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Four-Membered Ring Compounds Containing Bis(methylene)cyclobutene or Tetrakis(methylene)cyclobutane Moieties. Benzocyclobutadiene, Benzodicyclobutadiene, Biphenylene, and Related Compounds

Fumio Toda*

Department of Industrial Chemistry, Faculty of Engineering, Ehime University, Matsuyama 790, Japan

Peter Garratt*

Christopher Ingold Laboratories, Department of Chemistry, University College London, 20 Gordon Street, London WC1H OAJ, UK

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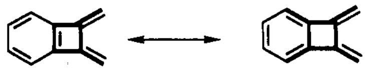
Contents

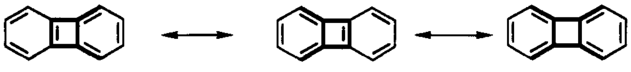
1 Introduction

The 3,4-bis(methylene)cyclobutene group occurs in many chemical species. It is a strained entity in that sp^2 hybridization would require bond angles of 120° at each of the four carbons of the 4-membered ring. Nevertheless, 3,4-bis(methylene)cyclobutene (**1a**) is itself formed by a thermal rearrangement (section 2.1) and is a stable, well characterized compound. Formally introducing a double bond to join the methylene atoms gives benzocyclobutene (**2**),[§] a compound of considerably less stability. The bis(methylene)cyclobutene structure **2a** is the most important of the contributing canonical structures, since structure **2b** incorporates a cyclobutadiene moiety. Annelating a benzene ring to **1a** gives bis(methylene)benzocyclobutane **3**, and annelation to benzocyclobutadiene gives biphenylene (**4**). Both **3** and **4** are more stable than **2**, and in both of these systems canonical forms containing the dimethylenecyclobutene are important but not exclusive, structures containing tetrakis(methylene)cyclobutane ([4]radialene) moieties (**3b**, **4c**) making a major contribution.


1a


2a 2b


3a 3b


4a 4b 4c

[§] Benzocyclobutene is the correct, but confusing, name for **2**, annelated systems ending in "ene" indicating complete unsaturation, unlike nonannelated nonaromatic systems. We prefer the name benzocyclobutadiene for **2** and will use it throughout this review.

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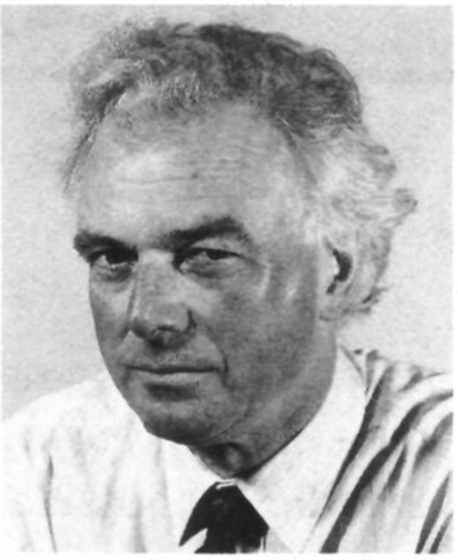
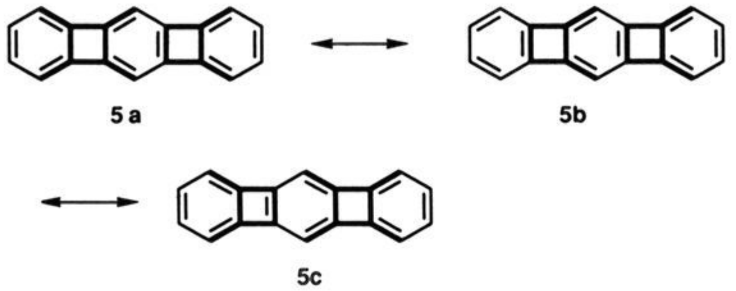
Fumio Toda received his Bachelor's, Master's, and Doctor's degrees from Osaka University at Osaka city, Japan in 1956, 1958, and 1960, respectively. After staying at Osaka University for four years as an Instructor and in United States for two years as a postdoctoral fellow, he obtained an Associate Professorship at Ehime University in 1966. He was promoted to full Professor in 1970. His research interests are in the area of strained small-ring compounds, host–guest inclusion compounds, solid-state chemistry, and reaction control in crystals.

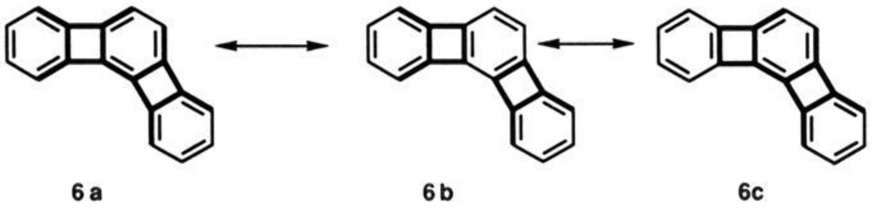


Peter Garratt obtained a B.Sc. in Biological Chemistry from Bristol University in 1956 and, after a period in teaching and a year with J. K. N. Jones in Canada, obtained a Ph.D. with T. J. Katz at Columbia University in 1964. He then returned to the UK as a NATO Fellow to work with F. Sondheimer at Cambridge University and was appointed a University Demonstrator and Fellow of Fitzwilliam College in 1966. He moved to University College London in 1967 and was made a Reader in 1974. His current research interests are in strained compounds, organic conductors, inhibitors of enzymes early in the pyrimidine biosynthetic pathway, ion channel blockers, and probing the structure of the melatonin receptor.

Extending the number of bis(methylene)cyclobutene structures from biphenylene can be done in two modes, linearly or angularly, as in **5** and **6**, respectively. In **5** at least one 3,4-bis(methylene)cyclobutene structure must be retained (**5a,c**), whereas in **6** a structure with only tetrakis(methylene)cyclobutane moieties can be accommodated (**6a**).



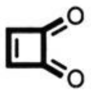
5a 5b 5c



6a 6b 6c

4-Methylenecyclobuten-3-one (**7**), cyclobutene-3,4-dione (**8**), 3,4-bis(methylene)cyclobutane-1,2-dione (**9**), and 2,4-bis(methylene)cyclobutane-1,3-dione (**10**) have related structures with similar strain effects. Again, these entities can participate in benzannelated structures such as **11** and **12**, but as with bis(methylene)benzocyclobutane, other canonical structures make important contributions.

7



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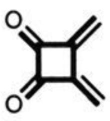

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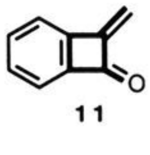

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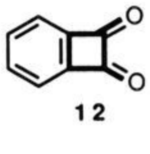


12

This review will examine the behavior of compounds possessing the bis(methylene)cyclobutene moiety, or a related structure, and will examine the limits that can be placed on these structural entities and the effects that they engender. Compounds of this type were reviewed in the classic text of Cava and Mitchell,[1] and certain aspects of the chemistry of such compounds may be found in other reviews.[2,3]

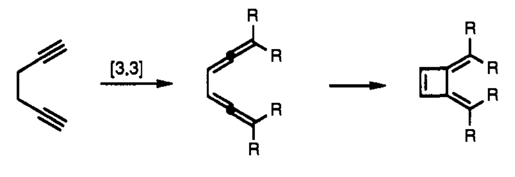
2 n-kis(methylene)cyclobutene Derivatives

2.1 3,4-Bis(methylene)cyclobutene and Nonbenzannelated Derivatives

2.1.1 Preparative Methods

3,4-Bis(methylene)cyclobutene (**1a**), although experiencing considerable bond-angle strain, is well known, being initially prepared, albeit in only 1% yield, by Blomquist and Maitlis in 1961 through the Hofmann degredation of 3,4-bis[(trimethylammonio)methyl]cyclobutene dihydroxide.[4] Currently, the main synthetic route to **1a** and substituted derivatives involves the electrocyclic rearrangement of hexa-1,2,4,5-tetraene or a substituted derivative. Thus **1a** can be derived thermally from **13a**.[5] The tetramethyl derivative **1b** can be similarly prepared from the corresponding tetramethylhexatriene **13b**, a higher temperature being required (250 °C, cf. 150 °C).[6,7] The *meso*-diallene **14** rearranged slowly at 150 °C but much more rapidly in boiling THF in the presence of copper(I) chloride,[8] in both cases to give **15** by conrotatory ring closure. The same catalytic effect of copper(I) was also observed in the formation of **1a**.[7]

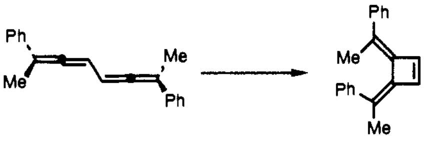
The first, and still probably the best, preparative route to 3,4-bis(methylene)cyclobutene (**1a**) was by the thermal rearrangement of hexa-1,5-diyne (**16**), the initial [3,3] sigmatropic rearrangement to **13a** being much slower than the subsequent electrocyclic ring closure of **13a** to **1a**.[9–11]



16

13a R = H
b R = Me

1a R = H
b R = Me



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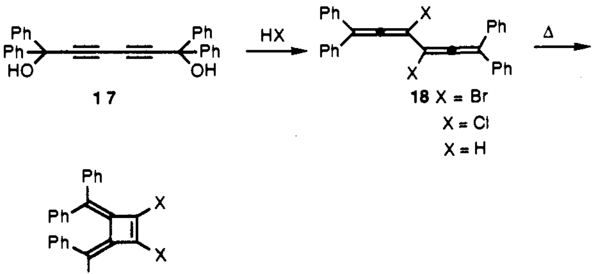
15

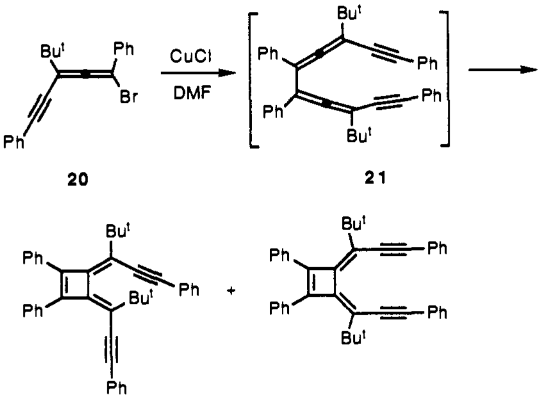
Thermolysis of the dibromotetraene **18**, readily prepared from the diol **17** by treatment with HBr, gave the dibromobis(diphenylmethylene)cyclobutene (**19a**)in almost quantitative yield.[12] The dichloride **19b** could be similarly prepared, and the cyclobutenyl halides were reactive, the bromine in **19a** being readily replaced by hydrogen to give **19c** by treatment with $LiAlH_4$. Coupling of the bromoallene **20** with copper(I) chloride gave a mixture of the bis(methylene)cyclobutenes **22** and **23**, presumably via the bisallene dimer **21**.[13]



17

18 X = Br
X = Cl
X = H

19a X = Br
b X = Cl
c X = H



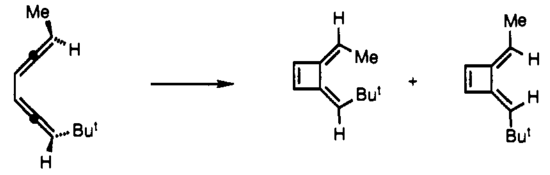
20

21

22

23

Pasto and co-workers[14,15] have investigated the mechanism of the bisallene to bis(methylene)cyclobutene rearrangement and have confirmed the original observations of Skattebol and co-workers.[8] In solution the reaction is catalyzed by Cu(I) salts, and the transformation proceeds at around 60 °C, whereas in the gas-phase temperatures of ca. 300 °C are required. Thermolysis of the *threo*-bisallene **24** gave a mixture of the two cyclobutenes **25** and **26** in the ratio 10.4:89.6 in the gas-phase reaction and 24.0:76.0 in solution. Both products are formed in a conrotatory process, compound **26** being much less sterically crowded than compound **25**.



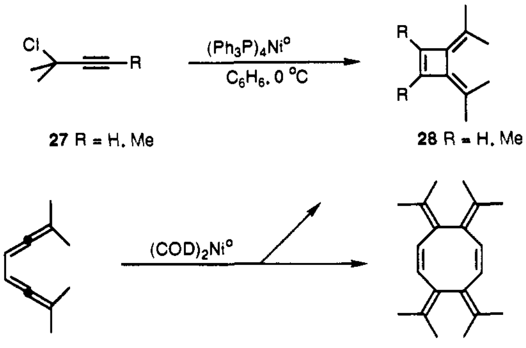
24

25

26

The mechanism of the rearrangement of 1,5-hexadiene was studied by Henry and Bergman,[16] who showed that, after rearrangement, the deuterium atoms of 1,6-dideuteriohexa-1,5-diyne appeared in the 1,2-positions of 3,4-bis(methylene)cyclobutene (**1a**). At higher temperatures **1a** rearranged to benzene and fulvene.

Treatment of the propargyl chlorides **27** with tetrakis(triphenylphosphoranyl)nickel in benzene under argon gave the 2-dipropenylcyclobutenes (**28**).[17] 2,7-Dimethylocta-2,3,5,6-tetraene (**29**) gave a trimer under these conditions but a mixture of 3,4-di-2-propylenecyclobutene (**28**, R = H) and 3,4,7,8-tetra-2-propylenecycloocta-1,5-diene (**30**) on reaction with dicyclooctadienenickel.[18]



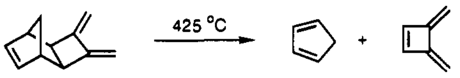
27 R = H, Me

28 R = H, Me

29

30

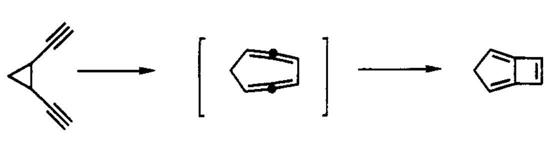
Bis(methylene)cyclobutene (**1a**) can also be prepared by the retro-Diels–Alder cleavage of **31** at 425 °C, the latter being prepared in three steps from the Diels–Alder adduct of quadricyclane with maleic anhydride.[19]

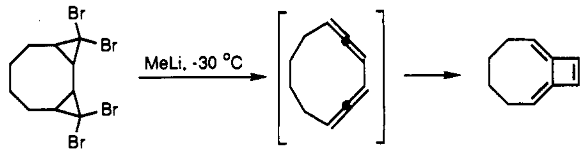


31

1a

Thermolysis of 1,2-diethynylcyclopropane (**31a**) at atmospheric pressure gave bicyclo[3.2.0]hepta-1,4,6-triene (**33**), presumably via the highly strained bisallene **32**.[20] *cis*-1,2-Diethynylcyclobutane on thermolysis gives, by contrast, mainly 1,2-dihydropentalene and very little bicyclo[4.2.0]octa-1,5,7-triene.[21,22] Bicyclo[6.2.0]deca-1,7,9-triene (**36**) is obtained when the tetrabromide **34** is treated with methyllithium at −30 °C, presumably through the intermediacy of the bisallene **35**.[23]


31a **32** **33**



34 **35** **36**

2.1.2 Structure and Spectroscopic Properties

A detailed microwave analysis has been carried out on **1a**.[24] The structure is shown in Figure 1. The molecule is flat, the C1–C4 and C2–C3 bonds are single, the bond angles in the ring are close to 90°, and the exocyclic bond angles are ca. 135°.

