BENZOCYCLOBUTENE AND ITS DERIVATIVES

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Contents

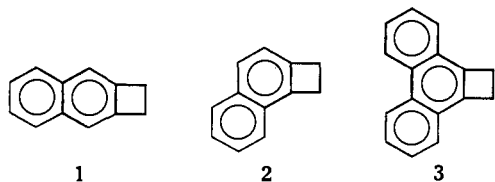## I. Introduction

The first reported synthesis of the benzocyclobutene ring system was that of Finkelstein,[1] a student of Johannes Thiele, who prepared 1,2-dibromobenzocyclobutene[2] as the first part of his doctoral theses in 1909. The field of benzocyclobutene chemistry then lay dormant for 47 years until Cava[3] repeated Finkelstein's synthesis. From 1956 until the end of 1968 at least 134 reports on the chemistry of benzocyclobutene have been published. It is the purpose of this review to present a survey of the literature on methods of synthesis and reactions of benzocyclobutene and its derivatives. *Chemical Abstracts* has been reviewed through December 1968. A few scattered papers that appeared late in 1968 or early in 1969 have also been included.

Several related systems such as **1**, **2**, and **3** are known but will not be included in this review. Condensed benzocyclobutenes derived from benzocyclobutadiene by Diels–Alder

reactions and other products from benzocyclobutadiene can be found in the book by Cava and Mitchell.[4]

II. Synthesis of Benzocyclobutenes

A. *o*-QUINODIMETHANE INTERMEDIATES

The original synthesis involved reacting a boiling alcoholic solution of $\alpha,\alpha,\alpha',\alpha'$-tetrabromo-*o*-xylene with sodium iodide.

Two possible mechanisms exist for the formation of 1,2-dibromobenzocyclobutene (Scheme I). The first of these involves a concerted elimination reaction giving rise to a highly reactive *o*-quinodimethane derivative which then cyclizes spontaneously to the observed dibromide **4**. The second possibility assumes the generation of an intermediate carbanion which displaces a bromide ion from the opposite and very close carbon atom. The reaction has been shown to proceed *via* the quinodimethane intermediate, as its Diels–Alder ad-

Scheme I

(1) (a) H. Finkelstein, Doctoral Dissertation, University of Strassburg, 1909; (b) *Chem. Ber.*, **43**, 1528 (1910) (the compound is mentioned only in a footnote in this paper); (c) *ibid.*, **92**, XXXVII (1959).

(2) The numbering of positions is according to M. P. Cava and D. R. Napier, *J. Amer. Chem. Soc.*, **79**, 1701 (1957).
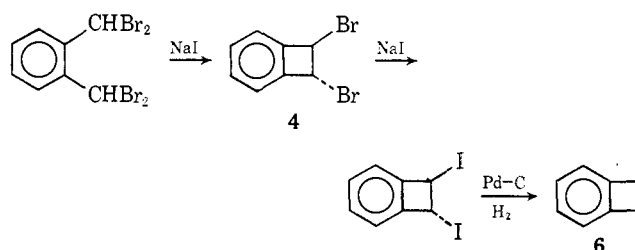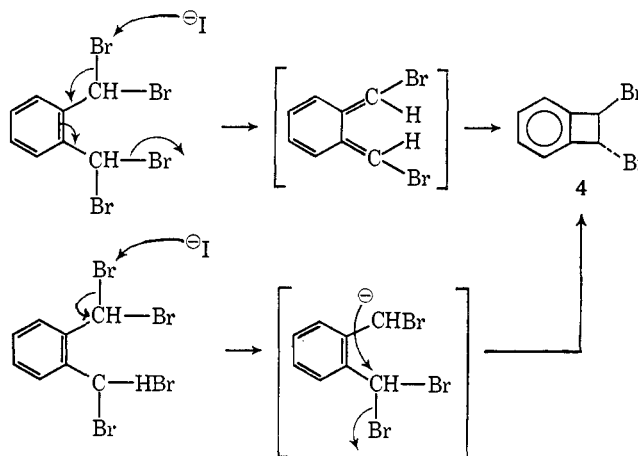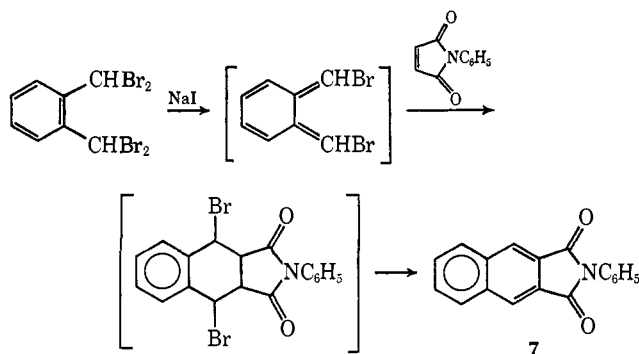
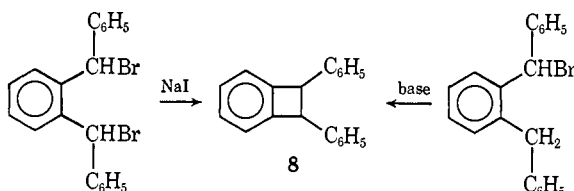(3) M. P. Cava and D. R. Napier, *ibid.*, **78**, 500 (1956).

(4) M. P. Cava and M. J. Mitchell, "Cyclobutadiene and Related Compounds," Academic Press, New York, N. Y., 1967.

duct with N-phenylmaleimide could be isolated in 65% yield.[5] The intermediate could also be trapped with maleic anhydride and quinone.
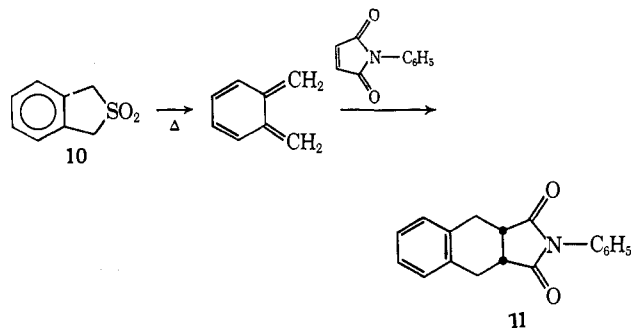

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A similar procedure has been used to prepare 1,2-diphenyl-benzocyclobutene (**8**).[6]

8

Another route for the synthesis of benzocyclobutene involving an o-quinoid-type intermediate has been reported.[7] This was the pyrolysis of 1,3-dihydroisothianaphthene 2,2-dioxide (**10**) over a hot Nichrome wire. To prove that the reaction proceeded via the primary formation of o-quinodimethane, the

9

10   **6**
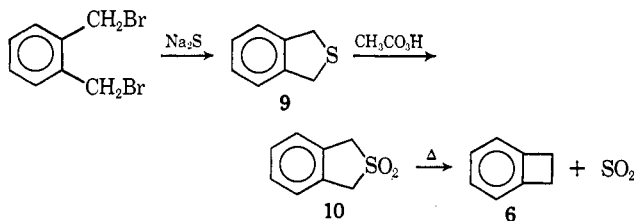
pyrolysis was carried out by fusing the sulfone in the presence of N-phenylmaleimide. Under these conditions no benzocyclobutene was formed; instead the Diels–Alder adduct **11** was isolated in 78% yield. Originally the yield of benzocyclobutene, starting with α,α'-dibromo-o-xylene, was 25.5%, but this has now been improved to 56.5%.[8] The main improvement was in the formation of the sulfide in the first step. It has

10

11

(5) M. P. Cava, A. A. Deana, and K. Muth, *J. Amer. Chem. Soc.*, **81**, 6458 (1959).

(6) F. R. Jensen and W. E. Coleman, *ibid.*, **80**, 6149 (1958).

(7) M. P. Cava and A. A. Deana, *ibid.*, **81**, 4266 (1959).

(8) J. A. Oliver and P. A. Ongley, *Chem. Ind.* (London), 1024 (1965).

been shown that when working at temperatures lower than that used by Cava or Ongley, in the range of 300–350° instead of 650–770°, the yield of benzocyclobutene can be increased by irradiation with ultraviolet light as shown in Table I.[9]

Table I

**Decomposition of 1,3-Dihydroisothionaphthene 2,2-Dioxide**

| | —————% yield[a]————— | |
Temp, °C	*Without irradiation*	*With irradiation*
200	2.6	4.0
250	17.5	24.9
300	30.7	39.2
350	42.0	53.2

[a] The yield of benzocyclobutene is based on total amount of the sulfone used.

Attempts to use the sulfone pyrolysis method to prepare 1,2-diphenylbenzocyclobutene have been investigated.[10] Pyrolysis of 1,3-diphenyl-1,3-dihydroisothianaphthene 2,2-dioxide (**12**) was carried out at 250°; neither 1,2-diphenylbenzocyclobutene nor a dimer of this substance was obtained. There was isolated instead, in 94% yield, 9-phenyl-9,10-dihydroanthracene (**13**). Heating a pure sample of 1,2-diphenyl-benzocyclobutene[6] caused it to rearrange to **13**.

12   **13**
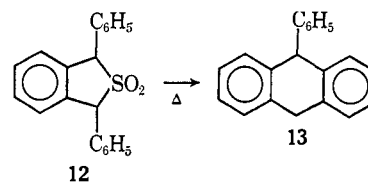
A novel synthesis of benzocyclobutenes has been reported.[11] It involves heating an o-trichloromethylxylene that is sterically hindered to cause the loss of hydrogen chloride with the formation of a 1,1-dichlorobenzocyclobutene. This reaction has been interpreted as proceeding through a quinodimethane intermediate. Several differently substituted benzocyclobutenes have been prepared by this method.[11b]

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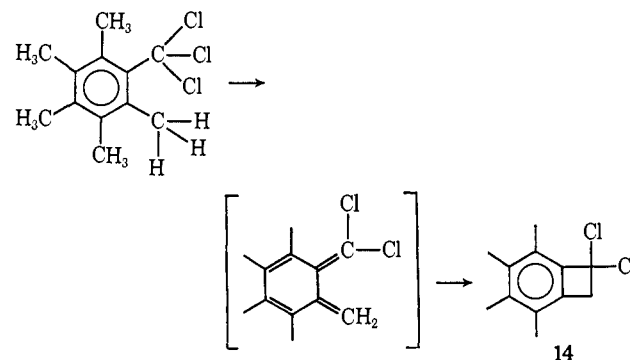
The photochemical expulsion of carbon monoxide from substituted 2-indanones is also reported to produce an o-quinodimethane intermediate.[12] trans-1,2-Diphenylbenzocy-

(9) Y. Odaira, K. Yamaji, and S. Tsutsumi, *Bull. Chem. Soc. Jap.*, **37**, 1410 (1964).

(10) M. P. Cava, M. J. Mitchell, and A. A. Deana, *J. Org. Chem.*, **25**, 1481 (1960).

(11) (a) H. Hart and R. W. Fish, *J. Amer. Chem. Soc.*, **82**, 749 (1960); (b) H. Hart, J. A. Hartlage, R. W. Fish, and R. R. Rafos, *J. Org. Chem*, **31**, 2244 (1966).
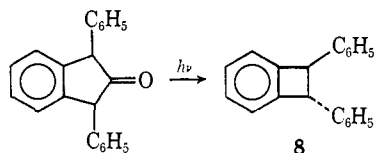
(12) (a) G. Quinkert, K. Opitz, W. W. Wiersdorff, and J. Weinlich, *Tetrahedron Lett.*, 1863 (1963); (b) G. Quinkert, W. W. Wiersdorff, M. Finke, and K. Opitz, *ibid.*, 2193 (1966); (c) J. Rigaudy and H. Paillous, *ibid.*, 4825 (1966).

clobutene (8) has been prepared by this method.[12a] Attempts to prepare 1,1,2,2-tetraphenylbenzocyclobutene (15) by this method[12b] and 2,2-diphenylbenzocyclobutenone (16) resulted in the formation of ring-expanded products.[12c]
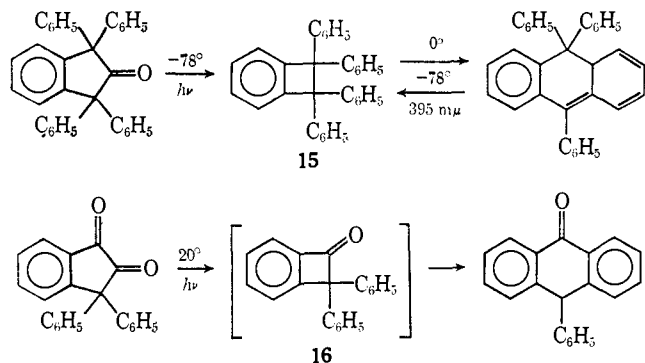

An observation that o-alkylbenzophenones are converted to an o-quinodimethane on irradiation prompted the photolysis of sterically hindered aromatic ketones which produced a number of benzocyclobutene alcohols 17.[13] These products revert to the starting ketones on pyrolysis.
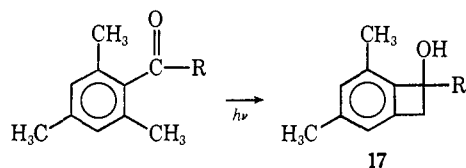

| R	% yield	R	% yield
CH_3	70	i-Pr	61
C_2H_5	63	i-Bu	0

The preparation of benzocyclobutene and 1,2-diphenyl-benzocyclobutene by the base-catalyzed elimination of nitrogen from the appropriate dihydroisoindole has been accomplished.[14]

