent. If one resonance form were found to contribute significantly more than the other

to the resonance hybrid, then bond fixation properties might become observable, as they are, for example, in naphthalene. If the 1,2:3,4 fusion of two cyclobutene rings induces some bond alternation, then the fusion of three rings in tricyclobutabenzene should make this effect more pronounced. The physical properties (NMR, IR, UV, and mass spectra) of **7** correlate exceedingly well with the higher homologues **45** and **46**, indicating this molecule to be a fully delocalized benzenoid system. The molecule is thermally stable up to 325 °C but is almost fully destroyed at 380 °C.

It is interesting to note that breaking the internal bridging bonds in **7a** would generate **77** directly, while
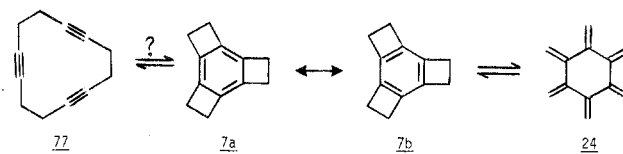
breaking the external CH_2–CH_2 bonds in **7b** would generate **24**. The thermal conversion of **77** to **24** has been demonstrated, but the involvement of **7** as an intermediate has not.[54] This reaction clearly merits further careful study.

The perfluoro analogue of tricyclobutabenzene can be prepared via the copper-bronze coupling of 1,2-diiodoperfluorocyclobutene[55] and is found to be a colorless, crystalline solid (mp 135–136 °C) with unremarkable spectral properties. A single crystal X-ray analysis of this molecule was carried out at –35 °C[56] to test the theories of bond localization set forth above. It showed a highly regular geometry with the bond lengths and bond angles in the central ring essentially identical with those of benzene itself. Related X-ray structure analyses on compounds **46** and **50**[29] also fail to show any clear or significant bond alternation as the result of small-ring fusion.

One property of bisannelated benzenes which does appear to vary significantly depending on the size and orientation of the fused rings is the ultraviolet absorption spectrum. Durene and prehnitene show very similar λ_{max}, indicating that for unstrained systems the substitution pattern of 1,2:3,4 vs. 1,2:4,5 has little influence on the electronic properties of the molecule. The 1,2:3,4-bisannelated benzenes analogous to **76** all correspond well with the tetramethylbenzenes. For the 1,2:4,5-fused isomers, however, a consistent shift of 10–11 nm to longer wavelength is observed. Such shifts previously have been attributed to increased strain. Our data indicate that it is the position at which this strain is introduced into the benzene ring which is critical in determining the electronic nature of the molecule.

An increment in extinction coefficient is observed when comparing 1,2:4,5- to 1,2:3,4-fused bisannelated benzenes and also as the size of the fused rings is decreased. Such changes have often been associated with increased strain. However, it is not evident that such strain should directly influence the allowedness of an electronic transition (ε). Arnold explains the higher extinction coefficient of benzocyclobutene as compared

(52) J. L. Lawrence and S. G. G. MacDonald, *Acta Crystallogr., Sect. B*, 25, 978 (1969).

(53) For an update on the "Mills-Nixon" effect, see: P. J. Garratt and D. N. Nicolaides, *J. Org. Chem.*, 32, 2222 (1974), and references contained therein.

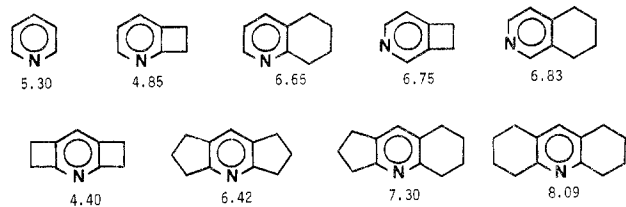(54) A. J. Barkovitch and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, 98, 2667, (1976).

(55) R. L. Soulen, S. K. Choi, and J. D. Park, *J. Fluorine Chem.*, 3, 141 (1973/74).

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Table II
Basicities of Some Annelated Pyridines (pK_a)

to indan or tetralin by claiming that out-of-plane vibrations in the less planar systems provide for poorer overlap between electronic states leading to a less likely transition.[57] Thus, the magnitude of the extinction coefficient is more strongly linked to the planarity of the ground state than to the strain inherent in the molecule. Examination of the photoelectron spectra of these molecules further suggests that changes in the hyperconjugative abilities of the fused rings may be correlated with changes in the orbital energies of the system and thus explain to some extent the observed variations in ionization potential as well as UV absorption energy and intensity.[58]

The basicity of the pyridine molecule provides a useful feature for studying the effect of cyclobutene ring fusion. The ability of a pyridine nitrogen to acquire a proton (pK_b, measured more conveniently as pK_a of the conjugate acid) directly reflects the availability of the nitrogen lone pair for bonding. The availability of this

electron pair, existing in the plane of the σ framework, should be affected by changes in σ bonding and hybridization. Table II presents the basicities of some annelated pyridines.[59] Normally, the electron-releasing inductive effect of cycloalkyl substitution increases the basicity (raises the pK_a) of pyridine. A 2,3-fused cyclobutene ring, however, has the opposite effect and diminishes basicity by 0.45 pK_a unit, while the fusion of a second cyclobutene ring in the 5,6 position further reduces the basicity to an equivalent extent. On the other hand, 3,4-cyclobutapyridine shows almost no change when compared to its unstrained analogue.

The Streitwieser–Finnegan model for rehybridization of bridgehead carbons can again be invoked to explain this basicity behavior. The lone pair of electrons on nitrogen is held more tightly when that atom is bonded to a carbon atom by using an orbital of higher s character. A consistent variation of basicity with the size of annelated rings may be seen for the 2,3:5,6-bisannelated series shown in the bottom half of Table II. Similar observations have been made for cyclobutene-fused quinolines, quinoxalines, and naphthyridines.[60]

(57) W. R. Moore, E. Marcus, S. E. Fenton, and R. T. Arnold, *Tetrahedron*, 5, 179 (1959).

(58) (a) C. Santiago, R. W. Gandour, K. N. Houk, W. Nutakul, W. E. Cravey, and R. P. Thummel, *J. Am. Chem. Soc.*, 100, 3730 (1978); (b) F. Brogli, E. Giovannini, E. Heilbronner, and R. Schurter, *Chem. Ber.*, 106, 961 (1973).

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Bimolecular Reactions of Nucleophiles in the Gas Phase

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The reactions which occur between nucleophiles and electrophiles are among the most common and important of all molecular processes. Such a reaction in solution is often dependent upon the nature of the solvent. This has been elegantly demonstrated[1] for the reaction $Cl^- + MeBr \rightarrow Br^- + MeCl$, which has rate constants, at 25 °C, of 8.2×10^{-27}, 1.1×10^{-26}, and 6.7×10^{-22} cm^3 molecule^{-1} s^{-1} for reactions in water, methanol, and dimethylformamide, respectively.

Solvent dependence is seldom encountered if the reaction is carried out in the gas phase at low pressure in a mass spectrometer. The rate constant for the above nucleophilic substitution reaction is 2.1×10^{-11} cm^3 molecule^{-1} s^{-1} in the gas phase, and thus more than 10^{11}-fold faster than in the most favorable of the three solvents mentioned. Moreover, the activation energy for this reaction in water as solvent is 24.7 kcal/mol, whereas in the gas phase the calculated activation energy is only 2.6 kcal/mol.[1] Indeed, it may be that the gas-phase reaction requires no activation energy. It is therefore apparent that reactivity in the gas phase is most truly representative of the intrinsic reactivity of a particular nucleophile or electrophile.

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