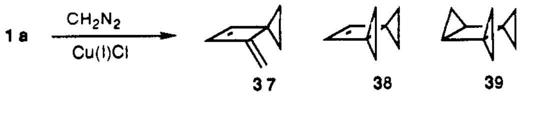
An earlier electron diffraction study by Skancke[25] had given values of values 135.7 pm for C_1–C_2, 148.8 pm for C_1–C_2 (C_3–C_4), and 151.6 for C_2–C_3. The compound has a large dipole moment (0.617 D) for an alternant hydrocarbon.[26,24] In the ^1H NMR spectrum the cyclobutene protons are at δ 6.84 and the two types of methylene protons at δ 4.59 and 4.70.[10] The detailed vapor infrared spectrum has been analyzed,[27] and the electronic spectrum is broad, showing a band at 240 nm (log ϵ 4.2) and at 294 nm.[4,27]

In 3,4-bis(diphenylmethylene)cyclobutene, the protons on the aromatic ring appear as two bands centered on δ 6.8 and 8.2 in the ratio 1:1. The higher field δ 6.8 band is attributed to the inner benzene rings which are mutually shielding (Figure 2), and this phenomena is observed in related derivatives.[28]

A variety of calculations have been carried out for **1a**. The calculated enthalpy of formation is in good agreement with the experimental value determined from hydrogenation[29] and indicates that the system is nonaromatic. Earlier calculations had suggested that **1a** had a small, negative resonance energy per electron (REPE), comparable to that of benzocyclobutene (**2**) (**1a**, −0.028 β, **2**, −0.027 β).[30]

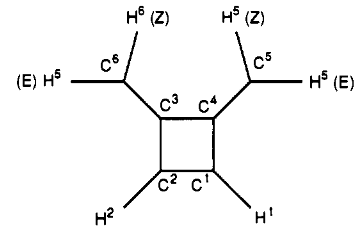
2.1.3 Reactions

Although **1a** is sterically ideally set up as a Diels–Alder diene, this type of reaction does not occur, presumably because the ensuing product has to have a cyclobutadiene ring. Addition of diazomethane to **1a** gave the spiro derivatives **37–39**.[31]



37 **38** **39**

Halogens add to the tetraphenyl derivatives **19a,b** on the cyclobutene double bond to give the corresponding tetrahalocyclobutanes **44a,b**.[32] The endo double bond of the tetraphenyl derivatives **19a,c** is also photosensitive. Irradiation of a benzene solution of **19a** under an oxygen atmosphere gave **42a** as crimson prisms.[32] The corresponding irradiation of **19c** gave 2,3-bis(diphenylmethylene)butane-1,2-dione (**43a**).[33,34] This reaction probably proceeds via a dioxetane intermediate whereas the photooxidation of **19a** may proceed through the radical intermediate **40**, which then undergoes a 1,2-shift of a bromine atom to give the radical **41**. Unlike the bromo derivative, the dichloride **19b** is inert to photooxidation but can be readily oxidized by dioxygen in the presence of a catalytic amount of diethyl ether peroxide to **43b**.



Bond	Length (pm)	Angle	Degrees
C_1-C_2	136.80	< C_1 - C_2 - C_3	93.54
C_2 - C_3	147.92	< C_2 - C_3 - C_4	86.46
C_3 - C_4	149.68	< C_3 - C_4 - C_5	135.75
C_4 - C_5	133.79	< C_4 - C_5 - H_5 (E)	133.68
C_1 - H1	107.99	< H_1 - C1 - C2	121.01
C_5 - H_5 (E)	108.59	< C_4 - C5 - H5 (Z)	120.33
C_5 - H_5 (Z)	108.41		

Figure 1. Structure of 3,4-bis(methylene)cyclobutene by microwave spectroscopy.

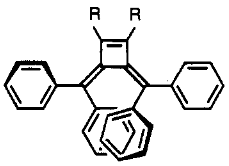
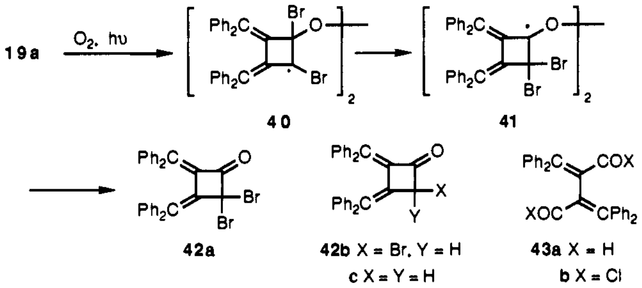


Figure 2. Structure of **19** showing overlap of inner benzene rings.



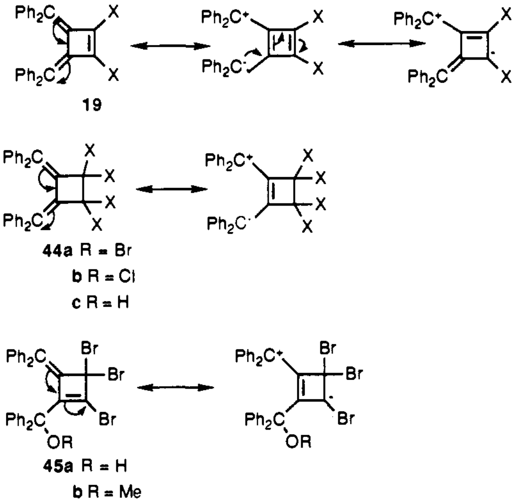
A comparison of the electronic spectra of the dihalocyclobutenes **19a–c** with the saturated derivatives, obtained after the addition of halogen, is revealing. The unsaturated compounds are colorless, with absorption bands in the ultraviolet, whereas the saturated derivatives are colored, with absorption bands in the visible region (Table 1). This finds a satisfying explanation in that the canonical contributions to **19** to allow conjugation require antiaromatic cyclobutadiene containing structures whereas those for **44** do not (Scheme 1).[35]

Reaction of **19a** with $AgClO_4$ in the presence of water gave the hydroxycyclobutene derivative **45a**, while the same reagent in the presence of methanol gave the corresponding methoxy derivative **45b**. These compounds have very similar electronic spectra to **19**, presumably because of a similar dipolar contribution to the ground state (Scheme 1).

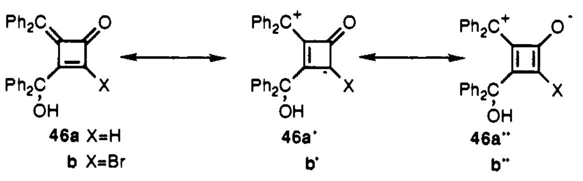
Table 1. Electronic Spectra of Bis(diphenylmethylene)-cyclobutene and -cyclobutane Derivatives

compd	solvent	λ_{max}, nm ($10^{-2}\epsilon_{max}$)
19a	CH_3Cl	290 (364)
19b	CH_3Cl	285 (364)
19c	CH_3Cl	280 (308)
44a	CH_3Cl	295 (135), 400 (162)
44b	CH_3Cl	290 (126), 388 (159)
44c	CH_3Cl	260 (235), 357 (209)
45a	EtOH	275 (131)
45b	EtOH	271 (158)
46a	EtOH	277 (103)
46b	EtOH	280 (154)

Scheme 1

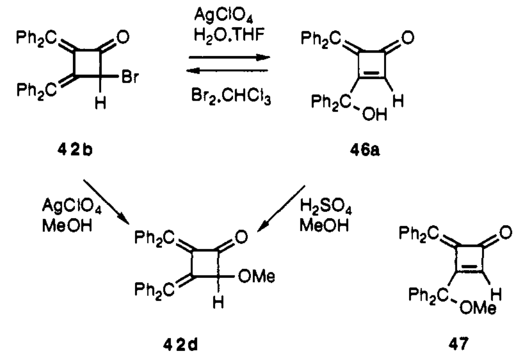


The first derivative of 4-methylenecyclobut-2-enone, 3-(diphenylhydroxymethyl)-4-(diphenylmethylene)cyclobut-2-enone (**46a**), was obtained by treatment of **42b** with aqueous $AgClO_4$.[35] Similar treatment of the dibromide **42a** gave the corresponding monobromo derivative **46b**.[35] The UV spectra of **46a** and **46b** are both similar to that of 3,4-bis(diphenylmethylene)-cyclobutene (**19c**), again indicating that cyclobutadiene-like structures do not greatly contribute to the ground state. The IR spectra of **46a** and **46b** show the C=O stretching bands at ca. 1770 cm^{-1} (**46a**, 1765 cm^{-1}; **46b**, 1790 cm^{-1}), the higher frequency suggesting that the carbonyl group is not highly polarized, again attributable to little contribution from **46″**.



The corresponding ethers could not be prepared by substituting MeOH for H_2O in the above reactions. In the case of **42b**, treatment with $AgClO_4$ in the presence of MeOH gave **42d** by a simple substitution of bromine. The attempted preparation of **47a** by methanolysis of **46a** with MeOH in the presence of H_2SO_4 also gave **42d**, presumably through an acid catalyzed rearrangement. Treatment of **46a** with bromine led to the reformation of **42b** rather than substitution of the hydroxyl group. Presumably, whereas the tautomer **46a** is preferred over the nonconjugated form, the bromide and methoxyl tautomers **42b** and **42d** are more stable than the conjugated systems. This may reflect a subtle balance between ring strain (there are four sp^3-C atoms in **47** and only three in **42d**) and conjugation (Scheme 2).

Scheme 2

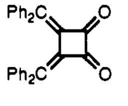


2.2 Cyclobutene-1,2-dione, 2,4-Bis(methylene)-cyclobutane-1,3-dione, and Nonbenzannelated Derivatives

2.2.1 Preparative Methods

The majority of methods for preparing cyclobutene-diones rely on the hydrolysis of geminal dihalides or geminal hydroxy halides to form the carbonyl groups. The methods have been reviewed by Schmidt and Ried.[36] Methods for the construction of the 4-membered ring include photochemical and thermal [2 + 2]-cycloaddition,[37-40] dimerization of tetrahaloethene with subsequent nucleophilic addition, elimination,[41-43] thermal [2 + 2]-cycloadditions between electron-rich and electron-poor ethenes,[44] intramolecular cyclization of hexatrienes,[45,46] rearrangement of cyclopropene derivatives,[47,48] and the addition of terakis[arylisocyanide] nickel to diphenylethyne.[49] The conversion of one cyclobutenedione, particularly the 2-halo or 2,3-dihalo derivatives, into another has also been a fruitful method of formation (see Schmidt and Ried, ref 36). General examples of some of these methods are shown in Scheme 3.

3,4-Bis(diphenylmethylene)cyclobutane-1,3-dione (**48**) was obtained in almost quantitative yield by treatment of **44a** with $AgBF_4$ in wet MeCN. Interestingly, increasing the water content to 10% gave **49** as the major product (44%) together with some **45a** (27%).[32] Substituting $AgClO_4$ for $AgBF_4$ in wet MeCN gave 3,4-bis(diphenylmethylene)succinic anhydride (**50**) in 85% yield. In this latter reaction, **45a** is initially formed but is then oxidized by the $HClO_4$ produced in the course of the reaction. This is substantiated by the ready oxidation of **48** with aqueous $HClO_4$, as well as with aqueous H_2O_2 and HNO_3.[32]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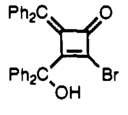
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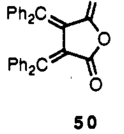
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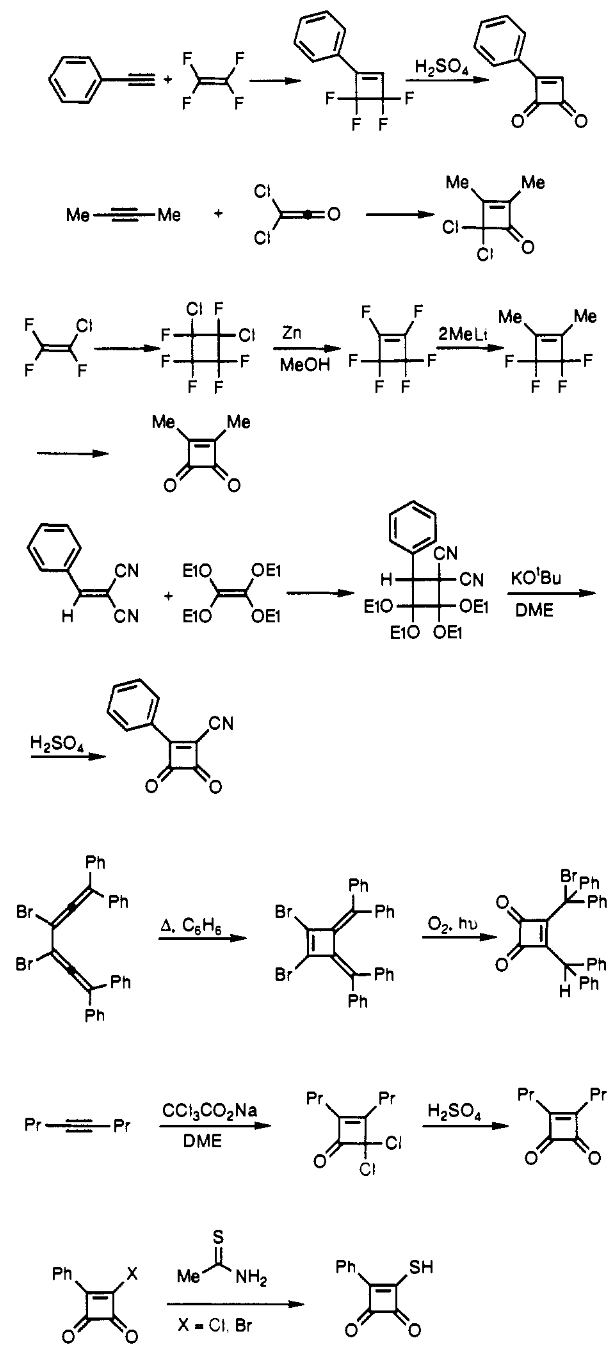
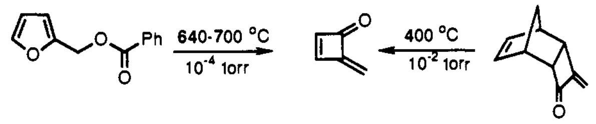
4-Methylenecyclobut-2-enone (**7**) was first prepared in 1973 by Trahanovsky and Park by the flash pyrolysis of furfuryl benzoate (**51**) at 640–700 °C.[50,51] Martin and co-workers have prepared **7** in a similar manner to

Scheme 3



their preparations of 3,4-bis(methylene)cyclobutene (**1a**) and cyclobutene-1,3-dione (**8**) by the pyrolysis of the adduct **52**.[19,52] Methylene cyclobutene was observed as a minor component in the pyrolysis of 2-propynyl propiolate.[53]

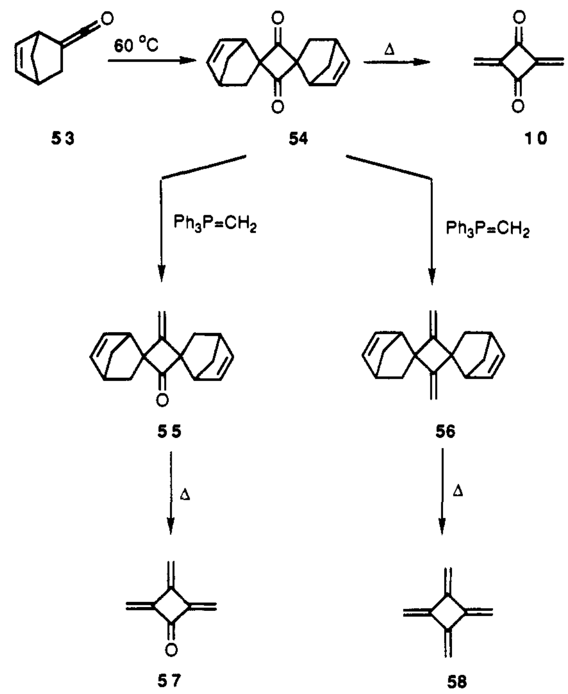


51 7 52

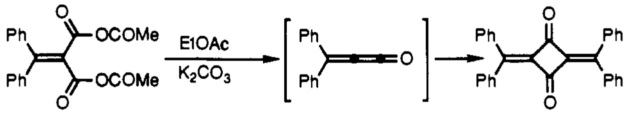
2,4-Bis(methylene)cyclobutane-1,3-dione (**10**) has been prepared by the flash photolysis of **54**, which in turn was prepared by dimerization of the ketene **53**.[54,55]

The dimer **54** reacted with methylenetriphenylphosphorane to give the monomethylene and bis(methylene) derivatives **55** and **56** and these in turn underwent flash

Scheme 4



pyrolysis to give tris(methylene)cyclobutanone (**57**) and tetrakis(methylene)cyclobutane (**58**) (Scheme 4).[55] Earlier, 2,4-bis(diphenylmethylene)cyclobutane-1,3-dione (**61**) had been prepared by the decomposition of the mixed anhydride **59**, presumably by way of the transient intermediate propadienone **60**.[56,57]

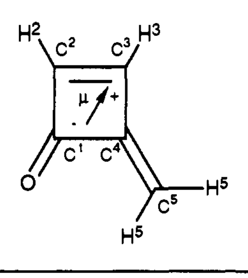


59 60 61

2-(Diphenylmethylene)-4-benzylidenecyclobutane-1,3-dione (**63**) was prepared by base condensation of 2-(diphenylmethylene)cyclobutane-1,3-dione with benzaldehyde.[58] The dione **62** was prepared from the bromide **46b** by base-catalyzed hydrolysis followed by elimination of HBr and benzophenone and subsequent protonation of the resultant enolate anion. Condensation of **62** with diphenylcyclopropenone rather than benzaldehyde gave the methylenecyclopropene **64**.[58] Both **63** and **64** added methoxide under basic conditions to give the cyclobutenyl enolate ions **65** and **66** (Scheme 5).