6, $R_1 = R_2 = H$ (16%)
8, $R_1 = R_2 = C_6H_5$ (40%)
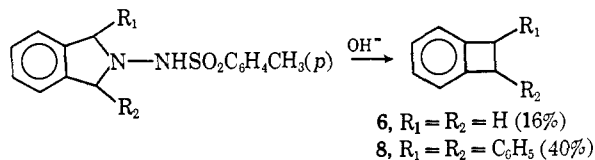
cis- and trans-1,2-diphenylbenzocyclobutene and 1,1,2-triphenylbenzocyclobutene have been prepared by oxidation of the corresponding N-aminodihydroisoindoles.[15]
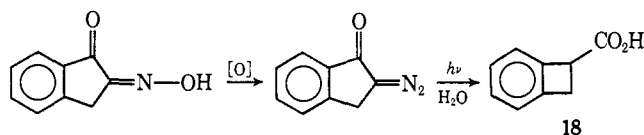

$R_1 = R_3 = C_6H_5; R_2 = H$
$R_1 = R_2 = R_3 = C_6H_5$
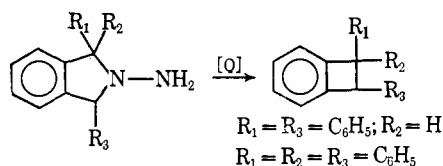
The conversion of 3,4-dihydrophthalazine to benzocyclo-butene in 48% yield has been reported.[16] There is no discussion as to the mechanism of formation, but a Diels-Alder adduct from o-quinodimethane and maleic anhydride was isolated. It is conceivable under the reaction conditions that there is an isomerization to a cyclic 1,4-dihydrophthalazine and then homolytic cleavage of the carbon-nitrogen bonds to form a diradical which can form o-quinodimethane or closes directly to benzocyclobutene.
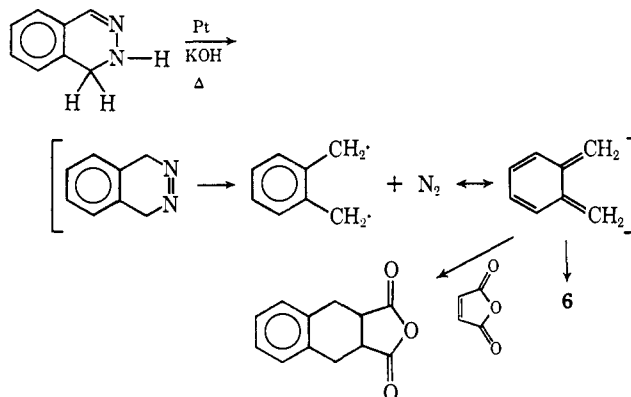

B. WOLFF REARRANGEMENT

Several groups[17] have employed the Wolff rearrangement of α-diazoindanones to produce substituted benzocyclobutene-carboxylic acids. This method allows a great variety of sub-

stituted benzocyclobutenecarboxylic acids to be prepared, but the scale of the reaction is limited by the size of the photolysis apparatus. The pyrolysis of an α-diazo β-diketone has been utilized to prepare a β-keto ester 19.[18]
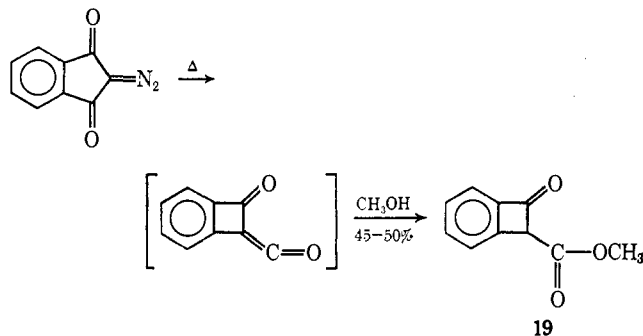
The photolysis of α-diazo ketones has also been used to prepare naphtho-1′,2′,2,3-cyclobutene-1-carboxylic acid (20)

(13) T. Matsuura and Y. Kitaura, *Tetrahedron Lett.*, 3309 (1967).

(14) (a) W. Baker, J. W. McOmie, and D. R. Preston, *Chem. Ind.* (London), 1305 (1960); (b) *J. Chem. Soc.*, 2971 (1961).

(15) (a) L. A. Carpino, *J. Amer. Chem. Soc.*, 84, 2196 (1962); (b) *Chem. Commun.*, 494 (1966); (c) *J. Org. Chem.*, 34, 461 (1969).

(16) Y. S. Shabarov, N. I. Vasil'ev, and R. Y. Levina, *Zh. Obshch. Khim.*, 31, 2478 (1961); *Chem. Abstr.*, 56, 7312 (1962).

(17) (a) L. Horner, W. Kirmse, and K. Muth, *Chem. Ber.*, 91, 430 (1958); (b) W. Kirmse, *Angew. Chem.*, 69, 106 (1957); (c) M. P. Cava, R. L. Litle, and D. R. Napier, *J. Amer. Chem. Soc.*, 80, 2257 (1958); (d) L. Horner, K. Muth, and H. B. Schmelzer, *Chem. Ber.*, 92, 2953 (1959); (e) A. T. Blomquist and C. G. Bottomley, *Justus Liebigs Ann. Chem.*, 653, 67 (1962); (f) C. Kaiser and C. Zirkle, U. S. Patent 3,149,159; *Chem. Abstr.*, 62, 14530d (1965).
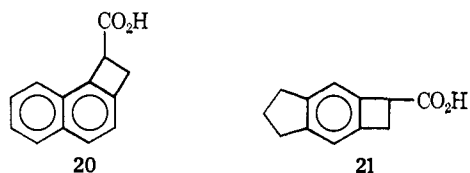
(18) M. P. Cava and R. J. Spangler, *J. Amer. Chem. Soc.*, 89, 4550 (1967).

and 4',5'-trimethylenebenzo-1',2',2,3-cyclobutene-1-carboxylic acid (21).[17a] The same sequence of reactions has been used
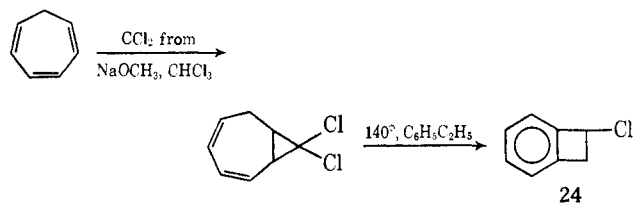

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21

to prepare 22 and 23.[17b]

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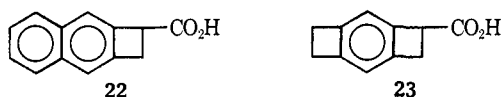
C. CARBENE REACTIONS

Benzocyclobutenes have been prepared from products resulting from carbene reactions with olefins. 1-Chlorobenzocyclobutene (24) was prepared from the mono dichlorocarbene adduct with cycloheptatriene in 10% overall yield based on the sodium methoxide used.[19]


The reaction of 1,4-dimethoxy-1,4-cyclohexadiene with dibromocarbene and then treatment of the product with silver nitrate or silver perchlorate gave a substituted benzocyclobutenone 25.[20] The carbene adduct can be more easily con-


25, R = H, NO$_2$
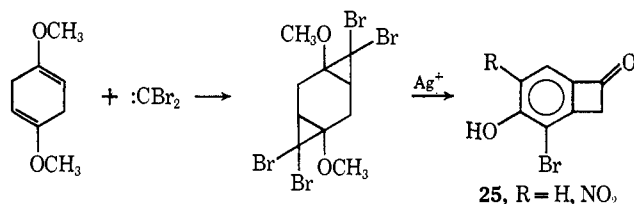
verted, although in somewhat lower yield, to the benzocyclobutenone by treating it with silver sulfate in 98% sulfuric acid.[21] The rearrangement to a benzocyclobutenone must be due to the presence of the methoxyl groups, since there is no trace of a benzocyclobutenone from the adduct of the parent compound, cyclohexa-1,4-diene.

D. ADDITION OF BENZYNE TO UNSATURATED COMPOUNDS

The reaction of benzyne with unsaturated compounds has also been used to prepare benzocyclobutenes. The reaction of benzyne, generated from o-fluorobromobenzene and magnesium in tetrahydrofuran, with bicyclo[2.2.1]heptadiene produced the substituted benzocyclobutene 26 in 15-21% yields.[22]


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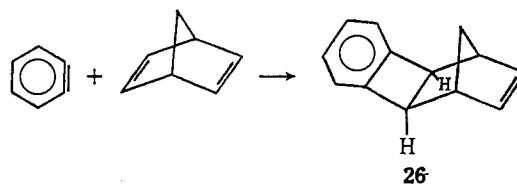
The reaction of tetrahalobenzyne (chloro and fluoro) with bicyclo[2.2.1]heptene and heptadiene has produced the expected exo-benzocyclobutene adducts along with another product from the heptadiene reaction.[23]

X = Cl or F

27

X = Cl or F

28
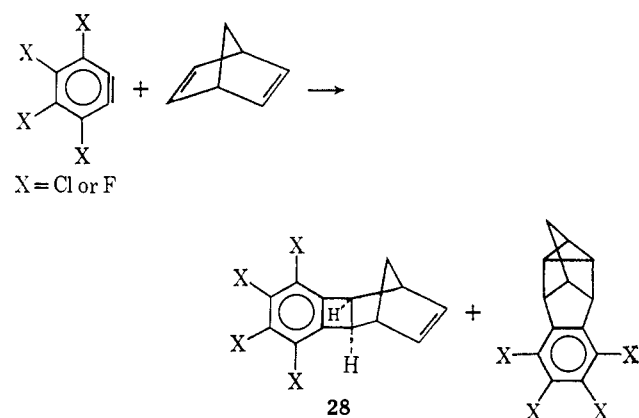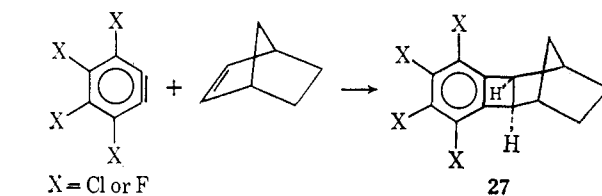
The reaction of benzyne with substituted butadienes[24] has been reported to give the normal Diels–Alder products along with an indirect addition product. The reaction with 2,3-dimethylbutadiene and benzyne gave 29 in 4–6% yield.

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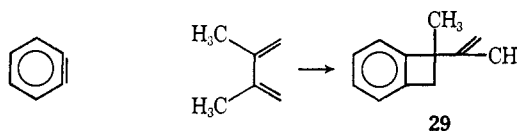
The reaction of benzyne with enamines has been examined.[25] It was found that the structure of the final products depended on the reaction conditions and the method employed for the generation of benzyne. Generation of benzyne from fluorobenzene and piperidyllithium in the presence of 1-pyrrolidino-

30
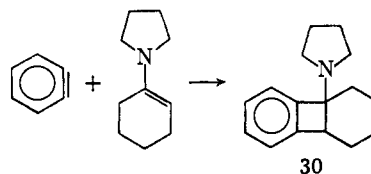
cyclohexene did not yield any of the benzocyclobutene 30. However, when butyllithium was used, the desired product was produced. When o-bromofluorobenzene and lithium amalgam were used to generate benzyne, only the benzocyclobutene

(19) (a) A. P. ter-Borg and A. F. Bickel, Proc. Chem. Soc., 283 (1958); (b) Rec. Trav. Chim. Pays-Bas, 80, 1217 (1961).
(20) A. J. Birch, J. M. Brown, and F. Stansfield, J. Chem. Soc., 5343 (1964).
(21) G. M. Iskander and F. Stansfield, ibid., 1390 (1965).
(22) H. E. Simmons, J. Amer. Chem. Soc., 83, 1657 (1961).

(23) H. Heaney and J. M. Jablonski, Tetrahedron Lett., 2733 (1967).
(24) G. Wittig and H. Durr, Justus Liebigs Ann. Chem., 672, 55 (1964).
(25) M. E. Kuehne, J. Amer. Chem. Soc., 84, 837 (1962).

derivative was obtained. Decomposition of o-benzenediazonium carboxylate at 40° in 1-pyrrolidinocyclohexene resulted in a violent detonation.

The reaction of benzyne, generated from o-bromofluorobenzene and magnesium, with the lithium salt of indole produced 2,3-phenylenedihydroindole (31) in 8% yield.[26]

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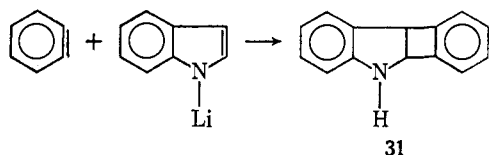
Several groups have reported the reaction of benzyne, generated from benzenediazonium-2-carboxylate, with olefins to form benzocyclobutenes. The synthesis of 1-ethoxy- (32) and 1-acetoxybenzocyclobutene (33) has been accomplished in fair yields by the above method.[27] Although no specific experimental details were given, it is assumed that these reactions were carried out on a small scale because of the explosive nature of benzenediazonium-2-carboxylate. The same reaction with ethyl acrylate and acrylonitrile has also been reported.[28]
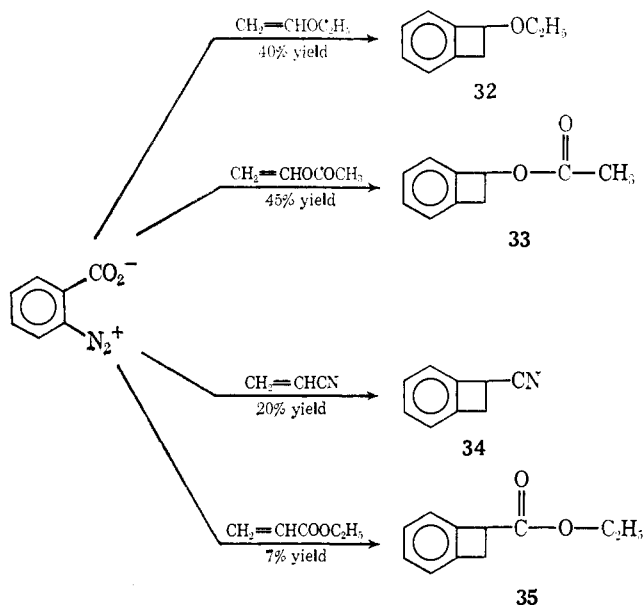
The stereochemistry of the addition of benzyne to olefins substituted with heteroatoms has been reported in a series of preliminary communications. The reaction of benzyne with cis- and trans-propenyl methyl ether gives mixtures of cis- and trans-benzocyclobutene adducts.[29] The reaction has been reported as being nonstereospecific with the cis-benzocyclobutene being the predominant product regardless of the composition of the starting material. It is postulated that the benzyne reacts as an aromatic diradical species.