2.2.2 Structure and Spectroscopic Properties

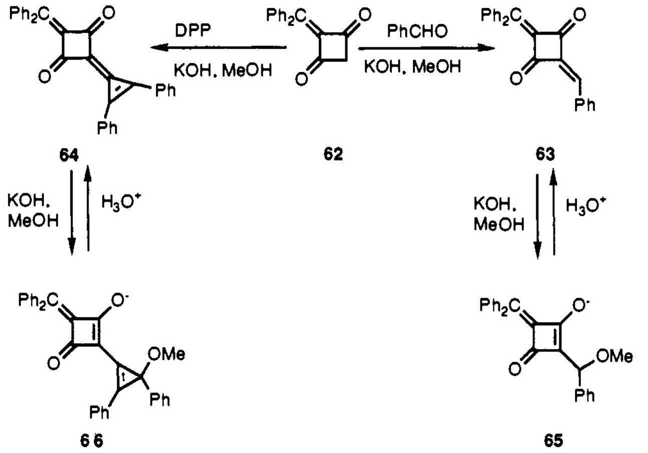
The ^{1}H NMR spectrum of 3-cyclobutene-1,2-dione (**8**) shows one signal at δ 9.73, the low-field value indicating a considerable contribution from dipolar forms. The IR spectrum shows a band at 1792 cm^{-1}, a considerably higher frequency than that of a simple ketone.[37] The IR spectrum of the bis(diphenylmethylene)cyclobutane-1,2-dione (**48**) also shows the carbonyl band at high frequency (1750 cm^{-1}). The microwave structure of 4-methylenecyclobut-2-enone (**7**) shows that it has a substantial dipole moment (3.39 ± 0.05 D) with the parameters shown in Figure 3. The ^{1}H NMR spectrum shows four doublets of triplets at δ 8.66 (H^3), 7.16 (H^2), 5.01 (H^5-Z), and 4.78 (H^5-E). The



Bond	Length (pm)	Angle	Degrees
$C^1 - C^2$	147.5	$O - C^1 - C^4$	134.5
$C^2 - C^3$	137.5	$C^1 - C^2 - H^2$	132.3
$C^3 - C^4$	147.5	$C^2 - C^1 - C^4$	86.1
$C^1 - C^4$	156.6	$C^1 - C^4 - C^3$	86.1
$C^4 - C^5$	134	$C^4 - C^5 - H^5$	121.5
$C^1 - O$	119		
$C^2 - H^2$ ($C^3 - H^3$)	108.3		
$C^5 - H^5$	108.6		

Figure 3. The structure of 4-methylenecyclobut-2-enone from the microwave spectrum.

Scheme 5

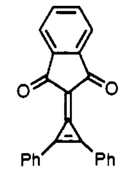


IR spectrum has bands at 1783 (C=O), 1688 (C=C), and 823 cm^{-1} (C=CH$_2$).

2,4-Bis(diphenylmethylene)cyclobutane-1,3-dione (61) has the carbonyl and methylene groups bent slightly away from each other out of the ring plane, the angle between the carbonyl carbon and the substituted carbon of the phenyl ring being 6.2°.[59] 2,4-Bis(phenylmethylene)cyclobutane-1,3-dione is centrosymmetric and nearly planar, the phenyl groups being slightly twisted out of the plane of the 4-membered ring.[60]

The IR spectrum of the 1,3-dione 64 shows a band at 1655 cm^{-1} for the C=O stretch, at a considerably lower frequency than those of 63 (1680 cm^{-1}) and 62 (1710 cm^{-1}) but at a comparable frequency to that of the methylenecyclopropene 67,[61] indicating a major contribution from the dipolar form. All of these carbonyl stretching frequencies are significantly lower than those of the cyclobutene-1,2-diones or methylenecyclobutane-1,2-diones (see 8 and 48). This is probably due in part to the smaller dipolar contribution to the 1,2-diones because of dipole-dipole interaction, but it also probably reflects the interaction between the two carbonyl groups in the latter systems. The ortho protons on the phenyl rings of 63 (δ 8.23–8.33), 64 (δ 8.47–8.60), and 67 (δ 8.65–8.80) are deshielded, largely through the diamagnetic anisotropy of the carbonyl group.[61]

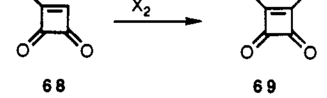
In the UV spectrum the absorption bands for the 1,2-diones are at a much longer wavelength than those for the 1,3-diones (Table 2) and this may also reflect a smaller contribution of the dipolar form to the ground state in the 1,2-diones.



67

2.2.3 Reactions

The reactions of substituted cyclobutene-1,2-diones have been reviewed.[62] The double bond is reactive and, for example, the proton of 3-phenylcyclobutene-1,3-dione (68) can be substituted by treatment with halogen to give the corresponding 4-halo derivative 69.[39]

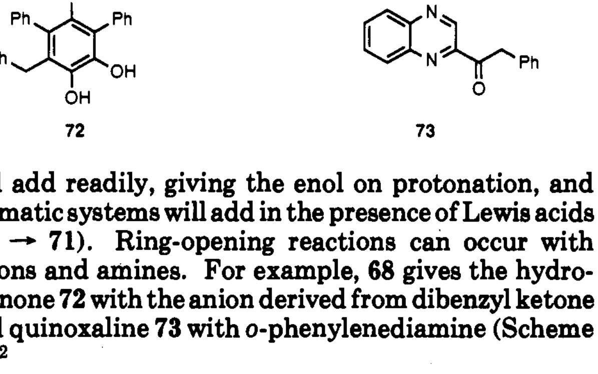


68 69

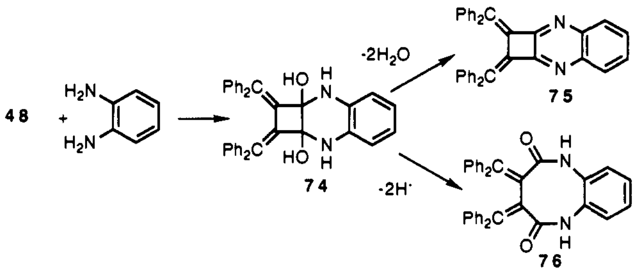
Nitrogen and phosphorus ylides act as nucleophiles to displace bromine from 66,[63] but Wittig reactions can also be carried out on the carbonyl groups.[64-66]

1,4-Addition to the double bond can also occur to give keto enols (68 → 70), the latter being stabilized by hydrogen bonding. Besides acids and thiols, carbanions will add readily, giving the enol on protonation, and aromatic systems will add in the presence of Lewis acids (68 → 71). Ring-opening reactions can occur with anions and amines. For example, 68 gives the hydroquinone 72 with the anion derived from dibenzyl ketone and quinoxaline 73 with *o*-phenylenediamine (Scheme 6).[62]

Scheme 6

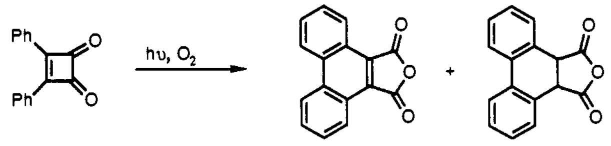


The bis(diphenylmethylene)butane-1,3-dione (48) reacts with *o*-phenylenediamine in CCl$_4$ containing AcOH to give the quinoxaline 75 in 98% yield. If the reaction is carried out in CCl$_4$ containing CBrCl$_3$ as a source of radicals, then the diazocine 76 was obtained in 85% yield together with a little 75.[67] In both cases addition of *o*-phenylenediamine to 48 gives the adduct 74, which dehydrates to 75 or rearranges to 76 by loss of hydrogen atoms.

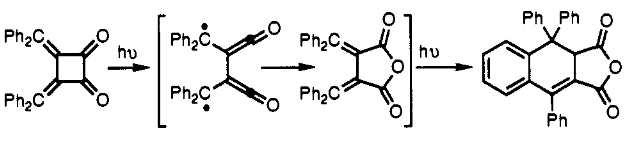


48 74 75 76

Photooxidation of diphenylcyclobutene-1,2-dione (77) in benzene or MeCN gave a mixture of 78 and 79.[68] Photoirradiation of 48 in 99% methanol gave 81 in 72% yield through initial ring opening to the bisketene 80 which oxidatively recyclized to the anhydride 50 and this in turn photocyclized.[69]

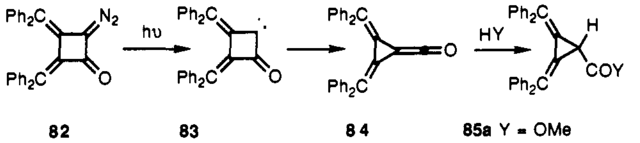


77 78 79



48 80 50 81

The diazo ketone 82, formed from the monotosyl hydrazone of 48 by treatment with basic alumina in $CHCl_3$, on irradiation in benzene containing a nucleophile gave the corresponding bis(diphenylmethylene)cyclopropane derivative. Thus with MeOH, 2-propanol, and aniline as nucleophiles the cyclopropanes 85a–c were obtained. The reaction presumably proceeds via a Wolff rearrangement of the initially formed ketocarbene 83 to the ketene 84.[70–72] This is the first observation of a Wolff rearrangement of a diazo ketone in a 4-membered ring.



82 83 84 85a Y = OMe

b Y = OiPr

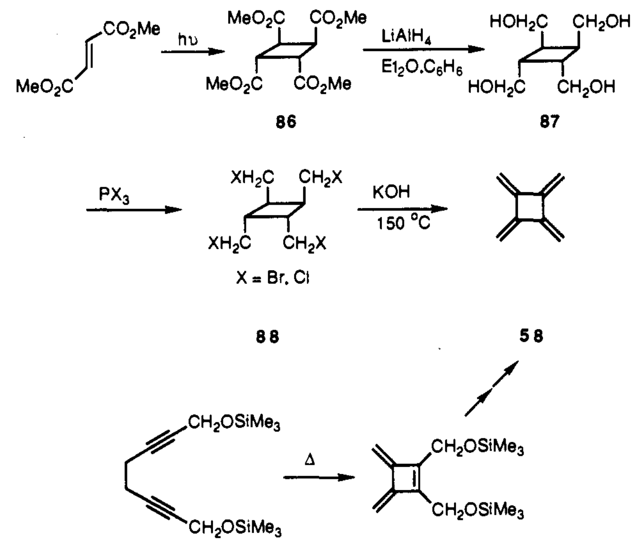
c Y = NHPh

2.3 Tetrakis(methylene)cyclobutane and Nonbenzannelated Derivatives

2.3.1 Preparative Methods

Tetrakis(methylene)cyclobutane (58), [4]radialene, was first prepared and identified by Griffin and Peterson in 1962,[73,74] but these authors noted that it had probably been prepared earlier by others as a component of mixtures. Their route to 58 involved as the last step a multiple 1,2-elimination from a number of symmetrical tetrasubstituted cyclobutanes, and the best precursors were found to be the tetrahalo derivatives 88. The synthetic route is shown in Scheme 7.

Scheme 7

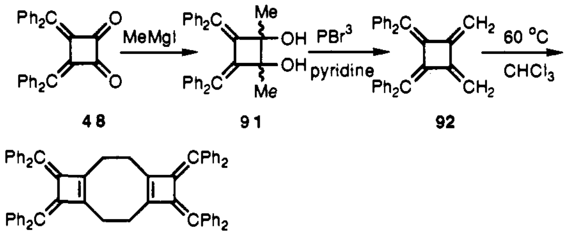


86 87 X = Br, Cl 88 58 89 90

A number of other methods for the preparation of 58 have been reported, one of which was illustrated in section 2.2.1.[55] Hopf and co-workers[75,76] adapted Huntsman and Wristers rearrangement of hexadiyne to the protected octa-2,6-diyne-1,8-diol 89 which, on thermolysis, gave the substituted bis(methylene)cyclobutene 90. Hydrolysis, conversion of the resulting diol to the dihalide and elimination gave 58.

At the same time that Griffin and Peterson reported the preparation of 58, a report on the synthesis of tetrakis(diphenylmethylene)cyclobutane (102) appeared involving the photodimerization of tetraphenylbutatriene.[77] The structure derived for 102 was largely based on the products of ozonolysis (see below).

A series of phenyl-substituted derivatives of 58 could be prepared from 3,4-bis(diphenylmethylene)cyclobutane-1,2-dione (48).[78] Addition of MeMgI to 48 gave a 2:3 mixture of the *cis*- and *trans*-diols 91 in 57% yield. The mixture, on treatment with PBr_3 in pyridine, gave the [4]radialene 92. This is not a very stable compound, and it dimerizes readily at 60 °C in $CHCl_3$ to give 93.



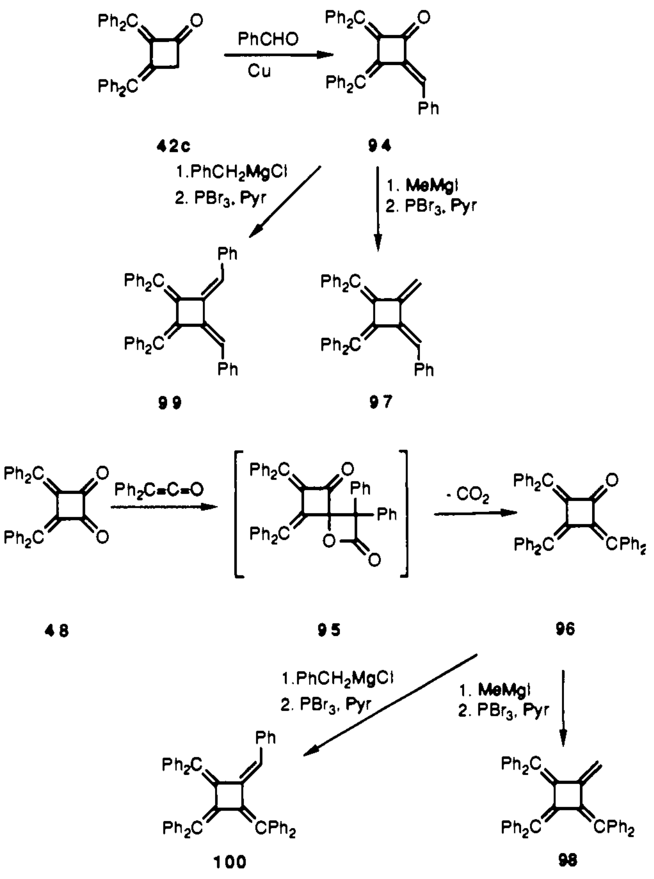
48 91 92

93

Tris(diphenylmethylene)cyclobutanone (96) was prepared by the sequence of reactions shown in Scheme 8.[78] Treatment of 42c with benzaldehyde in the presence of copper powder and cyclohexyl isocyanide gave the condensation product 94 in 52% yield. Treatment of 48 with diphenyl ketene gave 96 in 43% yield, presumably via 95 and loss of CO_2. Both 94 and 96 are stable compounds and serve as precursors to other tetrakis(methylene)cyclobutane derivatives.

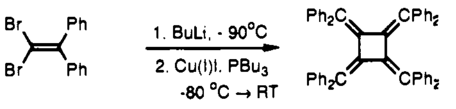
Treatment of 94 with MeMgI followed by phosphorus tribromide in pyridine gave the thermally stable radialene 97. A similar treatment of 96 gave the corresponding radialene 98. Substituting $PhCH_2MgCl$ for MeMgI in these reactions gave the radialenes 99 and 100, respectively.[78] Both the monomethylene

Scheme 8



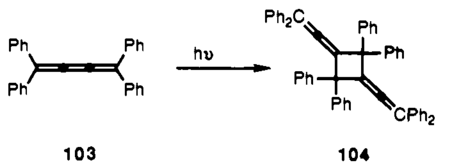
derivatives were obtained as yellow needles while the hexa- and heptaphenyl derivatives were red prisms.

Tetrakis(diphenylmethylene)cyclobutane (**102**) was prepared as deep red needles by the copper-assisted tetramerization of 1,1-dibromo-2,2-diphenylethene (**101**) and was, as were the radialenes **97–100**, a stable substance.[79]



101 **102**

The original report[77] that **102** could be formed from tetraphenylbutatriene (**103**) was shown to be incorrect,[80] the product being the asymmetric dimer **104**. The products reportedly obtained by ozonolysis[77,81] must also be incorrectly identified, and they differ in properties from the compounds above with the same assigned structure. Other compounds collated by Cava and Mitchell[1] in the chapter "Methylene Analogs of Cyclobutadienequinone" should also be considered to have different structures to those given.



103 **104**

An attempt to make **102** from the bromo ketone **42b** failed. Reaction of **42b** with Ph_3P gave the salt **105**, which could be readily converted into the ylide **106** with NaOMe. The ylide did not react with benzophenone, however, but it did react with ketene or phenyl isocyanate. The desired tris(methylene)cyclobutanes **107a,b** cyclized spontaneously to the naphthalene derivatives **108a,b** (Scheme 9).

Table 2. Electronic Spectra of Phenyl-Substituted Tetraradialenes as Solutions in $CHCl_3$

compd	λ_{max}, nm ($10^{-2}\epsilon_{max}$)
92	262 (326), 320 sh (94), 405 (57)
97	280 (248), 350 sh (93), 425 (53)
99	306 (402), 373 (181), 450 sh (54)
98	284 (283), 340 sh (196), 480 sh (28)
100	298 (319), 400 sh (138), 490 (25)

2.3.2 Structure and Spectroscopic Properties

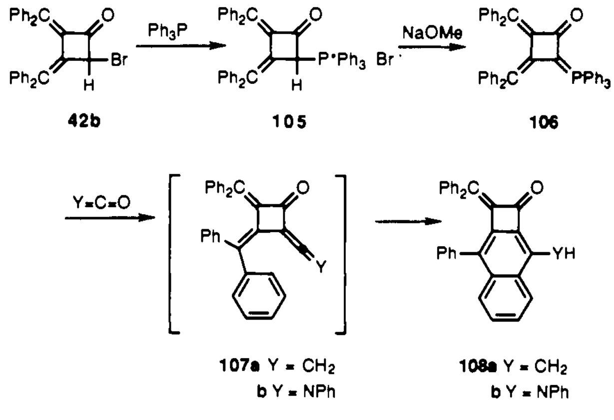
The ^1H NMR spectrum of tetrakis(methylene)cyclobutane (**58**) shows a singlet at δ 5.19, and in the IR spectrum there are absorption bands at 3095, 1760, 1710, 1400, and 880 cm^{-1}, the three high frequency bands being weak.[74] The IR and Raman spectra of **58** and its perdeuterated derivative are consistent with it having a planar ring with D_{4h} symmetry.[82] The photoelectron spectrum indicates that the ground state of the molecular ion is $^2B_{1u}$ and the ionization energy of a π-electron is 8.35 eV.[83] Numerous papers have appeared involving calculations on **58**.

As would be expected, in the phenylsubstituted derivatives the UV absorption bands move to longer wavelengths with increasing number of phenyl groups (Table 2).[78] An X-ray crystallographic structural analysis of the heptaphenyl derivative **100** shows that it has a puckered structure with the seven phenyl groups in an irregular arrangement.[84] In the octaphenyl derivative **102** the X-ray crystallographic structure shows it has the propeller-II rather than the propeller-I type structure, as shown in Figure 2,[79] and the 4-membered ring is very puckered (34.7°). The ^1H NMR spectrum of **102** shows a broad singlet at δ 6.80, and in the ^{13}C NMR spectrum the ring carbon is at δ 139.3 and the methylene carbon at δ 132.0.[79]

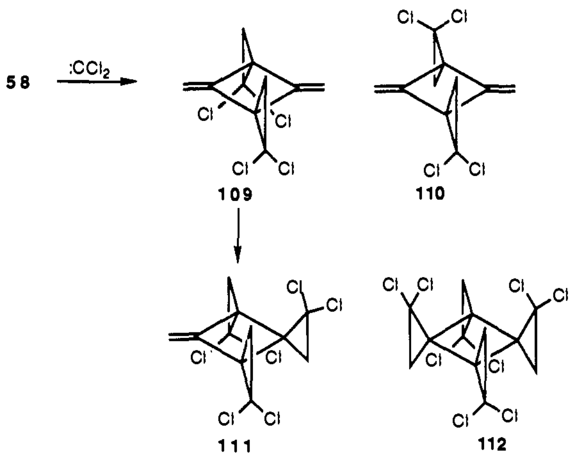
2.3.3 Reactions

Tetrakis(methylene)cyclobutane (**58**) adds carbenes to form spiro derivatives. Dichlorocarbene initially adds twice to give mainly the 1,3-dimethylene derivative **109** rather than **110**, and further treatment gives the tris and tetrakis adducts **111** and **112**.[76] Dibromocarbene

Scheme 9



gives only the bis adduct and diazomethane gives a complex mixture.



109 110 111 112

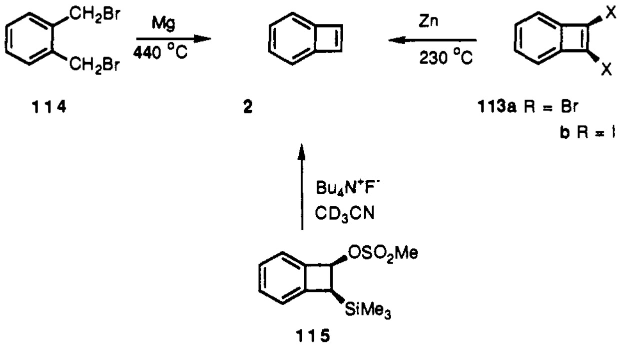
Dienophiles react only once to give bis(methylene)cyclobutene derivatives, the second addition being precluded because cyclobutadienes would be formed.[74] Gas-phase pyrolysis at 880 °C gave styrene and *o*-xylene.[74] Addition of bromine gave 3,4-dibromotetrakis(bromomethyl)cyclobutene, and addition of HBr gave 1-(bromomethyl)-3,4-dibromo-2,3,4-trimethylcyclobutene.[74] Hydrogenation gave *cis,syn,cis*-tetramethylcyclobutane.[74]

3 Benzocyclobutadiene and Related Systems

Benzocyclobutadiene (**2**) is a highly reactive compound that readily undergoes dimerization, and for many years its occurrence could only be demonstrated by trapping experiments,[1] including the preparation of an iron tricarbonyl complex.[85] Its spectroscopic properties have now been determined using either matrix isolation[86,87] or fast-flow techniques.[68] Naphthocyclobutadiene derivatives (e.g. **122**) and other annelated systems are much more stable and can be isolated.[1]

3.1 Preparative Methods

The majority of the methods of preparing benzocyclobutadiene (**2**) involve elimination from 1,2-disubstituted benzocyclobutenes. Early methods involved elimination of halogen from 1,2-dihalobenzocyclobutadienes (**113a,b**) with zinc,[1] and these methods were modified to produce **2** in the gas phase before cooling to 20 K in a matrix.[86] α,α-Dibromo-*o*-xylene (**114**) can also be dehalogenated to **2** over magnesium at a higher temperature (440 °C). Trahanovsky and Fischer[88] produced **2** in their flow NMR experiment by desilating the derivative **115** in CD_3CN by mixing with a CD_3CN solution of $Bu_4N^+F^-$.



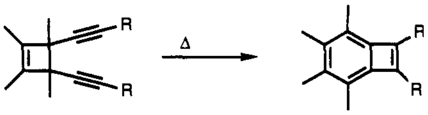
114 2 113a R = Br
b R = I

115

Alternative syntheses of **2** involve the rearrangement of octa-3,5-diene-1,7-diynes. Reaction of (*Z,Z*)-1,8-bis(trimethylsilyl)octa-3,5-diene-1,7-diyne (**116**) with NaOH in ethanol gave the dimer **117** of **2**, presumably by cleavage of the silyl groups, electrocyclization to cycloocta-1,2,4,6,7-pentaene followed by a second electrocyclization.[89] Thermal rearrangement of **116** gave 1,2-bis(trimethylsilyl)cyclobutadiene (**118**), the simplest benzocyclobutadiene derivative so far isolated.[90]

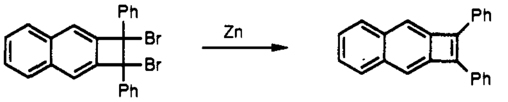
118 116 117

Thermolysis of substituted 1,2,3,4-tetramethyl-3,4-ethynylcyclobutenes **119** gave substituted benzocyclobutadienes **120**, the rearrangement occurring via octadienediynes, as above.[91] Some of these compounds (R = ^{t}Bu, mesityl) are stable systems but others dimerize thermally (R = H, Me, Ph), the nature of the product depending on the substituent.



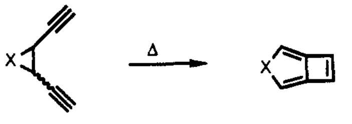
119 120

Naphthocyclobutadiene and anthrocyclobutadiene derivatives have been prepared by dehalogenation of the corresponding 1,2-dihalides (e.g. **121** → **122**).[92] Naphthocyclobutene itself dimerizes to dinaphtho[*a,c*]cyclooctatetraene.[93]



121 122

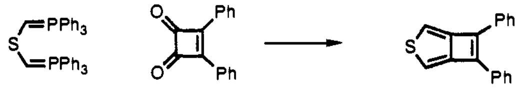
The heterocyclic analogues of benzocyclobutadiene have been prepared in which the benzene ring has been replaced by a 5-membered ring, either furan or thiophene. The parent systems were obtained by thermolysis of 2,3-diethynyloxirane (**123a**) and its sulfur analogue (**123b**).[94-96] In the case of thienocyclobutadiene (**124b**), extrusion of sulfur was a competitive process in the rearrangement.



123a X = O
b X = S

124a X = O
b X = S

6,7-Diphenyl-3-thiabicyclo[3.2.0]hepta-1,4,6-triene (**127**) was prepared by a Wittig reaction between the diketone **125** and the bisylide **126**.[97]



126 125 127

There have been numerous syntheses of benzocyclobutanedione (**12**) following the original synthesis from 1,2-diiodobenzocyclobutene by Cava and his coworkers,[98,99] and these methods have been extensively reviewed.[100–102] Many substituted benzocyclobutenediones have been prepared by modification of these methods and some examples are shown in Scheme 10.

3.2 Structure and Spectroscopic Properties

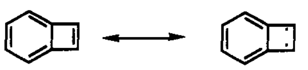
The ^1H NMR spectrum of **2** taken at a flow rate of 45 mL min^{-1} shows three bands at δ 6.36, 6.26, and 5.78. At a slower flow rate of 3 mL min^{-1} the two high-field signals are partially resolved as an AA′, BB′ system, showing these signals are due to the protons on the 6-membered ring.[88] The ^1H NMR spectrum of silyl derivative **118** shows signals at δ 6.30 and 5.75 in CD_3CN, with little solvent shift in CCl_4.[90] Table 3 lists the ^1H NMR spectrum chemical shifts for a number of benzocyclobutenes and related compounds. The high-field position of these bands, similar to the ring protons in 5,6-bis(methylene)cyclohexadiene, can be attributed to the paratropicity of the 8 π-system.

The ^{13}C NMR spectrum of the tetramethyl derivative **120** (R = ^tBu) shows ring carbons at δ 146.3 (C-1), 117.3 (C-2), 132.1 (C-3), and 156.0 (C-7).[91]

The matrix IR spectrum of **2** shows bands at 737 and 700 cm^{-1}, attributed to deformation of the protons on the 6- and 4-membered rings, respectively.[86]

The matrix electronic spectrum of **2** shows absorption maxima at 243, 246.5, 256, 264, 270, 281.5, and 289 nm,[86] and solution spectrum of **118** shows maxima at 236, 243, 404, 417 (sh), and 472 (sh) nm, the three long wavelength bands being weak.[90] The 1,2-diphenyl derivative **120** shows maxima at 207, 218 (sh), 278, and 468 nm[91] and the 1,2-diphenylthienocyclobutadiene (**127**) maxima at 266.5, 273.5, and 447 nm.[97] The latter compound is thermochromic, being deep reddish orange at room temperature and pale orange at lower temperatures.

The photoelectron spectrum of **2** has the lowest state of $^2B_1$ symmetry (7.87 eV) and is consistent with there being little contribution of the biradical to the ground state.[87]



The X-ray crystallographic structure of **120** (R = ^tBu) shows the 4-membered ring to be rectangular, with long bonds connected to the phenyl ring (153.4 pm), and short nonconnecting bonds (135.9, 141.6 pm).[91] The bond angles in the 4-membered ring are close to 90°. Similar alternation of bonds in the 4-membered ring is seen in the X-ray crystallographic structure of **127**, the connected bonds being 151.5 pm and the nonconnecting bonds 144.0 and 137.5 pm, the bond angles again being close to 90° but, as with **120**, the angle at the ring junction being slightly smaller than the other.[105] The phenyl rings are twisted out of the plane of the 4-membered ring by 23°. The X-ray structures of the substituted benzocyclobutadienes **175** and **177** (section 4.1.4) both show long connected bonds (**175**, 155.4 pm; **177**, 155.0 pm), short nonconnecting bonds (**175**, 133.6 pm; **177**, 135.0 pm) and some bond alternation in the benzene ring, the "bis(methylene)cyclobutadiene" benzene bonds being shorter (**175**, 136.5 pm; **177**, 136.0 pm).