The same reaction has recently been reported but with different results.[30] The reaction of benzyne with cis-methoxy-

propene gave mainly cis-1-methoxy-2-methylbenzocyclobutene (36, 80%) along with small amounts of the trans
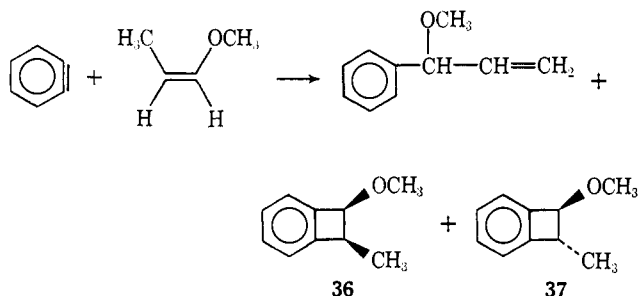
isomer 39 (10%) and some ene product, 3-phenyl-3-methoxypropene (9%). trans-Methoxypropene gave extensive amounts of the ene product (50%) and the cis- and trans-benzocyclobutene in a 1:1 ratio.

The reaction of benzyne, generated from benzenediazonium-2-carboxylate as has been the case in all studies of the stereochemical addition to olefins, has been studied with cis- and trans-ethyl propenyl ether.[31] Reaction with 100% cis-ethyl propenyl ether afforded cis-1-methyl-2-ethoxybenzocyclobutene (38, 51%), trans-1-methyl-2-ethoxybenzocyclobutene (39, 3.2%), and ethyl α-phenylallyl ether (40, 0.9%). With 100% trans-ethyl propenyl ether, the corresponding reaction with benzyne afforded the cis-cyclo adduct (38, 8.2%), the trans-cyclo adduct (39, 31%), and ethyl α-phenylallyl ether (40, 14%).
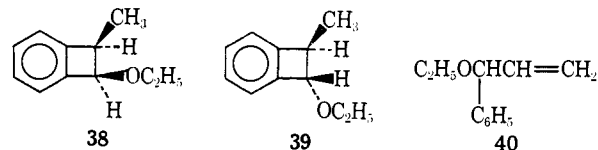
The stereochemistry of the addition of benzyne to cis- and trans-1,2-dichloroethylene has also been studied.[32] Reaction of benzyne with trans-dichloroethylene gave a mixture of cis- and trans-1,2-dichlorobenzocyclobutene in the approximate ratio 20:80. Reaction with the cis isomer gave the same two products in the ratio 68:32.
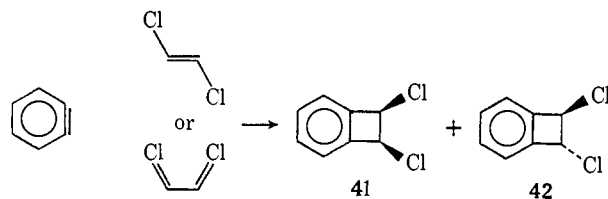
The reactions of benzyne with ethoxypropene, methoxypropene, and dichloroethylene have been explained as proceeding via a nonconcerted cycloaddition in which bond rotation is relatively slow compared with ring closure. The intermediates involved may be either dipolar or diradical.

A very recent report has been published on the 2 + 2 cycloaddition of benzyne to a nonpolarized olefin (one not containing any heteroatoms).[33] The addition of benzyne to trans-cyclooctene gives a mixture of 43 and 44. To rule out the isomerization of trans- to cis-cyclooctene during the reaction,

(26) M. Kuehne and T. Kitagawa, J. Org. Chem., 29, 1270 (1964).
(27) H. H. Wasserman and J. Solodar, J. Amer. Chem. Soc., 87, 4002 (1965).
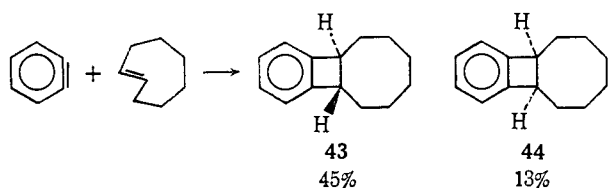(28) T. Matsuda and T. Mitsuyasu, Bull. Chem. Soc. Jap., 39, 1342 (1966).
(29) I. Tabushi, R. Oda, and K. Okazaki, Tetrahedron Lett., 3743 (1968).
(30) L. Friedman, R. S. Osiewicz, and P. W. Rabideau, ibid., 5735 (1968).

(31) H. H. Wasserman, A. J. Solodar, and L. S. Keller, ibid., 5597 (1968).
(32) M. Jones, Jr. and R. H. Levin, ibid., 5593 (1968).
(33) P. G. Gassman and H. P. Benecke, ibid., 1089 (1969).

43
45%

44
13%

the addition of benzyne to pure *cis*-cyclooctene was investigated. This gave a small amount of **44**, no **43**, and the ene product **45** not observed in the addition of benzyne to the *trans* olefin. The authors have presented evidence that seems


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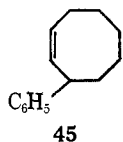
to rule out the presence of dipolar intermediates. It appears reasonable on the basis of the information presented that "simple" olefins react with benzyne in a 2 + 2 cycloaddition to form a diradical intermediate.

The reaction of benzyne with certain acetylenes[34] produces substituted benzocyclobutenes in very low yield ($\sim$1%).


46   **47**
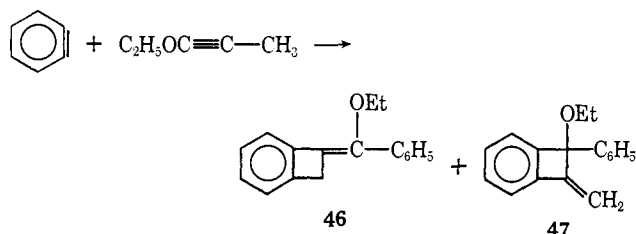
E. RING-CLOSURE REACTIONS

Benzocyclobutenes[35] have been prepared by homocyclic ring closure *via* benzyne intermediates. The ring closure was carried out with various functional groups in the side chain.[35a] The results are shown below. A double cyclization has been


Z	% yield
–COOEt	10
–CN	61
–SO$_2$C$_6$H$_5$	47
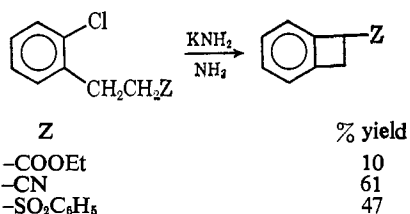
attempted but the expected product was not isolated.[35d] A monocyclized product could be prepared. Treatment of the


48
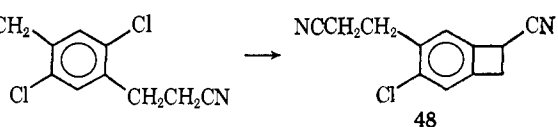
material containing one benzocyclobutene ring (**48**) with an excess of base resulted in decomposition of the starting material.

This method of ring closure seems to be the most versatile for the preparation of benzocyclobutenes substituted on the aromatic ring. The reaction of 3-bromo-4,5-dimethoxyhydrocinnamonitrile with sodium amide in liquid ammonia gave 1-cyano-4,5-dimethoxybenzocyclobutene (**49**) in 58% yield. Treatment of the same starting material with lithium diethylamide in tetrahydrofuran gave **49** in 46% yield.[36]


49
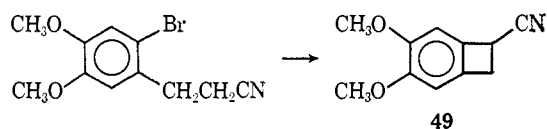
F. MISCELLANEOUS METHODS

The reaction of *p*-benzoquinones with enamines[37a–e] has been reported to result in the formation of 1-substituted amino-3,6-dihydroxybenzocyclobutenes. A more recent report shows this to be incorrect. This reaction actually gives benzofuran derivatives.[37f]

50
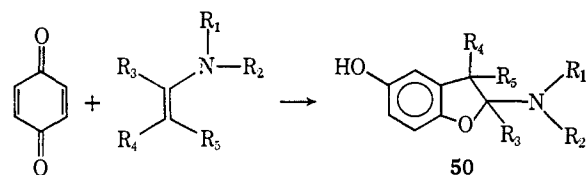
The synthesis of fluorinated benzocyclobutenes from aliphatic starting materials has been reported.[38] Condensation of 3,3,4,4-tetrafluorocyclobutene with butadiene gave the expected adduct **51** in 75% yield. When this adduct was refluxed with palladium on carbon catalyst, disproportionation occurs to give a mixture of the aromatic compound **52** and the reduced compound **53**. Treatment of the Diels–Alder adduct **51**

51   **52**   **53**

54
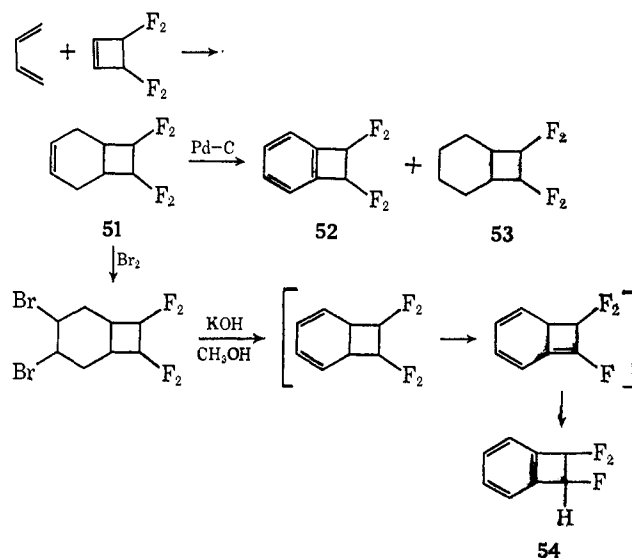
with bromine followed by reacting the dibromo adduct with methanolic potassium hydroxide resulted in the loss of 2 mol

(34) H. H. Wasserman and J. M. Fernandez, *J. Amer. Chem. Soc.*, 90, 5322 (1968).

(35) (a) J. F. Bunnett and J. A. Skorcz, *J. Org. Chem.*, 27, 3836 (1962); (b) Belgian Patent 635,901 (June 1964); *Chem. Abstr.*, 62, 3987 (1965); (c) J. A. Skorcz and J. E. Robertson, *J. Med. Chem.*, 8, 255 (1965); (d) R. Garst, *Diss. Abstr.*, 25, 4404 (1965); (e) I. L. Klundt and W. K. Hoya, *J. Org. Chem.*, 33, 3327 (1968).

(36) I. L. Klundt, unpublished observation.

(37) (a) K. Ley, H. Walz, and W. Redetzky, Belgian Patent 630,171; *Chem. Abstr.*, 60, 11962 (1964); (b) Netherlands Patent Appl., 6,410,558; *Chem. Abstr.*, 64, 3563 (1966); (c) Netherlands Patent Appl., 291,565; *Chem. Abstr.*, 64, 3813 (1966); (d) Netherlands Patent Appl., 6,411,154; *Chem. Abstr.*, 64, 5277 (1966); (e) K. Ley, H. Freytag, and W. Redetzky, Belgian Patent 653,645; *Chem. Abstr.*, 64, 17843 (1966); (f) G. R. Allen, Jr., *J. Org. Chem.*, 33, 3346 (1968), and references therein.