Scheme 10

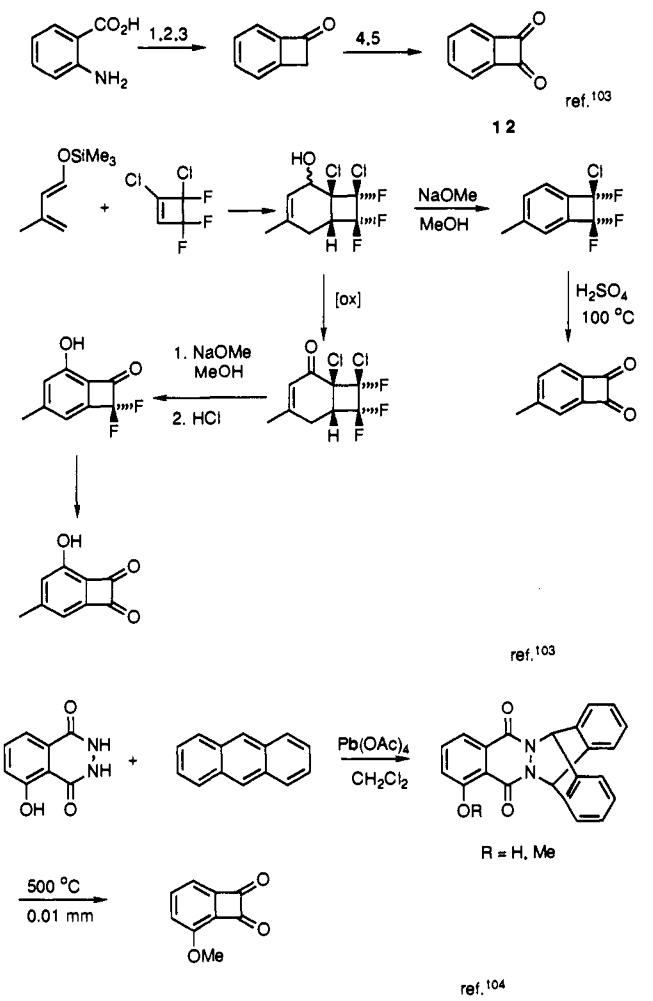
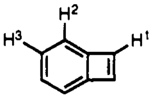
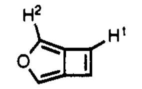
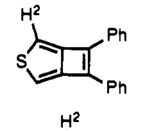
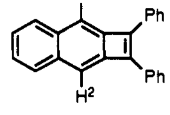
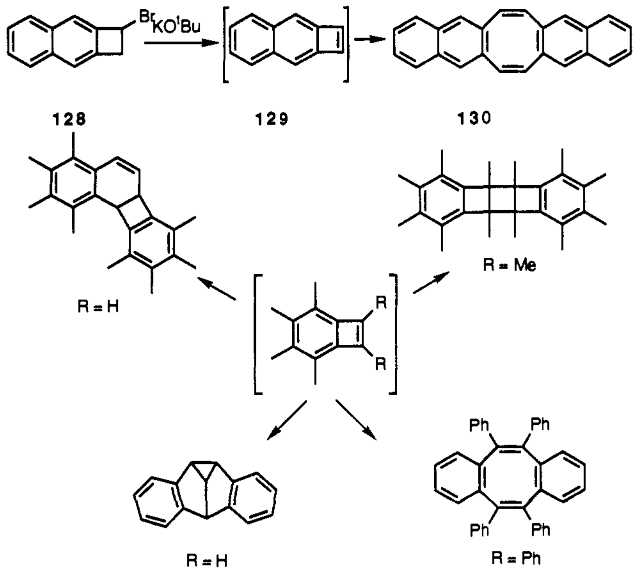


Table 3. Proton Chemical Shifts in the ^1H NMR Spectra of Benzocyclobutadiene and Related Compounds

compound	^1H NMR spectrum chemical shifts, δ H^1	H^2	H^3
	6.36	6.26 6.30	5.78 5.75
118 	6.33 6.75	6.11 6.01	
124b 		6.16	
		6.5	

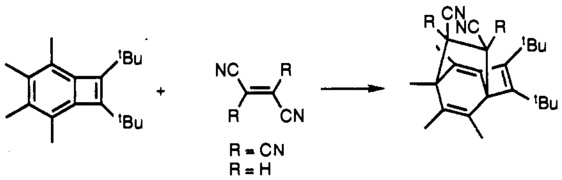
Scheme 11



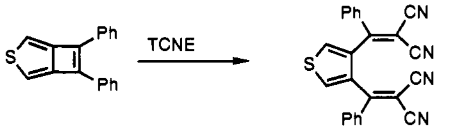
3.3 Reactions

Benzocyclobutadiene (**2**) is thermally unstable and dimerizes to the angular dimer **117**.[1] Naphtho[*b*]cyclobutadiene (**129**) is also thermally unstable, but in this case, dimerization gives the linear dimer **130**.[93] More highly substituted benzocyclobutadienes dimerize to various products depending on the substituents. 1-*tert*-Butylbenzocyclobutadiene is thermally unstable and the angular dimer is obtained,[106] while the 3,4,5,6-tetramethylbenzocyclobutadienes give angular, linear, and rearranged dimers depending on the nature of the 1,2-substituents (Scheme 11).[91]

Benzocyclobutadiene (**2**) undergoes Diels–Alder addition with dienes, and this was the original method of demonstrating its formation as a reactive intermediate.[1] Benzocyclobutadienes can also act as dienes, as in the dimerization reactions, and **120** (R = ^{t}Bu) reacts with tetracyanoethene (TCNE) and dicyanoethene across the 6-membered ring to give **131**.[107] The thienocyclobutadiene **127** adds TCNE to give the adduct **133**, presumably by a [2 + 2] addition followed by ring opening.[97] The bissilyl derivative **118** reacts with dimethyl acetylenedicarboxylate in a Diels–Alder manner to give dimethyl 3,4-bis(trimethylsilyl)naphthalene-1,2-dicarboxylate.[90]

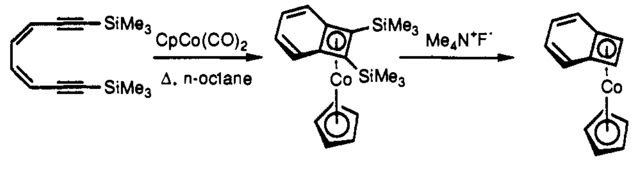


120 131



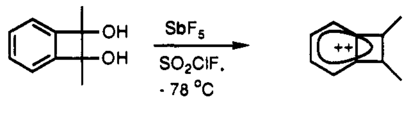
127 132

Benzocyclobutadiene and derivatives can be stabilized by forming organometallic complexes. Rearrangement of bis(trimethylsilyl)octa-3,5-diene-1,7-diyne with $CpCo(CO)_2$ gave the sandwich compound **133** which, on treatment with $Me_4N^+F^-$, gave the parent sandwich compound **134**.[108]

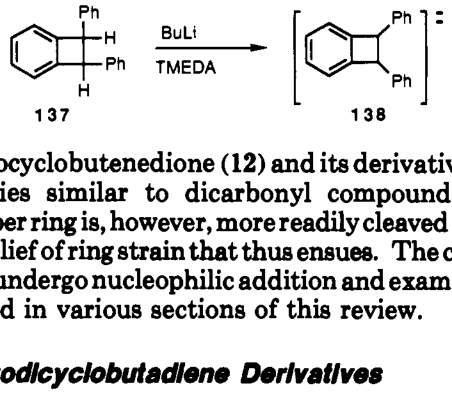


116 133 134

The benzocyclobutadienes are paratropic 8 π-electron systems and should add or lose 2 π-electrons to become 10 or 6 π-electron diatropic compounds. Dissolving the diol **135** in a mixture of SbF_5 and SO_2ClF at −78 °C gave the cation **136**,[109,110] while treating diphenylbenzocyclobutene (**137**) with BuLi in TMEDA gave the dianion **138**.[111] Whereas the dication appears to be a delocalized species, the dianion appears to have much of its charge localized in the substituents, presumably thus reducing electronic repulsion in the 4-membered ring.



135 136

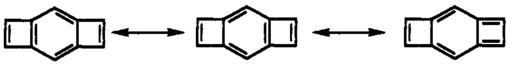


137 138

Benzocyclobutenedione (**12**) and its derivatives have properties similar to dicarbonyl compounds. The 4-member ring is, however, more readily cleaved because of the relief of ring strain that thus ensues. The carbonyl groups undergo nucleophilic addition and examples can be found in various sections of this review.

4 Benzodicyclobutadiene Derivatives

Benzodicyclobutadiene (**139**) has a 10 π-electron periphery, but as with most polycyclic systems, this is probably not significant and the compound is best considered as an annelated benzocyclobutadiene where the annelation ensures that there is a cyclobutadiene ring in all canonical forms.

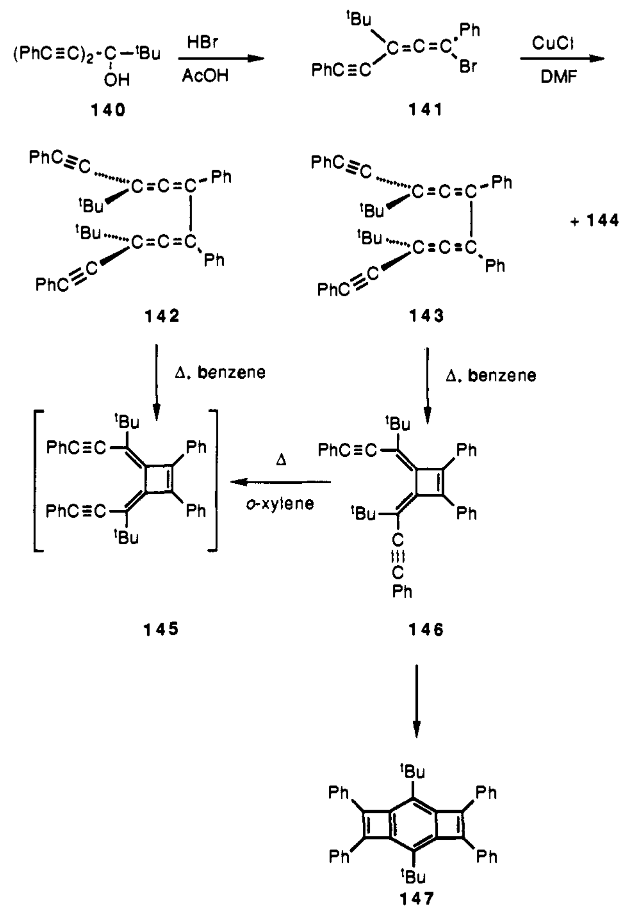


139a 139b 139c

Benzodicyclobutadiene would thus be expected to be a reactive, unstable compound, and it has not been prepared. One derivative, 2,7-di-*tert*-butyl-4,5,9,10-tetraphenyltricyclo[6.2.0.0^{3,6}]deca-1,3(6),4,7,9-pentaene (**147**) has been prepared[13,112] as shown in Scheme 12.

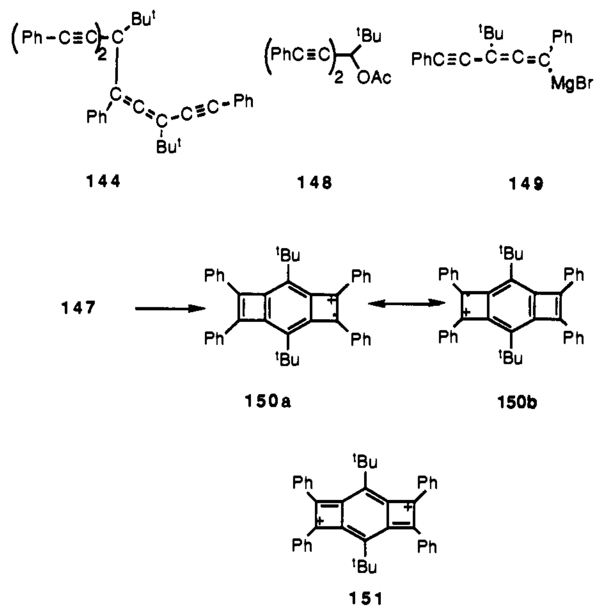
Treatment of the alcohol **140**, prepared from methyl pivarate and (phenylethynyl)magnesium bromide, with HBr in AcOH gave the bromoallene **141**. Treatment of **141** with CuCl in DMF by a previously reported method[113] gave *dl*-**142** and *meso*-3,8-di-*tert*-butyl-

Scheme 12



1,5,6,10-tetraphenyldeca-3,4,6,7-tetraene-1,9-diyne (**143**) together with 3,6-di-*tert*-butyl-1,5,8-triphenyl-6-phenylethynylocta-3,4-diene-1,7-diyne (**144**), in yields of 11%, 11%, and 54%, respectively.[112] The same compounds could also be obtained by CuCl treatment of the acetate **148** or the Grignard reagent **149**.[112] When **142** is heated in benzene it rearranges to the benzodicyclobutadiene **147** in 97% yield, probably by a disrotatory electrocyclization to **145** followed by a second electrocyclic ring closure and an allene dimerization, although these reactions do involve cyclobutadiene intermediates. Heating **143** in benzene provides support for this mechanism since the bis(methylene)-cyclobutene **146** is obtained by a disrotatory ring closure. Heating **146** in *o*-xylene then gives **147**.

The benzodicyclobutadiene **147** was obtained as greenish blue needles which melt at 296–297 °C and shows absorption bands in the UV spectrum in $CHCl_3$ solution at 394 and 643 nm. The compound is air sensitive but thermally stable under N_2, and no radical species is observed in the ESR spectrum.[114] The mass spectrum shows a peak at *m/e* 271 corresponding to the dication M^{2+} in addition to a peak at *m/e* 542 for the molecular ion.[112] The formation of the dication probably represents the stability of the species with an electron removed from each 4-membered ring (**151**). Attempts to obtain an X-ray crystallographic structure were unsuccessful, the crystal decomposing. Since there are no ring protons, the ^1H NMR spectrum cannot be used to probe the ring current. The nature of **147** has thus to be determined largely from its chemical properties.



4.1 Reactions

4.1.1 Oxidation

Treatment of **147** with 2 mol equiv of $Hg(OAc)_2$ together with 3 mol equiv of a nucleophile (NuH) in xylene at room temperature for 15–60 min gave 5,10-di-Nu-substituted 2,7-*tert*-butyl-4,5,9,10-tetraphenyltricyclo[6.2.0.0^{3,6}]deca-1,3,6,8-tetraene (**155**) (Scheme 13). The formation of **155** can be interpreted as a one-electron oxidation process. Electron transfer from **147** to Hg(II) gives the radical cation **150** which is then captured by the nucleophile to give the radical **152**. Oxidation of this radical (as though through the

Scheme 13

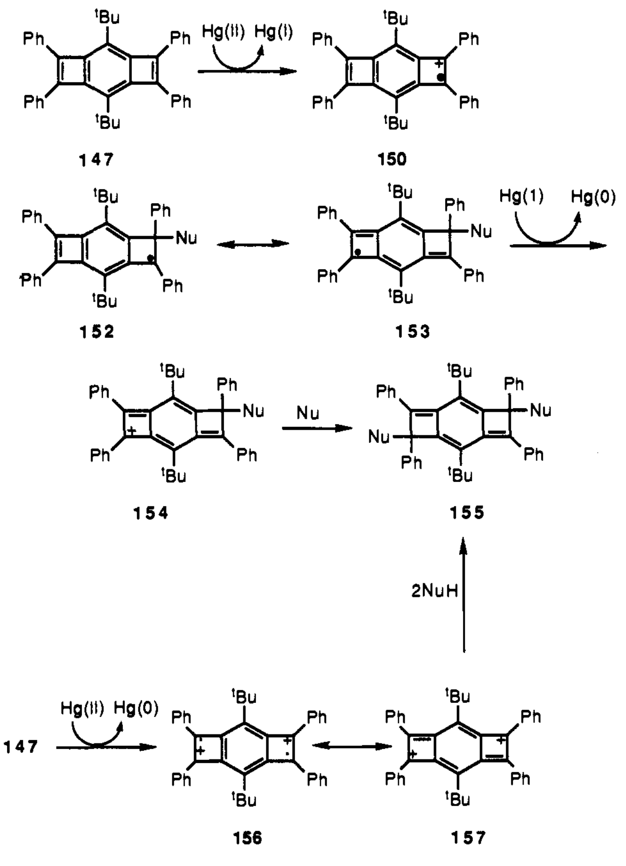


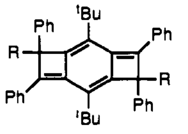
Table 4. Reaction of 147 with Nucleophiles and Mercuric Acetate in Xylene at Room Temperature

nucleophile	reaction time, min	product	yield, %
MeOH	15	**155a**	68
EtOH	60	**155b**	31
PhOH	15	**155c**	46
$PhNH_2$	15	**155d**	74
$4\text{-}MeC_6H_4NH_2$	15	**155e**	63
AcOH	30	**155f**	55
$PhCO_2H$	60	**155g**	17

canonical hybride **153**) by a second one-electron process gives the cation **154** which is in its turn captured by the nucleophile to give **155**. A considerable part of **155** formed is derived from the diradical dication **156**, which itself reacts with the nucleophile through its dication form **157** to give **155**. The yields and reaction times for a variety of nucleophiles are shown in Table 4.

Similar results to those tabulated were also obtained when a mercury(I) or silver(I) salt was used instead of the mercuric acetate. For example, reaction of **147** with methanol in the presence of Hg_2Cl_2 gave **155a** in 63% yield, and with AgOAc **155a** was obtained in 82% yield. When an equimolar amount of $Hg(OAc)_2$ rather than 2-fold excess was used, **155a** and mercury were obtained in 68% and 82% yields, respectively.[115]

These reactions, which are effectively 1,8-additions, are paralleled by the addition of benzoyl peroxide and azobisisobutyronitrile, which give **158a** and **158b**, respectively.

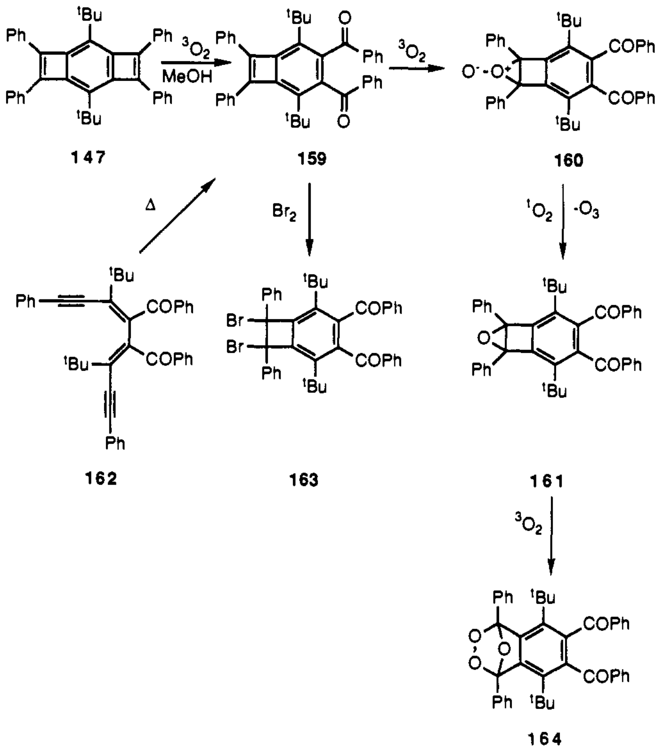


158a R = OCOPh
158b R = CMe_2CN

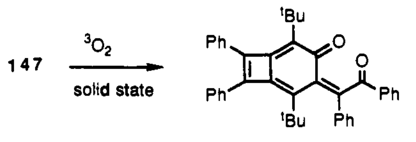
As might be expected from the results with mercury and silver, compound **147** is readily oxidized by other reagents, the products depending on the reaction conditions. Stirring a suspension of **147** in MeOH under oxygen for 1 h at room temperature gave **161** in 96% yield.[116] The same product was obtained with CCl_4, acetone, or petroleum ether as solvent. The oxidation probably proceeds by the sequence of reactions shown in Scheme 14. The intermediacy of the ring-cleaved dibenzoylbenzocyclobutadiene **159** in the sequence was supported by an alternative synthesis and its subsequent conversion to **161**. Bis(methylene)cyclobutene **146** was oxidized by $KMnO_4$ to the octadienediyne **162**, which was rearranged to **159** by heating to reflux in mesitylene. Compound **159** oxidizes immediately on exposure to air to give **161**, but it can be trapped as its dibromo derivative **163** by treatment with bromine. Oxidation of **147** proceeds in the dark and triplet dioxygen must be the oxidizing agent.[117-119]

The oxirane **161** is stable in the crystalline state at room temperature, but in benzene solution oxygen is gradually absorbed and the isobenzofuran peroxide **164** is obtained. Photooxidation of **161** in THF readily gives **164**.[116]

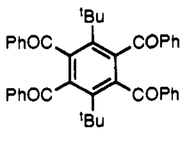
Scheme 14



Oxidation of **147** in the solid state proceeds by a different pathway to give the o-quinomethide derivative **165**.[116]



165



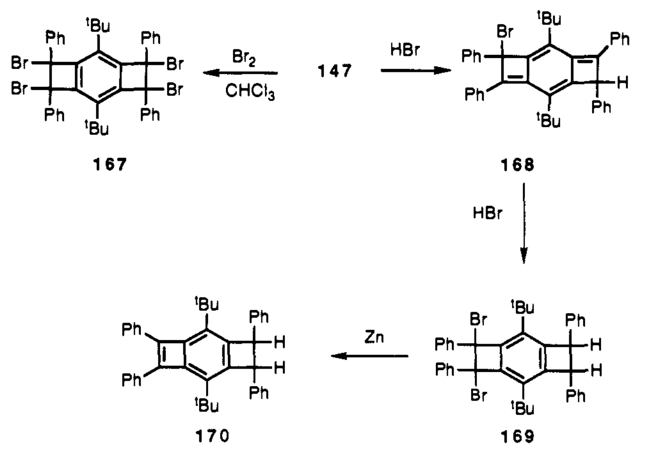
166

Oxidation of either **147** or **165** with $KMnO_4$ gave 1,2,4,5-tetrabenzoyl-3,6-di-*tert*-butylbenzene (**166**).[116]

These results clearly indicate that **147** is not an aromatic 10 π-system, the ready cleavage of one of the 4-membered rings presumably occurring because a cyclobutadiene structure is thereby removed. The formation of **165** in the solid-state photooxidation may be due to a decrease in delocalization of the central benzene ring due to the annelating cyclobutadiene rings, thus allowing it to be oxidized.

4.1.2 Addition

Bromine adds readily to **147** in $CHCl_3$ to give the tetrabromide **167**. Two equivalents of HBr add to **147** to give the dicyclobutabenzene derivative **169** in which the two bromine atoms are in the same 4-membered ring. Presumably an initial 1,8-addition of HBr occurs to give **168**, which then adds the second molecule of HBr regiospecifically in a 1,6-manner. Debromination of **169** with zinc gives the benzocyclobutadiene derivative **170**.[117]

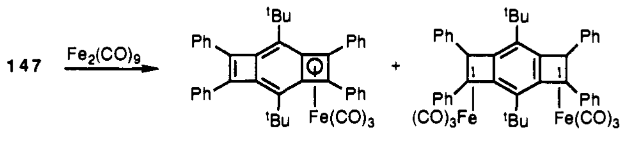


4.1.3 Complexes with $Fe(CO)_3$

Treatment of **147** with an equimolar amount of $Fe_2(CO)_9$ in boiling xylene under N_2 for 4 h gave a mixture of the red crystalline 1:1 complex **171** and the black red crystalline 1:2 complex **172**.[118,119]

X-ray crystallographic analyses of the two complexes showed that **171** is best represented by the structure in which the iron atom is bonded to one of the 4-membered rings as a cyclobutadienyl complex, the 4-membered ring being square (C—C, 146.4 pm) with the iron atom centrally situated. The remaining bismethylenecyclobutene unit has alternating double and single bonds (C—C, 150.9 pm, C=C 135.4 pm).[118,119] In **172**, both of the iron carbonyl groups are on the same side of the ring and are more strongly complexed to the nonbenzenoid double bond. The occurrence of both iron atoms on the same side may arise from simultaneous coordination of both iron atoms of a $Fe_2(CO)_9$ molecule.

The distribution of the 10 π-electrons of the ring system in the complex **172** should be indicated by the X-ray crystallographic structure. If both of the 4-membered rings contributed 4 π-electrons to an iron atom, then two electrons remain and a σ-bond might be expected between the 2,7-positions. The X-ray crystallographic structure parameters do not indicate this to be the case (see Figure 4).



4.1.4 Reaction with Dienophiles and Dienes

Considering the possible canonical contributors to the structure of **147**, there are a number of diene units which could be susceptible to reaction with dienophiles. In the "benzenoid" structure **147a**, reaction across the 1,6-positions would give a product in which the cyclobutadiene character of both 4-membered rings is lost and there is little ring strain (pathway a, Figure 5). Reaction across the 3,4-positions in structure **147a** (pathway b) and across the 3,6-positions in structure **147b** (pathway d) would also remove the cyclobutadiene ring character of both 4-membered rings, but the products would be highly strained. Reaction across the 4,5-positions in **147b** (pathway e) would give a benzocyclobutadiene structure and reaction across the 2,7-positions (pathway c) would give a product with two cyclobutadiene rings. Pathway a thus seems most probable, followed by pathway e, and pathway c seems the most unlikely.

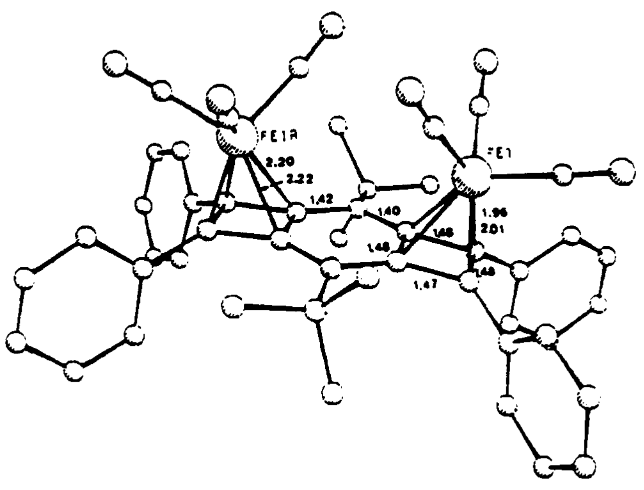


Figure 4. The X-ray crystallographic structure of the bis(iron tricarbonyl) complex **172**.

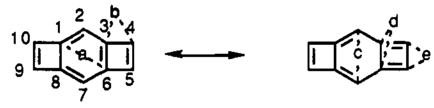


Figure 5. Possible sites for dienophile addition to **147**.

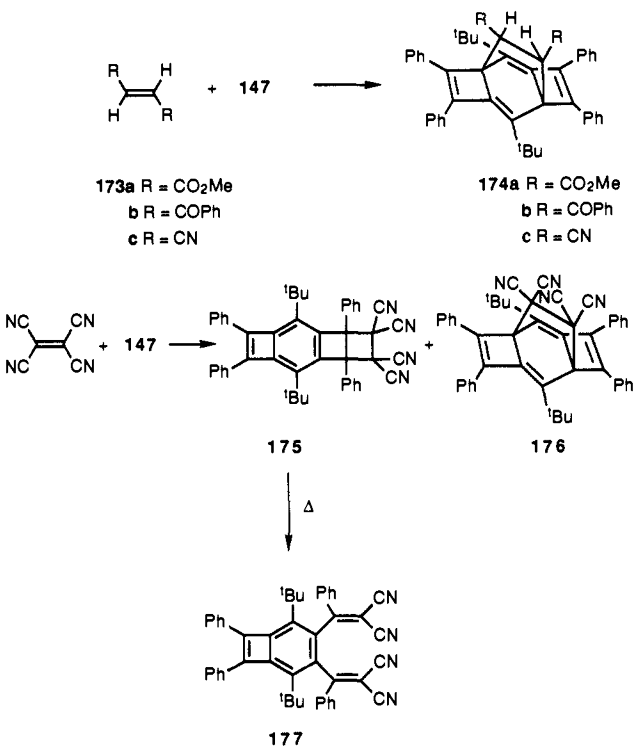
Heating a 1:1 mixture of **147** and dimethyl fumarate (**173a**) in *o*-xylene under N_2 gave the 1,6-addition product **174a** in 75% yield.[120] This reaction proceeds by pathway a, and the products from reaction with *trans*-dibenzoylethylene (**173b**) and *trans*-dicyanoethylene (**174c**) have analogous structures, **174b** and **174c**, respectively.[120,121] As the simple consideration of cyclobutadiene structures suggested, pathway a is preferred in this system. Heating TCNE with **147** gives, however, mainly the product **175**, together with a small amount of **176** (Scheme 15).[121] Pathway e is now preferred over pathway a, presumably because steric repulsion between the CN and *tert*-butyl groups in the transition state of pathway a raises its energy above that of pathway e. An X-ray crystallographic study of the product **176** clearly indicates the serious steric crowding that occurs in this compound.[122] A theoretical treatment of the reaction indicated that pathway a was energetically the most favorable.[122] Calculations of the nonbonded interaction energies for various modes of approach of TCNE to **147** suggest that there is a folding of the 4-membered ring of **147** in the transition state.[123]

Heating **175** converts it readily into **177**, an analogous reaction to that which gives **132** (section 3.3).[124,125] The X-ray structural analyses of **175**[123] and **177**[126] show the expected dominance of the dimethylenecyclobutene form as seen in other benzocyclobutadienes (section 3.2).

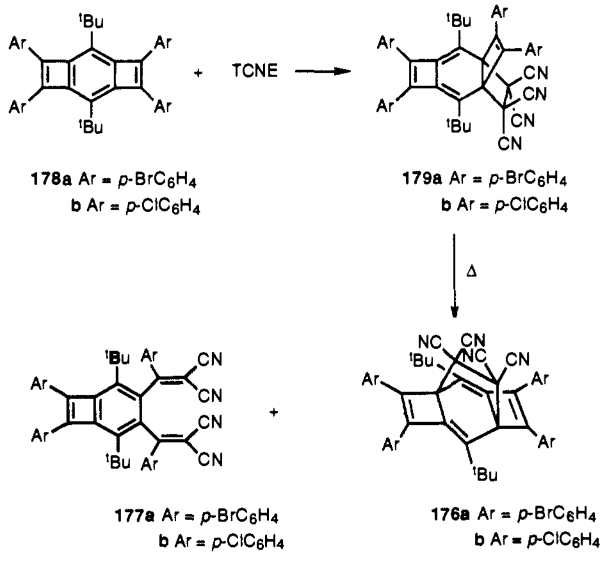
Interestingly, the Diels–Alder reaction between TCNE and benzodicyclobutadienes in which the phenyl groups have been substituted for *p*-halogenophenyl groups, **178a** and **178b**, takes a different course, via pathway d, to give the propellanes **179a** and **179b** in 66% and 84% yield, respectively.[121] The reason for this change in reaction pathway is not clear.