(38) R. J. Shozda and R. E. Putnam, *ibid.*, 27, 1557 (1962).

of hydrogen bromide and 1 mol of hydrogen fluoride to give the trifluorobenzocyclobutene **54**. A somewhat similar procedure has been utilized to prepare 4-substituted benzocyclobutenes.[39] The authors utilized dehydrogenation to introduce aromatic character into a bicyclo[4.2.0]cyclooctadiene (**55**).
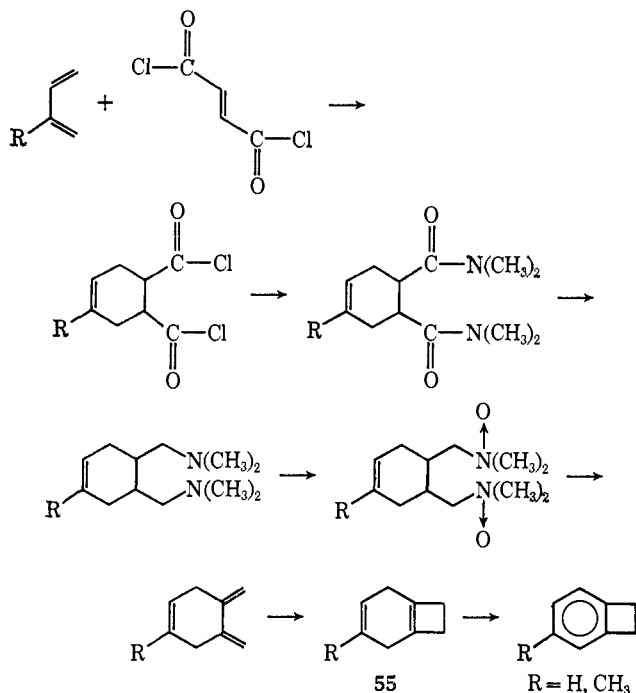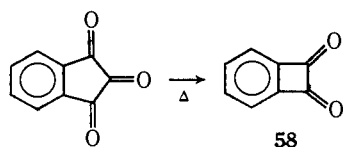

The preparation of perchlorobenzocyclobutene (**56**) via the dimerization of perchlorobutenyne has also been reported.[40]
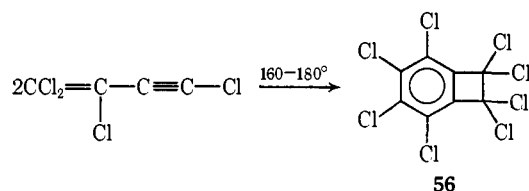
Pyrolysis of a hindered diaryldiazomethane in a sealed tube produced the substituted benzocyclobutene **57** in 78% yield.[41]
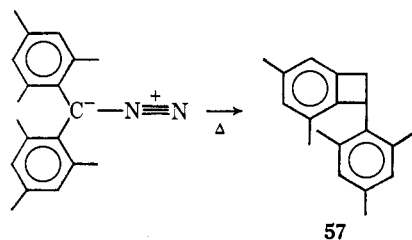

Pyrolysis of ninhydrin has also been shown to produce benzocyclobutene-1,2-dione in 17% yield.[42]

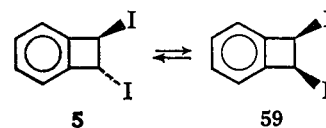# III. Reactions of Benzocyclobutenes

A. 1,2-DIHALOBENZOCYCLOBUTENES

Since the first benzocyclobutene to be prepared[1,3] was trans-1,2-dibromobenzocyclobutene (**4**), the reactions it undergoes will be examined first. Reaction of the dibromide with bromine at 150° gave the original tetrabromide in 48% yield.[2] Reaction of the dibromide with sodium iodide over a prolonged period produced 1,2-diiodobenzocyclobutene. These two dihalides
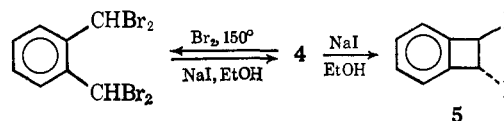
are strikingly different in their stabilities. The diiodide underwent decomposition when a dilute solution was irradiated with sunlight, and it also decomposed on attempted distillation at reduced pressure.

A solution of the dibromide was stable to sunlight and could be distilled at 140° under reduced pressure. The dibromide was completely stable to boiling aqueous alcohol and ethanolic potassium acetate.

Examination of the formation of 1,2-diiodobenzocyclobutene in more detail led to the isolation of the two isomeric diiodides.[43] The low-melting, known isomer **5**, prisms, mp 63°, comprised 91.6% of the mixture while the new isomer **59**, needles, mp 150°, comprised 8.4% of the reaction mixture. The diiodides are interconverted by refluxing them with sodium iodide in ethanol in the dark. It was shown that the isomerization would not proceed until free iodine appeared
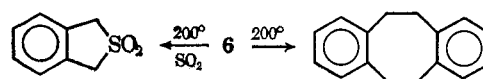

in the solution. The above isomerization could also be brought about by irradiation.

Reaction of 1,2-dibromobenzocyclobutene with maleic anhydride at 100° for 5 days gave a ring-opened product in 32% yield.[44] Pyrolysis of benzocyclobutene (**6**) either alone

$$X = Br, H, C_6H_5$$
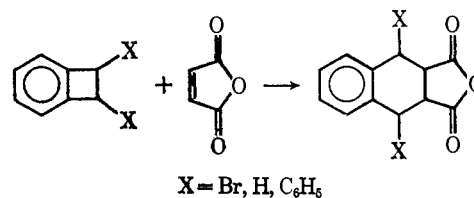
or in the presence of sulfur dioxide also caused the four-membered ring to rupture.

Treatment of 1,2-dihalobenzocyclobutenes with different bases causes the formation of different products. The reaction of 1,2-dibromobenzocyclobutene and 1,2-diiodobenzocyclobutene with potassium t-butoxide in t-butyl alcohol gave

(39) J. M. Garrett and G. J. Fonken, *Tetrahedron Lett.*, 191 (1969).
(40) A. Roedig and R. Kohlhaupt, *ibid.*, 1107 (1964).
(41) H. E. Zimmerman and D. H. Paskovich, *J. Amer. Chem. Soc.*, **86**, 2149 (1964).
(42) R. F. C. Brown and R. K. Solly, *Aust. J. Chem.*, **19**, 1045 (1966).

(43) F. R. Jensen and W. E. Coleman, *J. Org. Chem.*, 23, 869 (1958).
(44) F. R. Jensen, W. E. Coleman, and A. J. Berlin, *Tetrahedron Lett.*, 15 (1962).

similar results, the formation of 5-halobenzo[a]biphenylene.[45] The reaction of 1,2-dibromobenzocyclobutene with zinc gave a halogen-free dihydro derivative of benzo[a]biphenylene.[2]
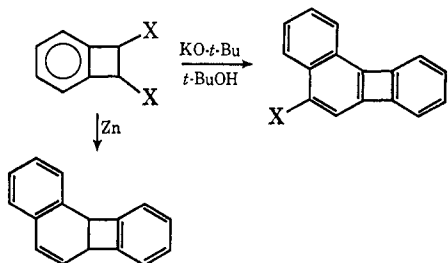

The reaction of trans-1,2-diiodobenzocyclobutene with dimethylamine at 60° produced two products.[46] The minor constituent, formed in 10% yield, was shown to be α-dimethylamino-o-tolualdehyde. The major component, 64% yield, was
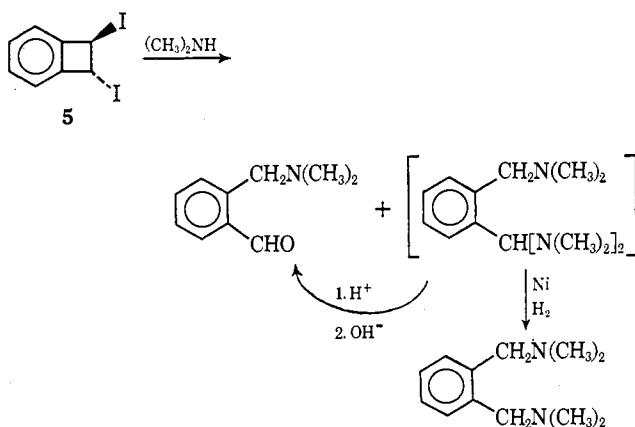

a very reactive liquid that began to decompose immediately. Reduction of the major component with Raney nickel gave α,α'-bisdimethylamino-o-xylene. Treatment of the unstable triamine with acid followed by base gave α-dimethylamino-o-tolualdehyde. The nmr spectrum confirmed the structure of the major product as being α,α,α'-trisdimethylamino-o-xylene.

Treatment of 1,2-diiodobenzocyclobutene (5) with silver nitrate in acetonitrile gave a mixture of nitrate esters 60 and 61 which were separated by fractional crystallization.[47] Either isomer when refluxed 1 hr with 1:1 methylene chloride-triethylamine gave, in 75% yield, 1,2-diketobenzocyclobutene (58). Additional work on the preparation of the dinitrate has
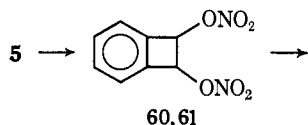

isomer A, mp 110°, cis (60)
isomer B, mp 55.5–56.5°, trans (61)
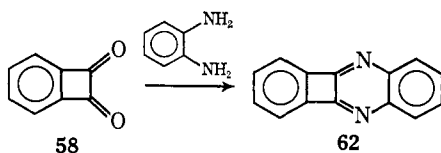
shown that it can be prepared from 1,2-dibromobenzocyclobutene.[48] Both nitrates reacted with lithium aluminum hydride to give phthalyl alcohol, not the desired diols. The dinitrates were subjected to reduction with hydrazine in the presence of palladium. Although the trans isomer gave only a brown gum, the cis isomer afforded the crystalline cis-diol.

Solvolysis of trans-1,2-dibromobenzocyclobutene (4) in acetic acid–silver acetate, containing 4% water, gave a 64% yield of cis-1-acetoxy-2-hydroxybenzocyclobutene (63). The monoacetate could be hydrolyzed to the cis-diol which was then converted to the acetonide 67 and the diacetate.[49] When the acetolysis was carried out in a mixture of acetic anhydride–acetic acid in the presence of silver acetate, trans-1,2-diacetoxybenzocyclobutene (64) was obtained in 82% yield. This was converted to the pure trans-1,2-diol 65 which was unstable upon heating in contrast to the cis isomer.
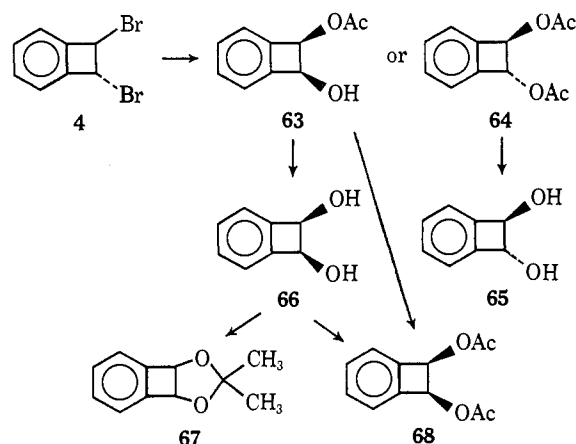
When trans-1,2-dibromobenzocyclobutene (4) is stirred under nitrogen with triphenylphosphine at 150° for 24 hr a quantitative yield of salt is obtained.[50] Treatment of the salt with butyllithium in DMSO or DMF gave a deep red solution which decomposed rapidly at room temperature but was stable for several hours at −40°. Treatment of a DMF solution of the bis ylide with excess benzaldehyde afforded a mixture of several products which was separated by chromatography.
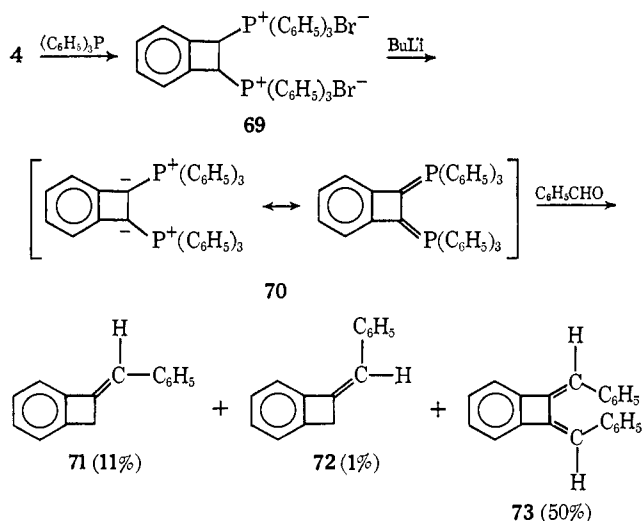
(45) (a) M. P. Cava and J. F. Stucker, J. Amer. Chem. Soc., 79, 1706 (1957); (b) M. P. Cava, K. W. Ratts, and J. F. Stucker, J. Org. Chem., 25, 1101 (1960).
(46) M. W. Hanna and S. W. Fenton, ibid., 26, 1371 (1961).
(47) M. P. Cava and D. R. Napier, J. Amer. Chem. Soc., 79, 3606 (1957).