Heating **179a** under reflux in *p*-xylene under N_2 for 30 min gave a mixture of **176a** and **177a** in 44% and

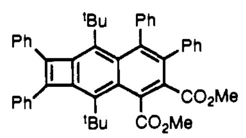
Scheme 15



40% yield, respectively.[121] This process may occur by a retro-Diels–Alder reaction to give **178a** and TCNE, followed by recombination by either pathway a or e. Some support for this mechanism is provided by heating **179a** in the presence of an equimolar amount of **147** when **178a** is formed in addition to **176** and **177**.[121]



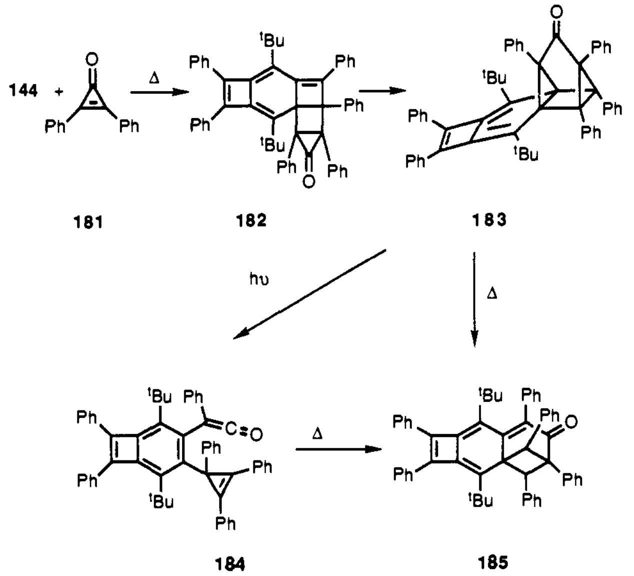
Diethyl acetylenedicarboxylate and dimethyl maleate both react with **147** by pathway b, the former dienophile giving the naphthocyclobutadiene **180**.[124,117]



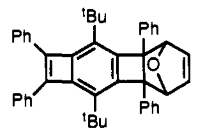
180

The reason that dimethyl maleate takes a different reaction pathway compared to diethyl fumarate is probably the greater steric hindrance in pathway a in the maleate case.[120] Diphenylcyclopropene (**181**) also reacts with **147** via pathway b to give the quadricyclanone **183** via the intermediate **182**.[127] Photoirradiation of **183** gave **184**, and thermolysis gave **185**. The former compound could be converted into **185** by thermolysis (Scheme 16).[127]

Scheme 16



With furan, **147** acted as a dieneophile, reacting through one of the cyclobutene double bonds to give the benzocyclobutadiene derivative **185a**.[117]

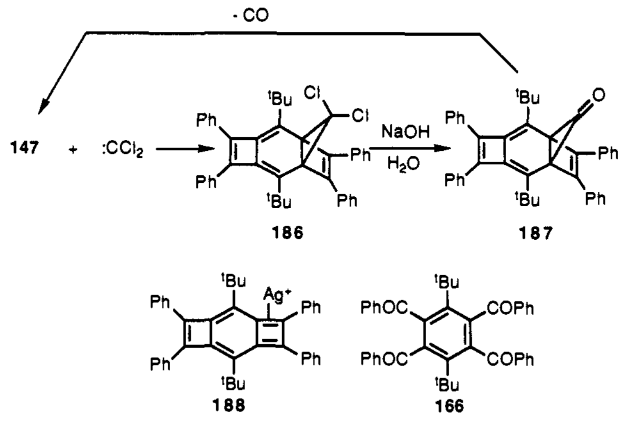


185a

4.1.5 Addition of Dichlorocarbene

Treatment of **147** with $CHCl_3$ and KOH under phase-transfer conditions gave the propellane derivative **186** in 20% yield as the sole isolable product[128] (Scheme 17). Similar treatment of **178a** and **178b** gave the corresponding propellanes in 18% and 24% yield, respectively.[128] Although these are highly strained systems, all three propellanes were stable substances.

Scheme 17

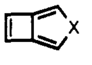


Hydrolysis of **186** by heating in acetone containing a small amount of aqueous NaOH for 2.5 h gave **147** in 72% yield. This reaction probably proceeds by hydrolysis of the *gem*-dichlorides to the ketone, followed by loss of CO.[128]

Hydrolysis with $AgClO_4$ in wet THF initially gave a greenish-blue solution, the color then fades gradually to give finally a mixture of AgCl, silver, and **166**. The color can be attributed to the 1:1 silver complex **188**. In support of this concept, a benzene solution of equimolar amounts of $AgClO_4$ and **147** was the same color and had the same spectral properties (λ_{max} 592 nm; ^1H NMR δ 1.09 (9 H, *t*-Bu), 1.24 (9 H, *t*-Bu), and decomposition of a dry benzene solution of **147** and excess $AgClO_4$ with water gave silver metal and **170** in 66% yield.

4.1.6 Insertion of Heteroatoms

Heteroatoms can be introduced between 4-C and 5-C of **147** to give tricyclic systems with 4-, 6-, and 5-membered rings. These compounds can be considered to be derived from the cyclobutenoheterocycles **189** and **190** (see section 3) by insertion of a benzene ring to give **191** and **192**. Inspection of the structure of **192** suggests it should be more stable than **190**, possessing a benzocyclobutadiene rather than a cyclobutadiene moiety, whereas **189** and **191** appear likely to have similar stabilities.



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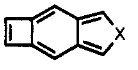
190



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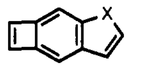


192

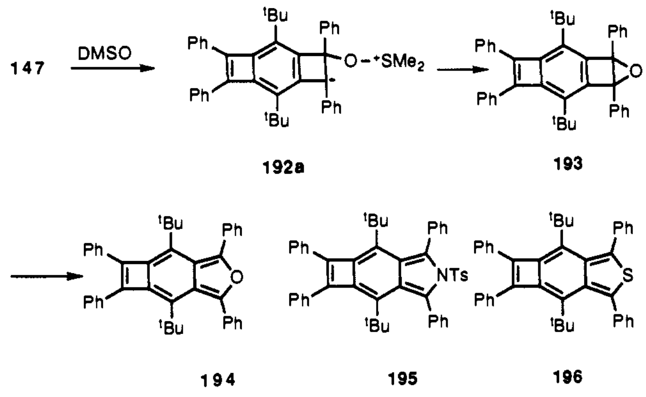
Heating **147** under reflux in DMSO under N_2 for 3 h gave the isobenzofuran derivative **194** in 54% yield. The reaction may proceed by the sequence shown (**192a** → **193**), addition of the DMSO followed by loss of dimethyl sulfide to form the oxirane and valence tautomerism to the furan (Scheme 18).[129]

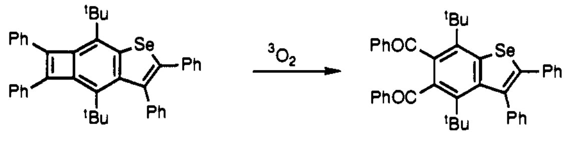
Heating **147** with tosylazide at 80 °C in *p*-xylene gave the pyrrole analogue **195** in 56% yield. The product from this latter reaction is in contrast with that from the addition of chlorocarbene and suggests that tosylnitrene is not the reactive species, probably reflecting the stability of tosyl azide.[130]

Treatment of **147** with sulfur in boiling benzene under N_2 gave the thiophene analogue **196** in 43% yield.

In all of these cases the hetero atom has been introduced between the 4,5-positions of the benzodicyclobutadiene. When **147** is heated with powdered selenium in boiling *p*-xylene under N_2, compound **197** is obtained in which the selenium atom has been inserted between the 3,4-positions. The derivative **197** was obtained in 89% yield as orange prisms. The reason for this change in regiospecificity may be steric, since the selenium atom is larger and in the selenium analogue of **196** the phenyl substituents on the heterocyclic ring will be crowded into the *tert*-butyl groups. In **197**, there will be only one such interaction. Tellurium could not be introduced into **147**, and this may reflect the greater steric interactions that would occur in both of the potential isomers. When **147** is heated with selenium dioxide in *p*-xylene then competition between insertion of oxygen and selenium occurs and a mixture of **194** (14%), **197** (32%), and **165** (22%) is formed.[129] The selenium derivative **197** is sensitive to oxygen, reacting even in the crystalline state, to give the dibenzoylselenophene **198** in quantitative yield.

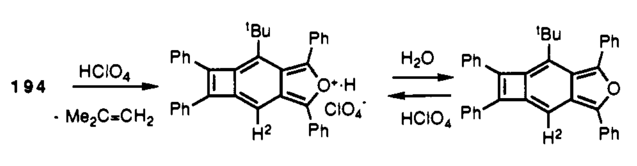
Scheme 18



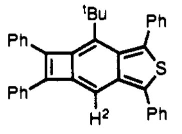


When compounds **194** and **196** are treated with perchloric acid, one of the *tert*-butyl groups is lost and the perchlorate salt is formed. Thus **194** gives **199** which, on treatment with water, gives the furan **200**. Similar treatment of **196** gave **201**. Both **200** and **201** are stable compounds that can be reprotonated back to the corresponding salts. In the ^1H NMR spectrum, **200** shows signals at δ 0.85 (s, ^tBu) and 6.50 (s, H^2), together with signals for the phenyl groups, and **201** shows signals at δ 0.79 (s, ^tBu) and 6.39 (s, H^2). The chemical shift signals for H^2 can be compared to that of the similar proton in diphenylnaphthocyclobutadiene **122**, H^2 δ 6.50.[92] The chemical shifts of each these H^2 protons suggests that the 4-membered rings in these compounds sustain a paramagnetic ring current, but that the paratropicity is less than that found in the benzocyclobutadiene and related compounds (see Table 3, section 3.2). The ease of protonation of **200** and **201** may indicate that the systems should be considered as a 12 π-electron antiaromatic systems, the destabilization being lost on protonation. The nitrogen analogue **195** and the selenium derivative **197** did not form salts with perchloric acid. It is of interest that the H^2 protons in **200** and **201** are derived from the departing *tert*-butyl group and not the perchloric acid, as was shown by the nonincorporation of deuterium when $DClO_4$ and D_2O were used.[129]

Treatment of the selenophene **197** with $Fe_2(CO)_9$ gave the complex **171** and selenium in 85% and 98% yield, respectively.[117] Treatment of **197** with TCNE gave the deselenated product **203**, presumably via the Diels–Alder adduct **202** which then loses selenium. The highly conjugated nature of **203** is reflected in the purple color



199 200



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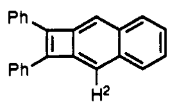
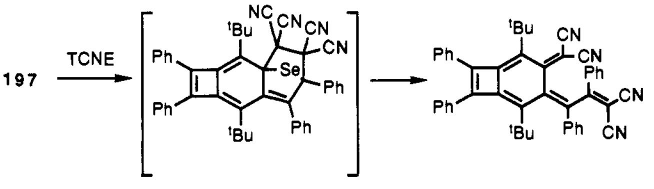


122

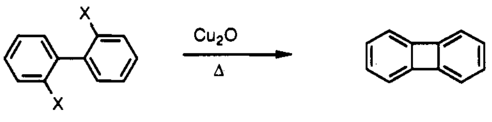
of its crystals and the electronic spectrum [λ_{max} 260 nm (ϵ 35 400), 332 (36 500), 555 (12 300)].[117]



202 203

5 Biphenylene and Related Compounds

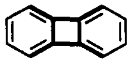
Biphenylene (4) was prepared by Lothrop[131] in 1941 by an Ullman reaction of 2,2′-dibromo- (**204a**) or 2,2′-diiodobiphenyl (**204b**) and was, for many years, the only known derivative of cyclobutadiene fused to benzene.



204a X = Br
b X = I

4

There are five canonical uncharged structures for biphenylene, two of which contain a cyclobutadiene ring and three which do not; the X-ray crystallographic structure shows that biphenylene is best represented by the structure shown in Figure 6 (section 5.2).[132] The bonds between the 6-membered rings approximate to single bonds in length and there is some bond alternation in the 6-membered rings, indicating that the canonical structure **4c** containing the tetrakis(methylene)cyclobutane moiety is the major contributor.



4c

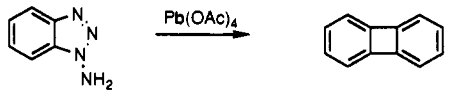
A variety of compounds related to biphenylene have now been prepared and the formation and properties of a number of these will be described in this section.

5.1 Preparative Methods

The three main methods of forming biphenylene and its derivatives are as follows: (a) by coupling a biphenyl at the ortho positions of the two rings, (b) by dimerization of benzyne, and (c) by extrusion of nitrogen or carbon dioxide and carbon monoxide from benzo[*c*]cinnolines or phthalic anhydrides.

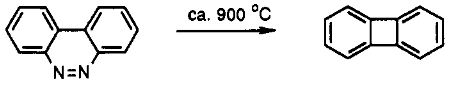
Method a is based on Lothrop's original synthesis and has been used to prepare a large variety of biphenylenes (see ref 133 and references therein). Copper powder appears preferable to the copper(I) oxide originally used as the cyclizing agent.[134]

Method b involves the dimerization of benzyne and the yield of biphenylene depends on the method of generation of the benzyne. The oxidation of 1-aminobenzotriazoles (**205**) with lead tetraacetate produces high yields of biphenylenes,[135] but substituted benzotriazoles are rather inaccessible.



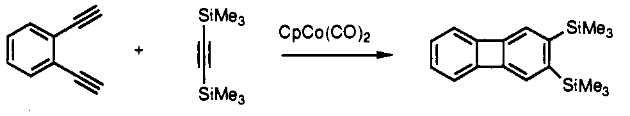
205 4

Method c utilizes flash vacuum pyrolysis and is only suitable for small amounts.[136-139] It is a highly versatile method, however, and a variety of biphenylenes and heterobiphenylenes have been prepared by this route.



206 4

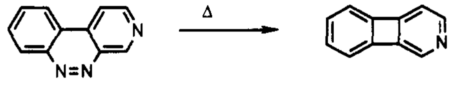
More recently, Vollhardt and his co-workers have introduced a method in which a 6-membered ring is constructed from a cobalt-catalyzed cyclization, the 4-membered ring arising because of the substrate chosen.[140] With bis(trimethylsilyl)acetylene (**208**) and *o*-diethynylbenzene (**207**), the 2,3-bis(trimethylsilyl)biphenylene (**209a**) is formed, which can be converted into biphenylene with trifluoroacetic acid.



207 208 209

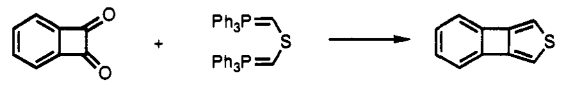
Method a, method c and Vollhardt's method have also been used to prepare benzobiphenylenes and poly(biphenylenes) as described below.

Analogues of biphenylene in which one of the benzene ring has been replaced by another heterocyclic ring have also been prepared. Pyrolysis of the appropriate N-substituted benzocinnoline (e.g. **210**) thus gives the pyridino biphenylene (e.g. **211**).[141-146]



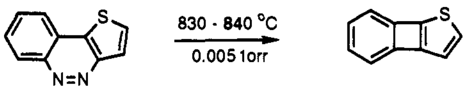
210 211

For the replacement of a benzene ring by a 5-membered heterocycle, two methods have been used. 2-Thianorbiphenylene (**213**) was prepared by a Wittig reaction between 1,2-benzocyclobutadienedione (**12**) and the preformed bis-ylide **212**.[64]



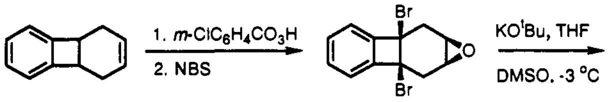
12 212 213

1-Thianorbiphenylene (**215**) was prepared by thermal extrusion of nitrogen from **214** and is much less stable than **213**, dimerizing to a number of products at 0 °C.[147]

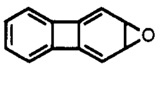


214 215

The oxirane **218** was prepared by oxidation of **216** with *m*-chloroperoxybenzoic acid to **217**, which was then converted to **218** by bromination with NBS, followed by dehydrobromination with KO^{t}Bu. Compound **218** shows no tendency to tautomerize to the oxepin.[148]



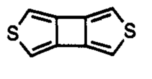
216 217



218

Two isomeric thionin derivatives were prepared using the bis-Wittig approach described above for 2-thianorbiphenylene.[149]

2,5-Dithiabisnorbiphenylene (**219**) and the tetraphenyl derivative (**220**) are the only known biphenylene derivatives in which both benzene rings are replaced by a 5-membered heterocycle,[150a,b] both being obtained in very low yield.