(48) M. P. Cava, D. R. Napier, and R. J. Pohl, ibid., 85, 2076 (1963).
(49) H. Nozaki, R. Noyori, and N. Kozaki, Tetrahedron, 20, 641 (1964).
(50) (a) A. T. Blomquist and V. J. Hruby, J. Amer. Chem. Soc., 86 5041 (1964); (b) ibid., 89, 4996 (1967).
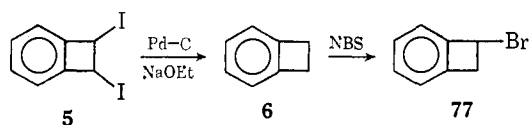
The reaction of the ylide **70** with substituted aldehydes in alcohol gave only monobenzylidines **75** and **76** with none of the bis-benzylidine derivative being obtained.
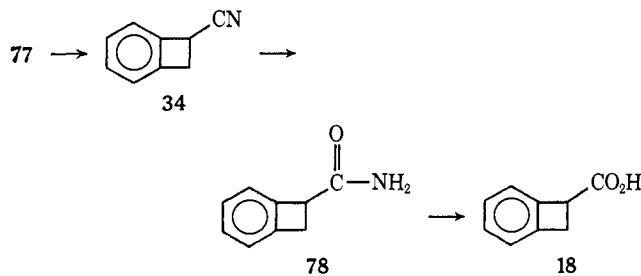

R'	Yield, %	
	75	**76**
C₆H₄NO₂-p	55	34
C₆H₅	56	14
C₆H₄Br-p	54	32
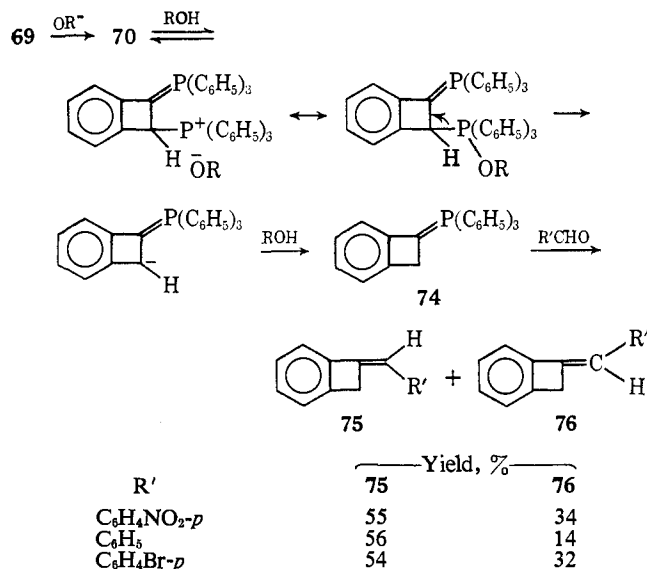
B. 1-SUBSTITUTED BENZOCYCLOBUTENES

Cava[51] was the first investigator to prepare benzocyclobutene. This was accomplished by reducing 1,2-diiodobenzocyclo-butene with palladium on carbon in the presence of aged sodium ethoxide. Benzocyclobutene is a colorless oil with a xylene-like odor. The ultraviolet spectrum resembles closely that of indan, both in the positions of the maxima and in the rather high values of their extinction coefficients. Benzocyclobutene was brominated with NBS to produce 1-bromobenzo-cyclobutene. The reaction of **77** with sodium cyanide pro-


ceeded very sluggishly under ordinary conditions; after 11 hr in refluxing methanol most of the bromide was unchanged, but infrared analysis indicated that about 30% of it had been converted to 1-cyanobenzocyclobutene.[52] However, when warm dimethyl sulfoxide was employed as the solvent in this reaction, 1-cyanobenzocyclobutene was produced in 93% yield after only 1 hr.


Oxidation of the nitrile **34** with alkaline hydrogen peroxide gave the corresponding carboxamide in 73% yield. Alkaline hydrolysis converted the amide **78** to benzocyclobutene-1-

carboxylic acid (**18**) in 97% yield. The acid **18** can also be prepared by direct hydrolysis of **34** with saturated alcoholic potassium hydroxide.[66]

1-Bromobenzocyclobutene is a common starting material for many reactions. It was used to prepare the magnesium Grignard reagent which was then carbonated to give benzo-cyclobutene-1-carboxylic acid in 53% overall yield.[63] The acid was converted to 1-aminobenzocyclobutene (**81**), and the methyl ester **79** was treated with various Grignard reagents to prepare several tertiary alcohols **80**.

R	R'
CH₃	OH
C₆H₅	OH
CH₃	O₂CCH₃
CH₃	Cl
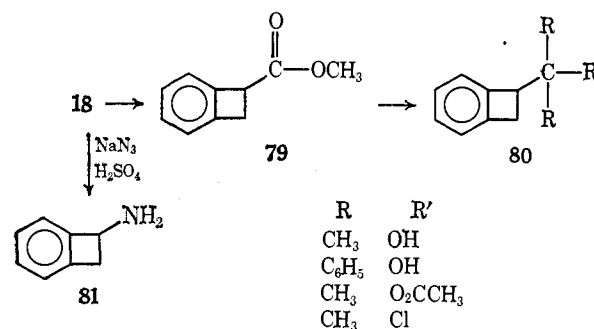
The reaction of 1-bromobenzocyclobutene with silver tri-fluoroacetate in benzene solution gave benzocyclobutenyl tri-fluoroacetate (**82**), a pleasant smelling oil, in 87% yield.[54] Benzocyclobutenol (**83**) was prepared in good yield by hy-drolysis of the ester **82**. The alcohol is not particularly sensi-tive to dilute mineral acids, but is surprisingly unstable in the
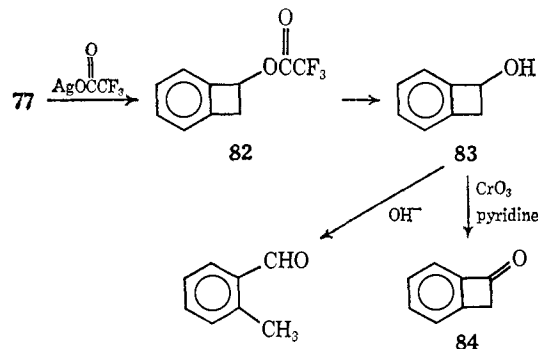
presence of sodium hydroxide. After standing with 0.25 N sodium hydroxide for 1 hr at room temperature, the alcohol was converted in 72% yield to o-tolualdehyde.

Mild oxidation of benzocyclobutenol with chromic anhy-dride in pyridine gave benzocyclobutenone (**84**) in 42% yield. The ketone is quite stable to dilute mineral acids and reacts rapidly with 2,4-dinitrophenylhydrazine in acidic media to give a normal derivative. Aqueous sodium hydroxide slowly destroys the ketone by a ring-opening process.

1-Bromo- and the isomeric 1,2-dibromobenzocyclobutenes have been used as starting material to prepare all of the possi-ble benzocyclobutenes having more than one bromine sub-stituted on the four-membered ring.[55] By using very pure start-ing materials, it is possible to convert 1-bromobenzocyclo-butene (**77**) to 1,1-dibromobenzocyclobutene (**85**) with N-bromosuccinimide. The reaction of pure trans-1,2-dibromo-benzocyclobutene (**4**) with NBS proceeds very slowly. From an incomplete reaction two new bromo derivatives were iso-

(51) M. P. Cava and D. R. Napier, J. Amer. Chem. Soc., 80, 2255 (1958).
(52) M. P. Cava, R. L. Litle, and D. R. Napier, ibid., 80, 2257 (1958).

(53) L. Horner, W. Kirmse, and K. Muth, Chem. Ber., 91, 430 (1958).
(54) M. P. Cava and K. Muth, J. Amer. Chem. Soc., 82, 652 (1960).
(55) M. P. Cava and K. Muth, J. Org. Chem., 27, 757 (1962).

lated, 1,1,2-tribromobenzocyclobutene (86) and 1,1,2,2-tetra-bromobenzocyclobutene (88). The corresponding reaction with cis-1,2-dibromobenzocyclobutene (87) proceeds very fast to give the tribromide. The removal of a hydrogen atom is subject to considerable steric hindrance by a cis substituent as large as bromine in a rigid small-ring system such as that of benzocyclobutene. Treatment of benzocyclobutenol (83) or
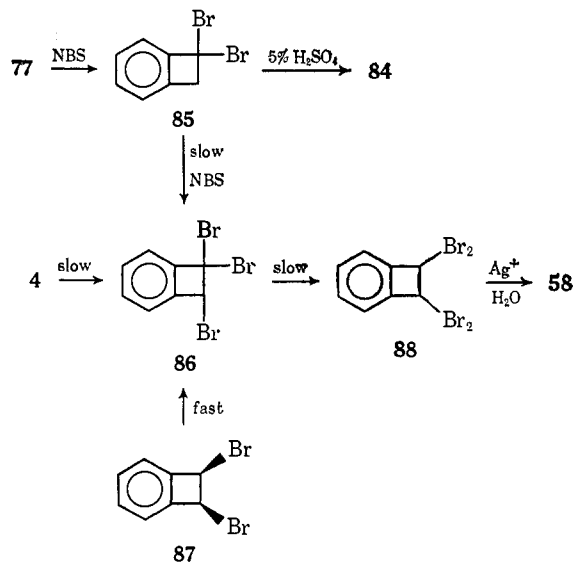
benzocyclobutenone (84) with NBS gave two different products depending on the amount of NBS used.[56] Either 2-bromo-benzocyclobutenone (89) or 2,2-dibromobenzocyclobutenone (90) could be isolated. Both of the bromo ketone derivatives were unstable to base and gave ring-opened o-xylene derivatives.
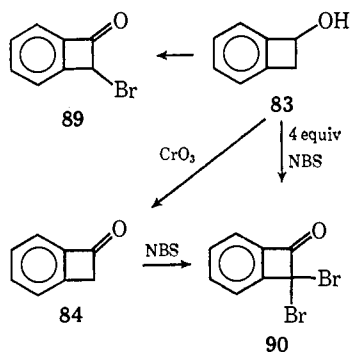

The reaction of 1-bromobenzocyclobutene with chromium trioxide in acetic acid produced 2-bromobenzocyclobutenone.[57]
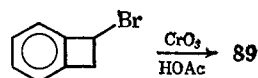
Reduction of benzocyclobutene-1-carboxylic acid with lithium aluminum hydride gave 1-hydroxymethylbenzocyclo-butene (91).[58] Treatment of the alcohol with tosyl chloride gave a crystalline tosyl ester 92. This ester was converted to methylenebenzocyclobutene (94) with potassium t-butoxide in t-butyl alcohol. The methylene derivative was reduced to 1-

methylbenzocyclobutene (93) which also was prepared by the lithium aluminum hydride reduction of the tosyl ester.
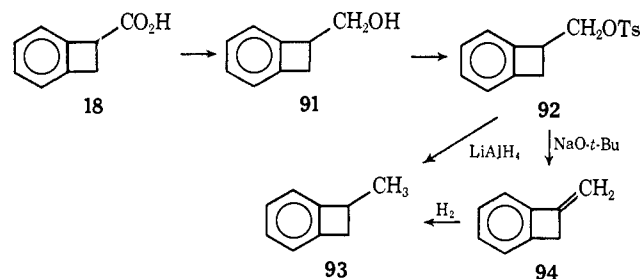
Solvolysis of benzocyclobuten-3-ylcarbinyl toluenesulfonate (92) in refluxing buffered acetic acid gives initially a 7:3 mixture of indan-2-yl acetate (95) and indan-1-yl acetate (96). The latter product is not stable under the reaction conditions and goes over to indene on prolonged reflux.[59] The authors postulated that the results require the formal intermediacy of a bicyclo[2.1.0]pentylphenonium ion (aryl migration) in this rearrangement.
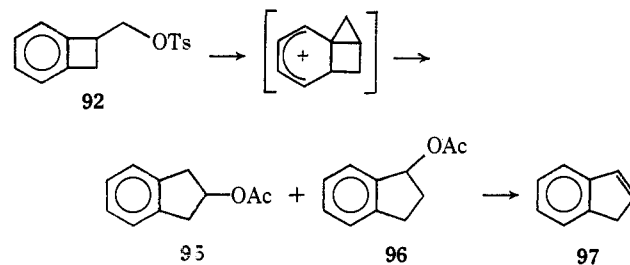
A double Arndt–Eistert homologation of benzocyclobutene-carboxylic acid (18) followed by reduction of the terminal carboxyl group to a methyl group has been applied to prepare 1-n-propylbenzocyclobutene.[60]
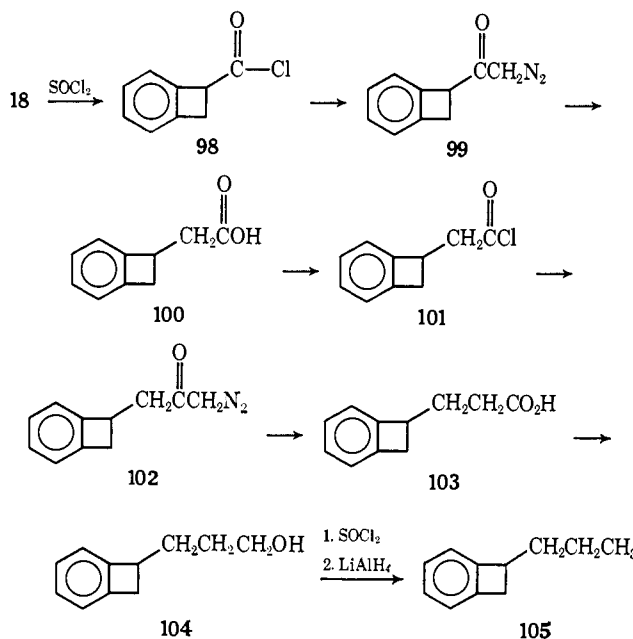
Substituted benzocyclobutenecarboxylic acids have been used by two groups as starting material for the preparation of

(56) M. P. Cava, D. Mangold, and K. Muth, J. Org. Chem., 29, 2947 (1964).
(57) L. Horner and P. V. Subramaniam, Tetrahedron Lett., 101 (1965).
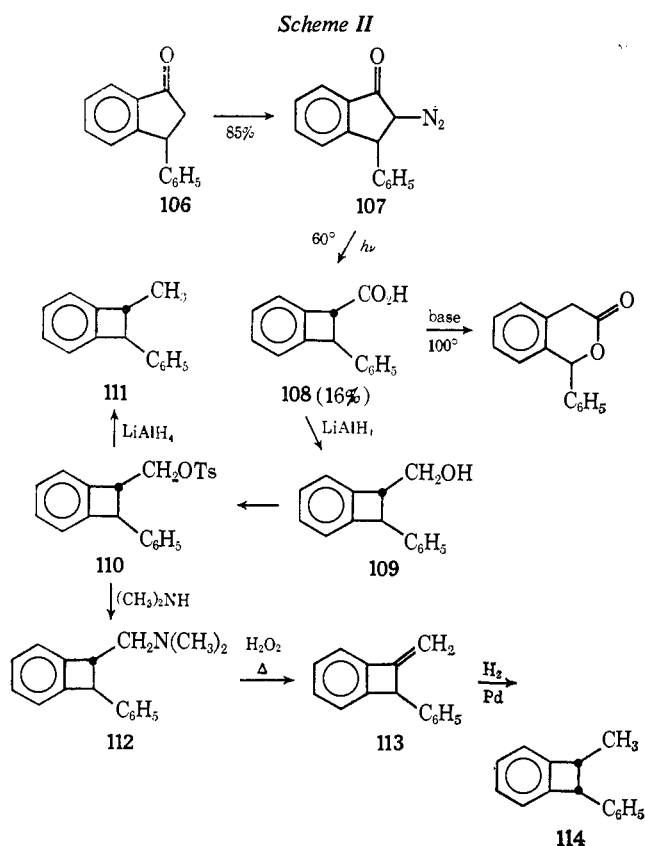(58) M. P. Cava and M. J. Mitchell, J. Org. Chem., 27, 631 (1962).

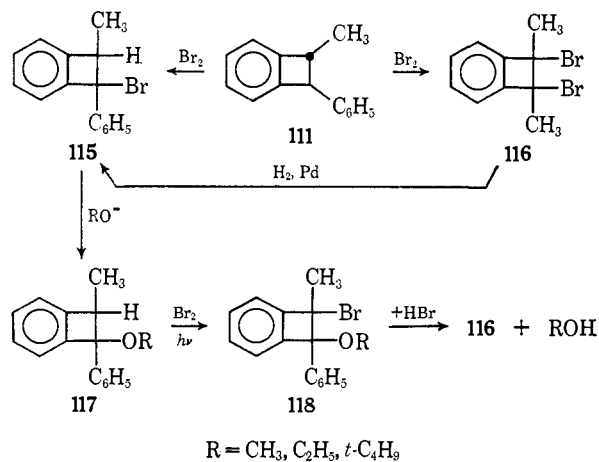(59) H. W. Whitlock and P. Fuchs, Jr., Tetrahedron Lett., 1453 (1968).
(60) C. D. Gutsche, G. L. Bachman, and R. S. Coffey, Tetrahedron, 18, 617 (1962).

other benzocyclobutenes. In both cases substituted indanones were converted to the corresponding diazo ketones and then photolyzed to produce the benzocyclobutenecarboxylic acids.[17e,f]

3-Phenyl-1-indanone (106) was utilized to prepare a series of 2-phenyl-1-substituted benzocyclobutenes[17e] (Scheme II).

C_2H_5) with acetyl bromide gave one isomer of the monobromide, 115, while light-catalyzed bromination of each of the three ethers gave the known dibromide 116.

Photolysis of indanone diazo ketone was used to produce benzocyclobutenecarboxylic acid (18) which was then converted to various derivatives (Scheme III).[17f] Unfortunately, yields and physical constants of most of these derivatives were not given.
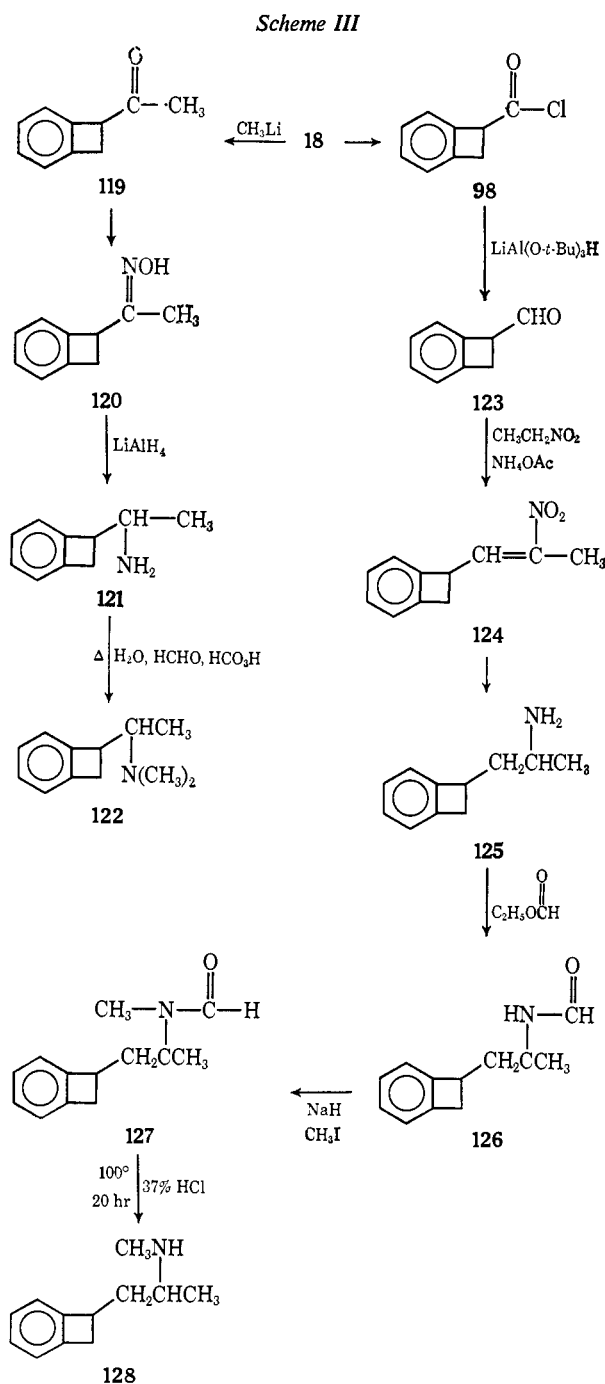
Scheme II

Scheme III

Bromination of *trans*-1-methyl-2-phenylbenzocyclobutene (111) in the presence of light can be controlled to give either the metastable liquid 2-bromo-1-methyl-2-phenylbenzocyclobutene (115) or the stable solid, 1,2-dibromo-1-methyl-2-phenyl-benzocyclobutene (116).[61] Treatment of the ether 117 (R =

R = CH$_3$, C$_2$H$_5$, *t*-C$_4$H$_9$

Many 1-substituted and 1,1-disubstituted derivatives of benzocyclobutene have been prepared by using 1-cyanobenzo-cyclobutene (34) as the starting material. Several papers and patents on the alkylation of 1-cyanobenzocyclobutene and on
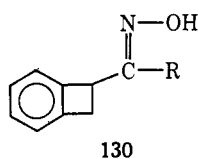
(61) A. T. Blomquist and C. G. Bottomley, *J. Amer. Chem. Soc.*, 87, 86 (1965).

the conversion of 1-cyanobenzocyclobutene to derivatives of 1-acetylbenzocyclobutene have been published.[62]
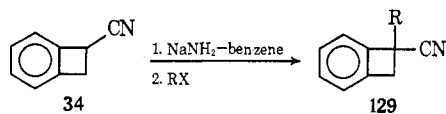
The isolation of a number of oximes of acylbenzocyclobutenes has been reported, but the stereochemistry was not determined.[62b] Samples of several of these oximes, **130**, were obtained by another investigator and their stereochemistry determined *via* nmr analysis and Beckmann rearrangement with phosphorus pentachloride in ether[63] (Table II).
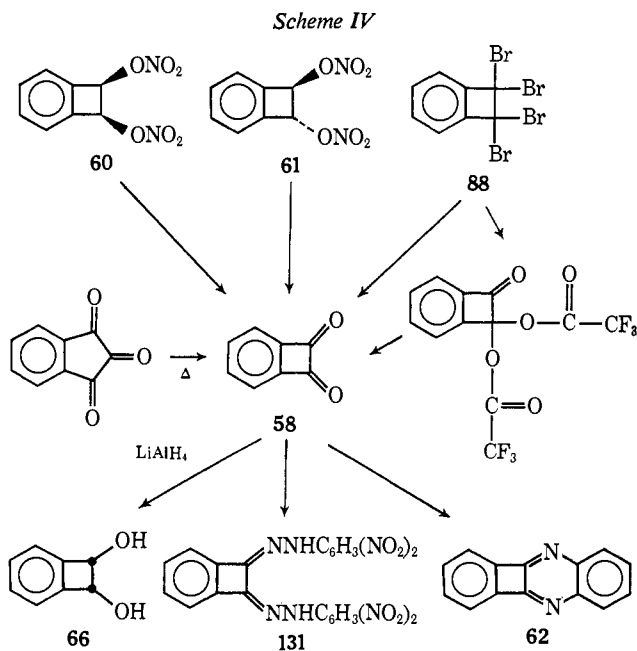
Table II

130

R	Oxime config[63] relative to R	Mp, °C[62b]
CH₃	syn	90–92
C₆H₅	anti	131–134
n-C₄H₉	syn	55–58
C₆H₅CH₂	syn	87–90
C₆H₁₁	syn	187–188

C. BENZOCYCLOBUTADIENOQUINONE (BENZOCYCLOBUTENEDIONE)

Benzocyclobutadienoquinone (**58**) forms pale yellow prismatic crystals, mp 133–135°, which possess a faint but musty qui-

Scheme IV

none-like odor. It appears to be quite stable thermally and sublimes unchanged at 100° under 0.2 mm pressure. The α-diketone system was cleaved readily in base. Several routes to the preparation of benzocyclobutadienoquinone have already been mentioned and they are summarized in Scheme IV.

Reaction of the diketone **58** with phenylmagnesium bromide gave diphenylisobenzofuran (**132**) in 60% yield.[48] The reaction
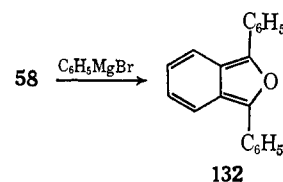
of benzocyclobutenedione (**58**) with triphenylphosphine–carbomethoxymethylene gave two different products in high yield depending on the amount of Wittig reagent used[64] (Scheme V).

Scheme V

Treatment of the diketone **58** with methylmagnesium bromide gave two colorless crystalline compounds of composition C₁₀H₁₂O₂.[65] These were shown to be the *cis* and *trans* isomers produced by normal Grignard addition. Assignment of configuration was based on the rates of oxidation by lead tetra-
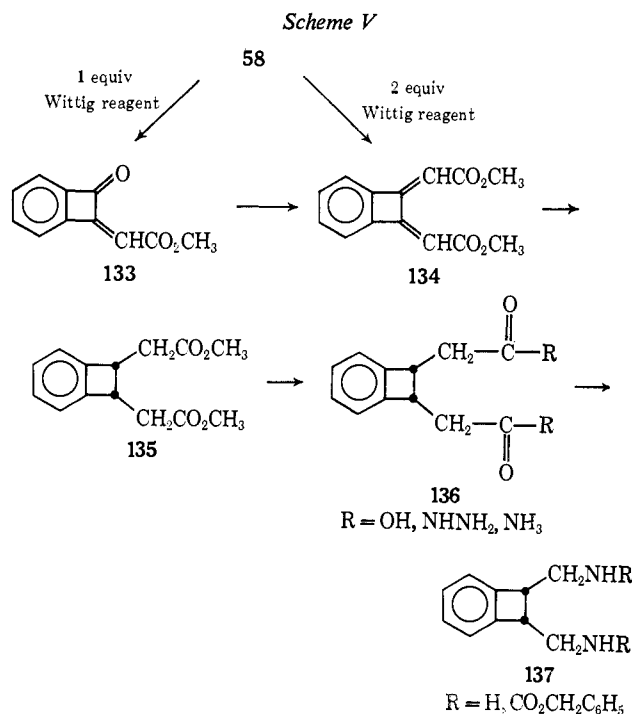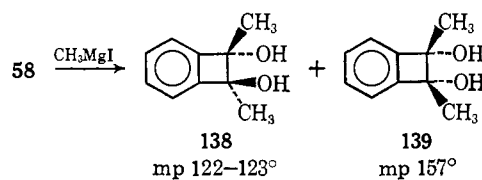

(62) (a) J. A. Skorcz and F. E. Kaminski, *J. Med. Chem.*, **8**, 732 (1965); (b) J. A. Skorcz, J. T. Suh, C. I. Judd, M. Finkelstein, and A. C. Conway, *ibid.*, **9**, 656 (1966); (c) J. A. Skorcz, U. S. Patent 3,359,300 (1967); *Chem. Abstr.*, **68**, 10112 (1968); (d) German Patent 1,235,903 (1967); *Chem. Abstr.*, **68**, 5732 (1968); (e) J. E. Robertson and J. A. Skorcz, U. S. Patent 3,308,157 (1967); *Chem. Abstr.*, **67**, 43590 (1967).
(63) C. F. Barfknecht, *J. Pharm. Sci.*, **56**, 1364 (1967).

(64) (a) M. P. Cava and R. J. Pohl, *J. Amer. Chem. Soc.*, **82**, 5242 (1960); (b) M. P. Cava, R. J. Pohl, and M. J. Mitchell, *ibid.*, **85**, 2080 (1963).
(65) M. P. Cava, M. J. Mitchell, and R. J. Pohl, *Tetrahedron Lett.*, 825 (1962).

acetate. The isomer, mp 122–123°, had a rate constant of 116 and was assigned the *trans* configuration **138**; the isomer, mp 157°, had a rate constant greater than 30,000 and was assigned the *cis* configuration **139**. Treatment of the diols with acetic anhydride and pyridine at steam-bath temperatures gave slowly a monoacetate and then a diacetate. The diol diacetates proved surprisingly stable to pyrolysis. When the *cis* diacetate **140** was passed over Sterchamol firebrick at 300°, cracking occurred to give 1,2-dimethylenebenzocyclobutene (**141**) in 27% yield. The diene was a colorless liquid which froze in an ice bath to give crystals, mp 15–16°. It polymerized to a thick
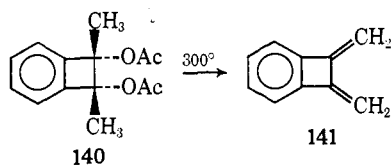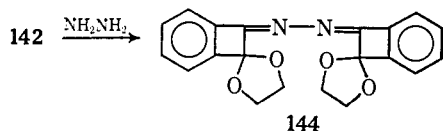

gum at room temperature after a few hours. The diene could be hydrogenated to give *cis*-1,2-dimethylbenzocyclobutene.