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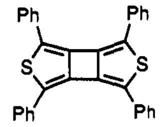
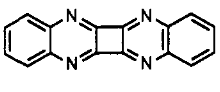


220

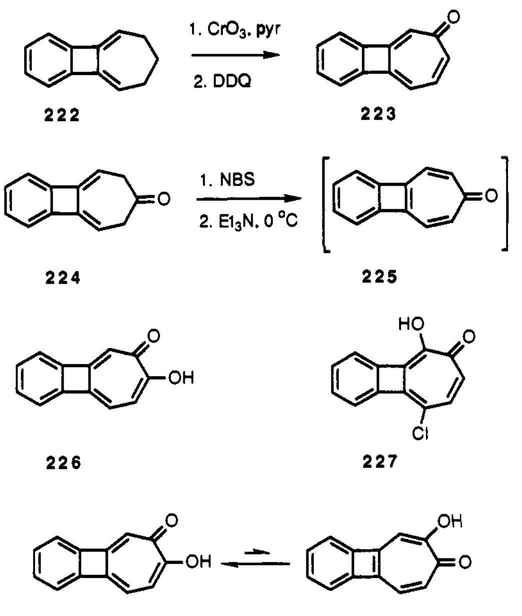
A dibenzobiphenylene **221** (tetraazanaphthylene) has been prepared with pyrazine rings in place of the benzene rings of the biphenylene moiety by two routes: condensation and polyphosphoric acid cyclization of squaric acid and *o*-diaminobenzene,[151] and by method c.[152]



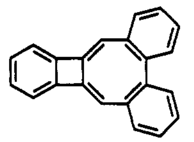
221

A number of compounds have been prepared in which one of the benzene rings has been replaced by larger carbocyclic system (Scheme 19). Two tropone isomers were prepared by Wege and co-workers,[153] the first **223** by allylic oxidation of **222** followed by dehydrogenation with dichlorodicyanoquinone (DDQ), and the second **225** by bromination and dehydrobromination of **224**. Compound **223** is much more stable than **225**, which could only be trapped with cyclopentadiene. Three chloro derivatives of **223** have also been prepared by dichlorocarbene addition to 1- and 2-methoxybiphenylene, followed by hydrolysis.[154] The tropolones **226** and **227** have been prepared, and it was shown that the tautomers with the bismethylene structure were preferred to those with the benzocyclobutadiene structure (e.g. **226a**).[155,156]

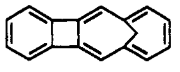
Scheme 19



Compounds with cyclooctatetraene **228** and methano-[10]annulene **229** rings were also prepared by the bis-Wittig procedure.[157,158]



228



229

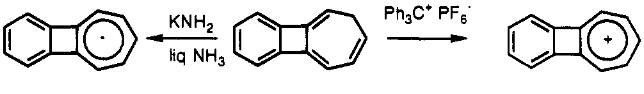
Biphenylene analogues have been prepared in which one of the benzene rings has been replaced by a charged $4n + 2$ π-electron system. The norbiphenylene anion **231** was prepared by a double Hoffman elimination from the 1,3-trimethyl ammonium salt **230** and is unstable, readily dimerizing.[159] The tropylium ion analogue, the homobiphenylene cation **230**, has been prepared from the cycloheptatriene **232**, obtained from the diene **232**, by hydride removal with triphenylmethyl hexafluorophosphate and can be isolated as a salt.[160] A benzo analogue has also been prepared.[161]

Reduction of the cyclooctatetraene derivative **228** with alkali metals gave the corresponding dianion, equivalent to replacing one of the benzene rings by a 10 π-electron system.[157]

The homobiphenylene anion (**234**), a biphenylene analogue with an 8 electron, $4n$ π-system replacing a benzene ring, has been prepared from **232** by treatment with potassium amide in liquid ammonia.[162]

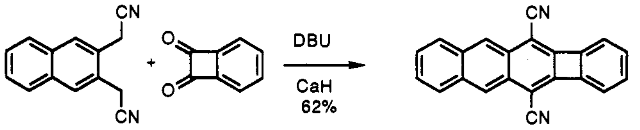
A large number of benzannelated biphenylene derivatives have been prepared by a variety of routes. Fusion can occur at either the a or b bond of the biphenylene to give linear or angular products, both

230 231



234 232 233

being known. Besides the application of a number of the methods described previously for biphenylenes and heterobiphenylenes, a method of considerable generality has been introduced by McOmie and co-workers.[163] A benzocyclobutaquinone is treated with *o*-bis(cyanomethyl)alkyne and a hindered base, DBU being preferred, in the presence of calcium hydride to remove the water formed in the reaction. An example is shown with the formation of the naphthalenobiphenylene **236** by reaction of **235** with **12**.



235 12 236

Compounds have also been prepared in which a number of biphenylene units have been incorporated. Vollhardt's method has been particularly successful in this area, but the earlier methods have also been used, and Barton and co-workers[164] have adopted a Diels–Alder approach, using bis(methylene)cyclohexadienes as the diene component and benzocyclobutenes as the dienophile.

Again, angular and linear compounds can be constructed and examples of the various methods are given in Scheme 20.

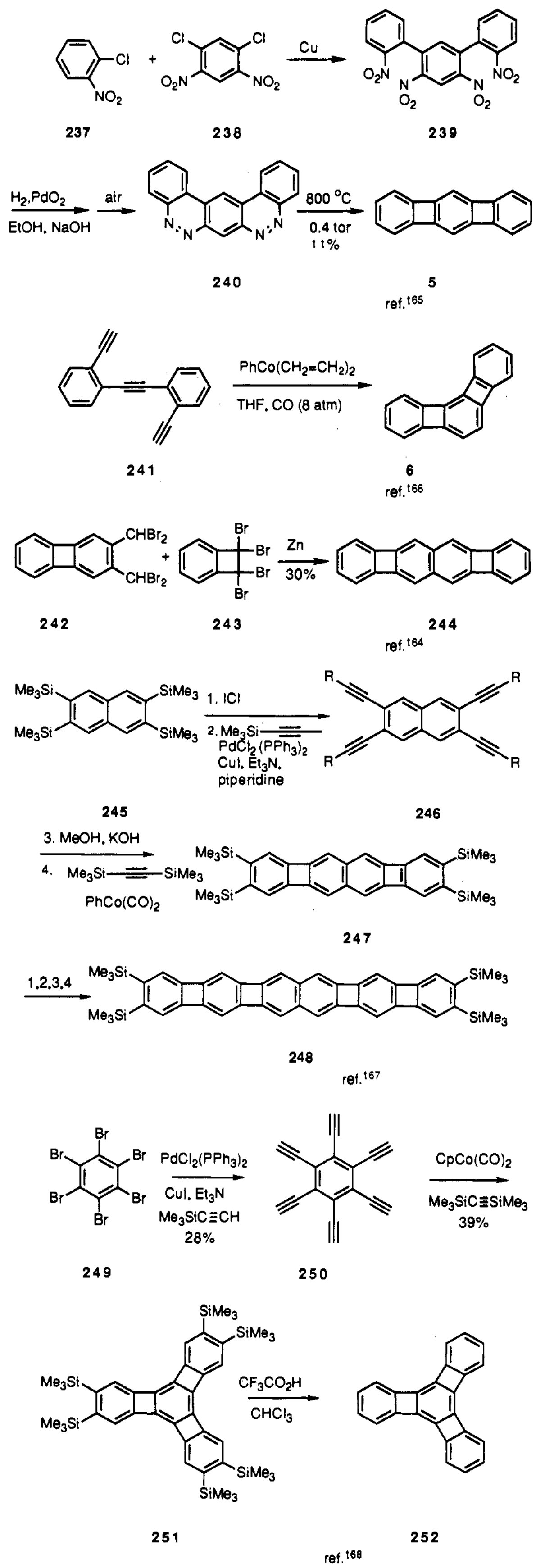
5.2 Structure and Spectroscopic Properties

Biphenylene (**4**) is a stable, pale yellow crystalline solid. The X-ray crystallographic structure[132] is shown in Figure 6.

The bonds between the phenylene rings are long. The X-ray crystallographic structures of a number of biphenylene derivatives and heterosubstituted biphenylenes have been obtained. These show similar bond lengths and angles to those of biphenylene itself. *N*-Ethyl-2,7-diazabiphenylene has long bonds (150 pm) between the two pyridinyl rings, the remaining bonds varying in length as in pyridine itself.[169] In angular [3]phenylene (**6**), the bonds between the phenylene rings are long (150.3 pm) and the central phenylene ring has alternating long and short bonds [134.5, 144.9 (annelated to 4-membered ring), 134.8, 144.6, 134.8, and 144.9.][166] The outer benzenes also show alternation, with the bonds exocyclic to the 4-membered ring shorter, but this effect is much less pronounced, resembling the situation in biphenylene.

The X-ray crystallographic structure of hexakis(trimethylsilyl)tris(benzocyclobutadieno)benzene (**251**) is shown in Figure 7.[168] This clearly shows that the central ring is cyclohexatriene rather than benzene, the double and single bonds alternating with the bis(methylene)cyclobutene structure dominant at each 4-membered ring.

Scheme 20



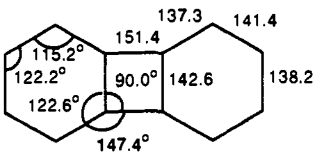


Figure 6. X-ray crystallographic structure of biphenylene. Bond lengths are in pm, and bond angles are in degrees.

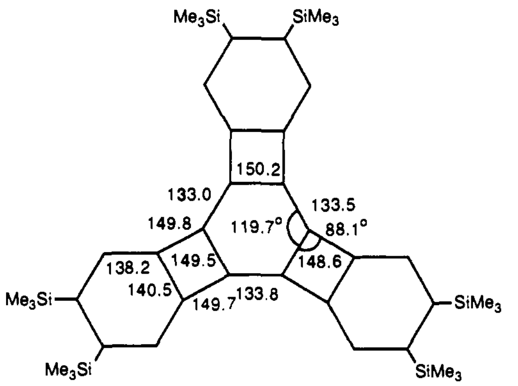


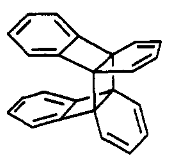
Figure 7. X-ray crystallography structure of hexakis(trimethylsilyl)tris(benzocyclobutadieno)benzene. Bond lengths are in pm, and bond angles are in degrees.

The ^{1}H NMR spectra of biphenylene shows the protons at a higher field than for simple benzenoid systems (H-1, δ 6.70; H-2, δ 6.60). The spectrum of 2-thianorbiphenylene (**213**) shows similar shifts (H-1, δ 6.49; H-4,5, δ 6.86), and this effect is presumed to arise from the paratropic effect of the antiaromatic 4-membered ring, since on oxidation of **213** to the sulfone, the phenyl signals move to lower field (H-4,5, δ 7.63), while the protons on the thiophene ring are virtually unaffected, indicating that the diatropic and paratropic contributions are of similar magnitude.[105] This effect is common in all of the biphenylene systems and becomes accentuated in annelated and polybiphenylenes.[170] In the polybiphenylenes, the protons on the inner benzene rings shift to still higher fields. For example, in the linear [3]phenylene **5**, the protons on the central ring resonate at δ 5.91, while in the angular system **6** they resonate at δ 6.13.[171] Similar effects have been observed with systems containing a central naphthalene ring; in **244** the naphthalene protons resonate at δ 8.06, in **247** at δ 6.69, and in **248** at δ 6.42.[167] Thus, in these systems it also appears that bond localization occurs on annelation, structures with bismethylenecyclobutene moieties predominating.

In the homobiphenylene cation (**233**), the H-2,4 protons resonate at higher field than the remaining tropylium ring protons, suggesting that a greater amount of positive charge resides on these carbons, as expected for the bis(methylene)cyclobutene structure.[160] The benzannelated derivative shows similar shift differences, and the destabilizing effect of the benzocyclobutadiene annelation on the tropylium ion appears to be similar to that of annelation by benzene.[105]

5.3 Reactions

Biphenylene undergoes classical electrophilic addition to give the 2-substituted derivatives. Under certain conditions, ring opening can occur to give benzocyclooctatetraene derivatives, possibly through addition followed by valence tautomerism of the tricyclo[6.4.0.0^{2,7}]dodecapentaene derivative.[172,173] Thermolysis of biphenylene gives tetraphenylene, presumably via the 2,2′-biphenyl diradical.[174-176] Photoirradiation of biphenylene gave the dimer **253**.[177]



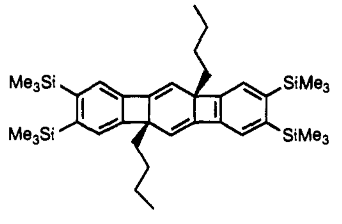
253

Reduction of biphenylene gives the monoanion and then the dianion, the latter a potential 14 π-electron system.[178-181] Oxidation of biphenylene gave the dication, the spectral properties of which indicate it is a delocalized 10 π-electron system.[182,183]

The thiophene ring of 2-thianorbiphenylene (**213**) is more reactive than a normal thiophene, readily adding bromine.[64] On oxidation **213** forms the sulfoxide and sulfone, neither of which undergo Diels–Alder reactions.

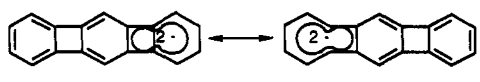
Hydrogenation of the polybiphenylenes, which occurs under very mild conditions, provides considerable insight into the structure of those compounds. With linear [3]phenylene (**5**), the central ring is reduced to the cis-syn-cis isomer, and reduction of **252** occurs in a similar fashion with reduction of the central ring to give the cis-syn-cis-syn-cis hexahydro derivative.[171,184] The ^{1}H NMR spectrum of the hexahydro derivative shows a singlet at δ 4.19 for the cyclohexane ring protons and the ^{13}C NMR spectrum for the compound shows only four absorption signals, substantiating the high symmetry.[184]

The reactivity of the central ring of the tetrakis(trimethylsilyl) derivative of [3]phenylene is also illustrated by the reaction with butyllithium. Treatment with butyllithium followed by iodobutane gives the dialkylated compound **254**, presumably arising from nucleophilic addition of the butyl anion followed by trapping of the resultant anion with the iodobutane.[171]



254

Reaction with [3]phenylene (**5**) with SbF$_5$ in SO$_2$ClF gave the dication, and with potassium in THF the dianion was formed.[171] The spectra of the dianion suggest that the two bis(methylene)benzocyclobutene structures (**255a** and **255b**) are the major canonical contributors.



255a **255b**

6 Conclusions

Two factors restrict the formation of compounds containing bis(methylene)cyclobutene and terakis-

(methylene)cyclobutane structural groups: strain and the introduction of cyclobutadiene structures. The wealth of synthetic and structural information, and the extensive body of knowledge on the reactions of compounds containing these moieties, suggest that the first restriction is less important than the second in limiting the preparation of these compounds. Those compounds in which contributions from canonical structure containing cyclobutadiene systems are minimized are more stable, as is illustrated by the series, 3,4-bis(methylene)cyclobutene (**1a**), benzocyclobutadiene (**2**), and biphenylene (**4**), and is now supported by many of the findings described above, for example in the different properties of 1-thia- and 2-thianorbiphenylene (**215** and **213**, respectively). Even where such structures are enforced, however, compounds can be prepared if access to reagents is prevented by suitable substitution. This is illustrated clearly in the formation of the benzodicyclobutadiene derivative **147** which, despite having one cyclobutadiene system in each of its canonical forms, is isolable. The preferences for structures without a cyclobutadiene contribution has been nicely demonstrated in the phenylenes, particularly by the work of Vollhardt and his collaborators. Phenyl rings are eventually persuaded to adopt cyclohexatriene structures as a means of limiting cyclobutadiene forms, as seen most spectacularly with tris(benzocyclobutadieno)benzene (**252**).

All of the compounds containing 4-membered rings described in this review do, however, involve degrees of bond angle strain and can be expected to undergo reactions in which this strain is lost or minimized. Such reactions are extensively illustrated in the sections above. Compounds containing bis(methylene)cyclobutene or tetrakis(methylene)cyclobutane moieties should thus continue to provide valuable reactive intermediates for the preparation of compounds with new, interesting structures.

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