The reaction of the dione **58** with hydroxylamine, hydrazine, or *p*-toluenesulfonylhydrazine gave ring-opened derivatives of phthalic acid.[66] Treatment of the dione **58** with either 1 or 2 equiv of ethylene glycol led to two derivatives (**142** or **143**) of benzocyclobutene as shown.
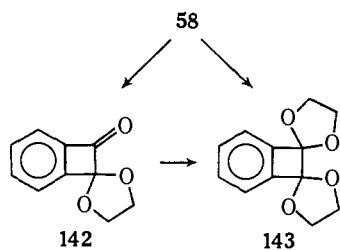
The reaction of the monoketal **142** with hydrazine gave the azine of the monoketal.

Benzocyclobutene-1,2-dione (**58**) has been shown to undergo photochemical dimerization by several different groups to produce at least the three products (**145–147**) shown.[67]
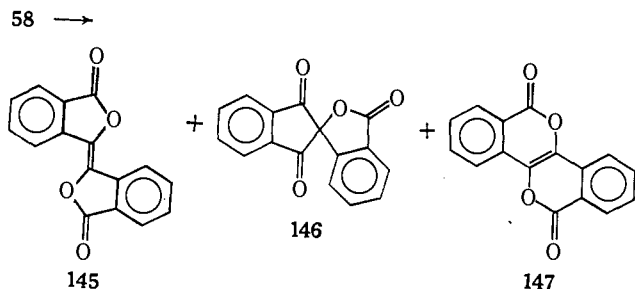
D. ELECTROPHILIC SUBSTITUTION

Several groups have investigated the electrophilic substitution of benzocyclobutenes. Two major questions have come forth: (1) what effect does the four-membered ring have on the rate of the reaction; (2) what effect does the four-membered ring have on the position of aromatic substitution. The rate of an electrophilic substitution reaction was obtained by studying the rate of benzoylation of benzocyclobutene, using benzoyl chloride–aluminum chloride.[68] No attempt was made to isolate any of the products (see Table III).

Table III

Rates of Aluminum Chloride Catalyzed Benzoylation of Selected Benzene Derivatives in Ethylene Chloride
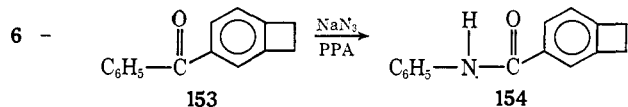
Aromatic	Relative rate
Benzene	1/1700
Toluene	1/13
o-Xylene	1
Indan	1.9
Tetralin	2.3
Benzocyclobutene	2.8

Nitration of benzocyclobutene has been studied by several groups.[69] The principle benzocyclobutene derivative formed is 4-nitrobenzocyclobutene. If any 3-nitrobenzocyclobutene is present it is produced in less than 5% yield.

Acylation in carbon disulfide using aluminum chloride does not give any substituted benzocyclobutene. A similar result is obtained using methylene chloride as a solvent. When nitromethane is used as a solvent for aluminum chloride acylation, the mixture obtained contains 4-acetylbenzocyclobutene (**148**), isolated in 27% yield after chromatography. This undergoes the normal reactions of aromatic methyl ketones.
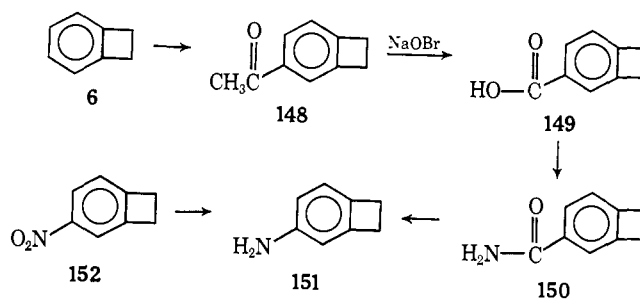
The ratio of ring-opened to ring-closed product in the benzoylation of benzocyclobutene depends on the solvent and the catalyst.[70] The ring-closed product has been shown to be 4-benzoylbenzocyclobutene (**153**). Schmidt azide rearrangement, in polyphosphoric acid, of **153** produced **154**

(66) M. P. Cava and R. P. Stein, *J. Org. Chem.*, **31**, 1866 (1966).
(67) (a) H. A. Staab and J. Ipaktschi, *Tetrahedron Lett.*, 583 (1966); (b) *Chem. Ber.*, **101**, 1457 (1968); (c) R. F. C. Brown and R. K. Solly, *Tetrahedron Lett.*, 169 (1966).

(68) F. R. Jensen and G. Maciel, *J. Org. Chem.*, **25**, 640 (1960).
(69) (a) J. B. F. Lloyd and P. A. Ongley, *Tetrahedron*, **20**, 2185 (1964); (b) L. Horner, H. G. Schmelzer, and B. Thompson, *Chem. Ber.*, **93**, 1774 (1960).
(70) J. B. F. Lloyd and P. A. Ongley, *Tetrahedron*, **21**, 245 (1965)

in about 40% yield. This reaction also produces a material identical (ir, phosphate ester) with that obtained when 4-benzocyclobutenylbenzamide (155) is treated with polyphosphoric acid, which suggests that both amides are formed in the rearrangement. The instability of 155 in acid is expected
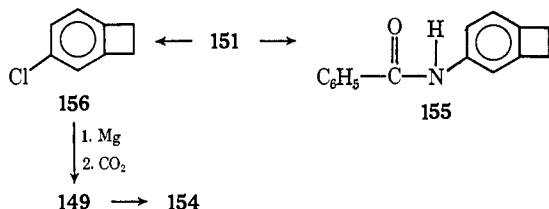

since the substituted amino group should facilitate a protodealkylation, just as it does in 4-acetamidobenzocyclobutene.[69] Sulfonation with dioxane–sulfur trioxide complex in ethylene chloride, bromination in acetic acid in the presence of iodine, and chlorination under the same conditions did produce the various 4-substituted benzocyclobutenes, respectively.[70] The structure of the chlorinated product was proven by independent synthesis from the 4-amino derivative 151 *via* a Sandmeyer reaction.

This seems to be the appropriate place to comment on the observation that electrophilic substitution of benzocyclobutene appears to take place predominantly, if not exclusively, in the 4 position. The rates of tritiodeprotonation of several fused strained ring systems have been studied, and the following generalization regarding the position of electrophilic substitution was presented.[71] "Aryl positions adjacent to a fused strained ring have enhanced acidity and reduced reactivity toward electrophilic substitution. The atomic orbitals of the fused aryl carbon used to construct the strained ring have higher p character; hence, the remaining orbital has higher s character. The *ortho* carbon is thus bound to an orbital of higher electronegativity."

It has been noted in studying the reactivity of other molecules containing a strained ring fused to a benzene ring, *viz.*, biphenylene, indan, and triptycene, that in all of these the α-aromatic position is less reactive than the β-aromatic position. A recent explanation of this has been attributed to the fact that in the transition state for α-aromatic substitution, the bond common to the two rings has a higher double-bond character than the transition state for β substitution, leading to increased strain in the fused ring and destabilization of the transition state.[72]

The oxidation of 4-hydrozybenzocyclobutene with Fremy's salt has been reported to produce benzocyclobutene-3,4-quinone (157).[69b] The relative unreactivity of the 3 position
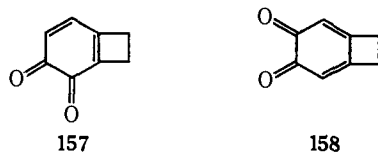

toward electrophilic substitution suggests that this position in a 4-substituted benzocyclobutene should also be unreactive. Reinvestigation of the oxidation of 4-hydroxybenzo-

cyclobutene proved that the oxidation product was benzocyclobutene-4,5-quinone (158), and not 157.[78]

R = H, CH₃CO
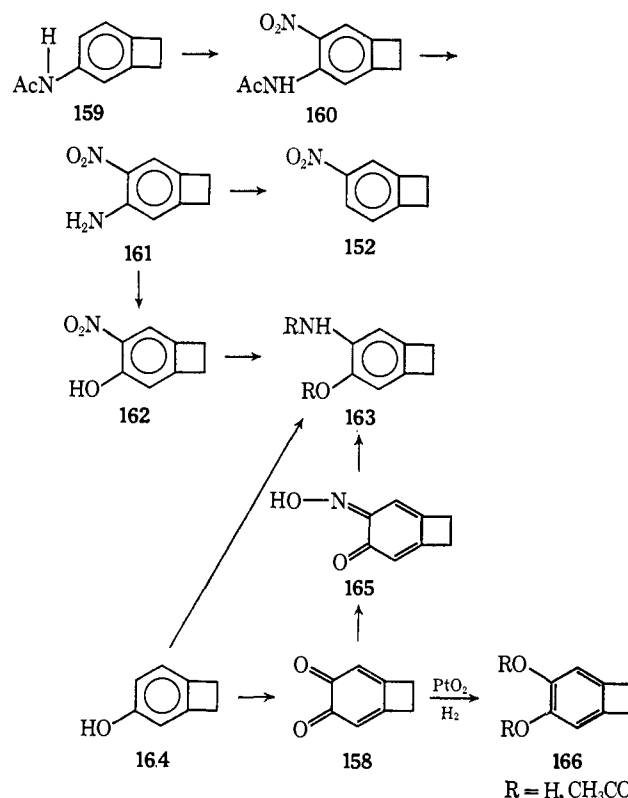
Iodination of benzocyclobutene produced the expected 4-iodobenzocyclobutene (167) in 57% yield.[74]
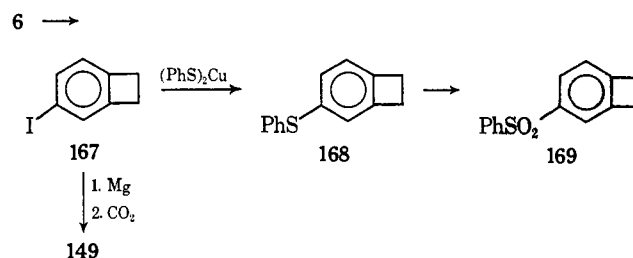
Very little work has been done on the position of electrophilic substitution in a 1-substituted benzocyclobutene. Nitration of 3-bromo-4-hydroxybenzocyclobuten-1-one (25) with nitric acid gave the 5-nitro derivative in 46% yield.[20] In this molecule there is only one pertinent position for electrophilic substitution, *i.e.*, the 5 position. Nitration of 1-cyanobenzocyclobutene has been shown to give predominantly if not exclusively 1-cyano-5-nitrobenzocyclobutene (170) as the only isolatable nitrocyanobenzocyclobutene.[85e]
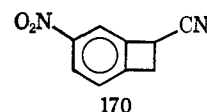
(71) A. Streitwieser, Jr., G. R. Ziegler, P. C. Mowery, A. Lewis, and R. G. Lawler, *J. Amer. Chem. Soc.*, 90, 1357 (1968).
(72) R. Taylor, G. J. Wright, and A. J. Homes, *J. Chem. Soc. B*, 780 (1967), and references therein.

(73) J. B. F. Lloyd and P. A. Ongley, *Tetrahedron*, 21, 2281 (1965).
(74) L. Horner, P. V. Subramaniam, and K. Eiben, *Tetrahedron Lett.*, 247 (1965); *Justus Liebigs Ann. Chem.*, 714, 91 (1968).

E. MISCELLANEOUS REACTIONS

The metalation of benzocyclobutene with sodium and potassium alkyls has been shown to take place at the 3 position.[75] This reaction proceeds in poor yield, 6% of pure benzocyclobutene-3-carboxylic acid (171) being isolated.
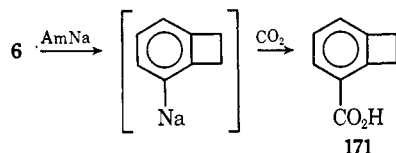

The esr spectrum on the anion radical of benzocyclobutenedione has been obtained.[76] The seven-line spectrum is readily assigned to isotropic proton coupling constants of 1.87 and 3.74 G for two sets of equivalent protons.

The preparation of stable benzocyclobutenyl cations in 96% sulfuric acid has been studied.[77] Several substituted benzocyclobutenols were prepared by treating the corresponding ketone with an aryl Grignard reagent. Solution of the compounds in 96% sulfuric acid gave intensely colored,

R	X	Y
H	CH₃	H
H	Cl	H
CH₃	CH₃	Cl
CH₃	Cl	CH₃
CH₃	CH₃	OCH₃
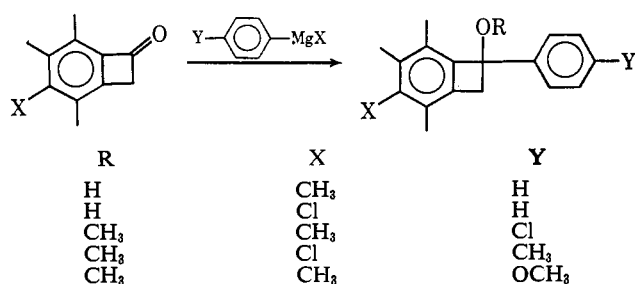
stable solutions whose electronic and nmr spectra were consistent with the formation of the corresponding carbonium ions. Hydrolysis or methanolysis of the acid solutions gave the starting alcohols or methyl ethers in high yield, indicating that no structural rearrangement had occurred. The nmr spectrum of the cation derived from 172 shows that considerable positive charge is delocalized to the benzo ring.
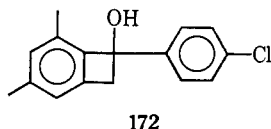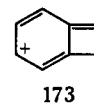

Both methyls (*ortho* and *para* to the carbonium ion center) are deshielded relative to their positions in carbon tetrachloride. The methylene protons experience an even greater downfield shift (about 1 ppm), being directly attached to the ionization site. Even the aromatic protons *meta* to the carbonium carbon are deshielded by ca. 0.7 ppm, showing that there is considerable positive charge on the *meta* carbon atoms of the benzo ring. When the derivative containing all aromatic positions substituted with methyl groups was examined, it was found that the deshielding effect is selective, being stronger at *ortho–para* positions than at *meta* positions. This suggests that the mechanism for transmitting the effect is probably *via* contributions from resonance forms such as
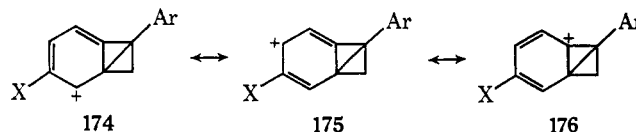

173, rather than a general inductive electron withdrawal by the carbonium ion carbon. Examination of the electronic spectra also led to the conclusion that the charge can also be delocalized by 1,3 π intermediates.

The formation and reactivity of the benzocyclobutenone anion has been reported in a brief communication.[78] Treatment of benzocyclobutenone (84) with a suspension of sodium hydride in DMF followed by acidic work-up gives the dimer 177 as the major product. When the reaction is
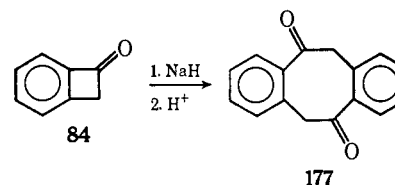
carried out in the presence of 1 equiv of benzaldehyde, the major product is the carboxylic acid 178. The carbonyl
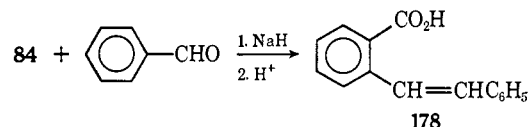
of benzocyclobutenone is more reactive toward condensation than a typical ketone, but less reactive than an aldehyde.

The crystal structure of several *cis*-1,2-dihalobenzocyclobutenes has been determined by single-crystal X-ray diffraction studies.[79] These are the chloride, bromide, and iodide. Within limits there is no significant difference in the shape and size (other than the C–X bond distance) among the three molecules. The chloride was shown to be monoclinic with the bromide and iodide being orthorhombic. In the dichloride the cyclobutene ring is planar rather than skewed. Its plane is the same as that of the benzene ring within 1.5° (Figure 1).[80] The crystal structure of benzo[1,2:4,5]dicyclobutene has also been reported.[81] The molecule is reported to be planar (Figure 2).

Several groups have reported on the nmr spectra of various benzocyclobutenes.[82] Examination of the 220-Mc spectra of several substituted 1-cyanobenzocyclobutenes produced the data in Table IV.[83] The aliphatic protons exhibit an ABX pattern.

(75) R. A. Finnegan, *J. Org. Chem.*, 30, 1333 (1965).
(76) D. H. Geske and A. L. Balch, *J. Phys. Chem.*, 68, 3423 (1964).
(77) H. Hart and J. A. Hartlage, *J. Amer. Chem. Soc.*, 89, 6672 (1967).

(78) D. J. Bertelli and P. Crews, *ibid.*, 90, 3889 (1968).
(79) G. L. Hardgrove, L. K. Templeton, and D. H. Templeton, *J. Phys. Chem.*, 72, 668 (1968).
(80) G. L. Hardgrove, UCRL Report 8803, 1959.
(81) S. G. G. MacDonald, J. Lawrence, and M. P. Cava, *Chem. Ind.* (London), 86 (1965).
(82) (a) Reference 17e; (b) ref 49; (c) G. Fraenkel, Y. Asahi, M. J. Mitchell, and M. P. Cava, *Tetrahedron*, 20, 1179 (1964); (d) ref 35e.
(83) I. L. Klundt, unpublished results. Spectra were determined by L. F. Johnson, Varian Associates.

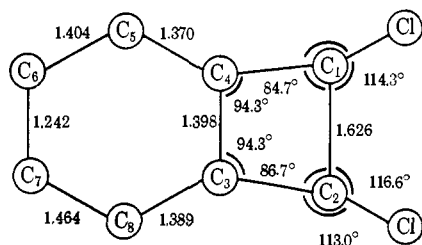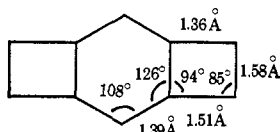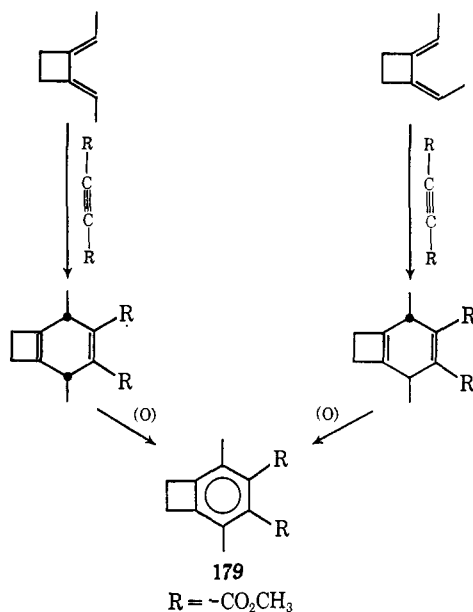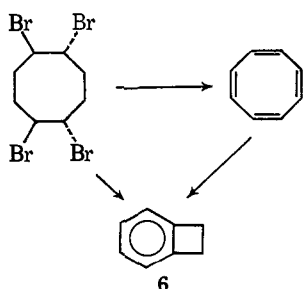**Figure 1.** Interatomic distances (Å) and angles in $C_8H_6Cl_2$ at 25°.

Figure 2.

IV. Addendum

Dehydrogenation of a preformed ring system has been used to prepare 3,6-dimethyl-4,5-dicarbomethoxybenzocyclobutene (179).[84]

179

$$R = -CO_2CH_3$$

The treatment of 1,2,5,6-tetrabromocyclooctane or cyclooctatetraene with a strong base has been shown to produce benzocyclobutene.[85]

6

Table IV

R_1	R_2	δ_{H1}	δ_{H2}	δ_{H3}	$J_{1,2}$	$J_{1,3}$	$J_{2,3}$
H	H	4.15	3.43	3.58	2.5	5.5	14
Cl	H	4.24	3.49	3.65	3.0	5.5	14
NO$_2$	H	4.42	3.67	3.85	3.0	5.5	15
HNCOCH$_3$	H	4.22	3.50	3.65	2.5	5.5	14
H	OH	4.17	3.45	3.61	2.25	5.5	14
H	OCH$_2$C$_6$H$_5$	4.13	3.45	3.58	3	5.5	14
OCH$_3$	OCH$_3$	4.17	3.45	3.60	2.5	5.25	13.5
Cl	NO$_2$	4.36	3.65	3.80	3	5.5	14.5

An attempt to prepare 1-cyano-2-phenylbenzocyclobutene has been reported.[86] The method utilized was to treat 2-*o*-chlorophenyl-2-phenylpropionitrile with sodium amide. This method failed to give a nitrogen-containing product. When the R group in **180** was a methyl or a benzyl group, the desired ring closure took place to give the benzocyclobutene **181**.

180   **181** .

$$R = C_6H_5, CH_3, -CH_2C_6H_5$$
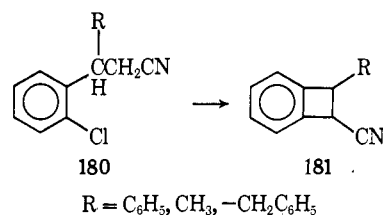
The reaction of benzyne with *cis*-3,4-dichlorocyclobutene to give a substituted benzocyclobutene has been reported.[87] The method of generation of benzyne was not mentioned. The product is assigned the *cis-exo* structure **182** on the basis of its nmr spectrum.

182

The rate of cleavage (protodesilylation) of some trimethylsilyl derivatives of benzocycloalkenes and *o*-xylene has been used to indicate the reactivity of the 3 and 4 positions in these molecules.[88] Chart I depicts the rates (10³*k*) of reaction of the various positions.

Treatment of 3,4,5,6-tetramethylbenzocyclobutene with peroxytrifluoroacetic acid–boron trifluoride at −30° produced the oxidation product **183** in 34% yield.[89]


183

(84) P. Heimbach and R. Schimpf, *Angew. Chem. Int. Ed. Engl.*, 8, 206 (1969).

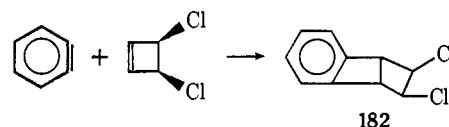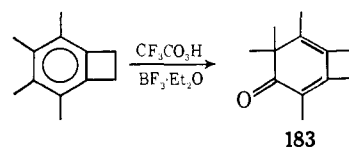(85) G. Eglinton, W. McCrae, R. A. Raphael, and J. A. Zabkiewicz, *J. Chem. Soc. C*, 474 (1969).

(86) N. Campbell and R. A. N. Morris, *Proc. Royal Soc. Edinburgh*, LXVIII, Part I, 23 (1968).

(87) R. N. McDonald and D. G. Frickey, *J. Amer. Chem. Soc.*, 90, 5315 (1968).

(88) A. R. Bassindale, C. Eaborn, and D. R. M. Walton, *J. Chem. Soc. B*, 12 (1969).

(89) R. J. Bastiani, D. J. Hart, and H. Hart, *Tetrahedron Lett.*, in press.

The availability of substituted 1,1-dichlorobenzocyclobutenes makes them an ideal starting material for the preparation of other benzocyclobutenes. A recent report details an excellent method for the removal of one or both halogen atoms. Treatment of the dichlorobenzocyclobutene with lithium in liquid ammonia removed both halogen atoms while treatment with Raney nickel and hydrogen at 2 atm produced the mono chloro derivative in good yield.[90]

Chart I
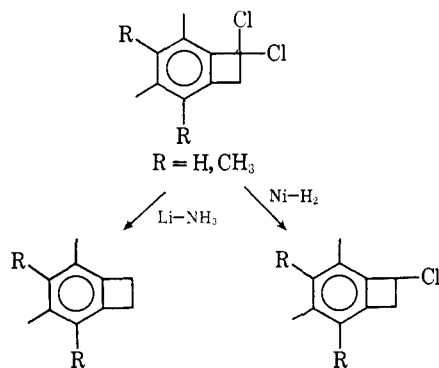
The Schmidt reaction reaction was applied to benzocyclobutenone and 4-methoxybenzocyclobutenone in sulfuric acid and trichloroacetic acid.[91] In sulfuric acid benzocyclobutenone gave a product resulting from aryl migration while that from 4-methoxybenzocyclobutenone involved alkyl migration. In trichloroacetic acid the rearrangement of the 4-methoxy derivative involved alkyl migration, but no reaction was observed with the parent ketone.
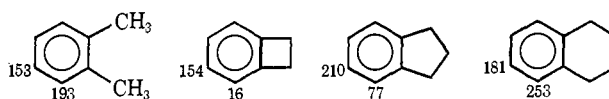
Attempts to prepare a benzocyclobutenyl carbene have been reported.[92] Pyrolysis of 4,6-dimethylbenzocyclobutenone *p*-toluenesulfonylhydrazone sodium salt (**184**), in acetamide gave the sulfone **185** and the acetamide **186**. Photolysis of this salt yielded sulfone **185** as well as a hydrocarbon tentatively identified as 1,1'-bis(4,6-dimethylbenzocyclobutylidene) (**187**). All of these products could arise through

the intermediate formation of the benzocyclobutenyl carbene **188**.

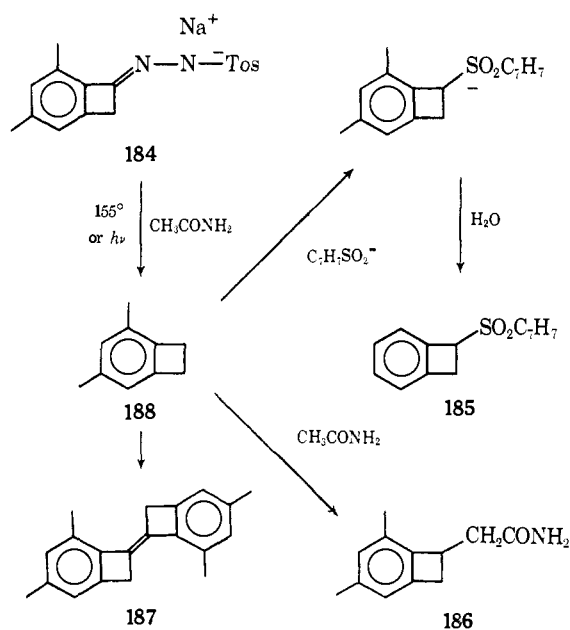(90) D. J. Hart and H. Hart, "Organic Preparations and Procedures," in press.
(91) M. Tomita, S. Minami, and S. Uyeo, *J. Chem. Soc. C*, 183 (1969).
(92) A. T. Blomquist and C. F. Heins, *J. Org. Chem.*, 34, 2906 (1969).