GENERATION AND INTERCEPTION OF 1-OXA-2,3-CYCLOHEXADIENE AND 1,2,4-CYCLOHEXATRIENE

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ABSTRACT. The cycloadducts 6 and 7 of tricyclo[4.1.0.0^{2,7}]-hepta-3,4-diene (5) with styrene and 1,3-butadiene rearrange to unusual products on thermolysis, namely the cyclohepta-triene derivatives 9 and 10. 1-Oxa-3,4-cyclohexadiene (20) is generated smoothly from 6,6-dichloro-3-oxabicyclo[3.1.0]-hexane (22) and n-butyllithium. 1-Oxa-2,3-cyclohexadiene (21) is formed from 6-exo-bromo-6-endo-fluoro-2-oxabicyclo-[3.1.0]hexane (30) and methyllithium. In the presence of activated olefins, this reaction provides an efficient route to 28 and 33 - 38, the trapping products of 21. Inter-estingly, [2+2]-cycloadditions do not take place at the same double bond of 21 as [4+2]-cycloadditions. The reactions of 1,3-cyclopentadiene and indene with bromofluorocarbene af-ford 6-exo-bromo-6-endo-fluorobicyclo[3.1.0]hex-2-ene (50) and its benzo derivative 45, respectively. On treatment of these compounds with methyllithium in the presence of sty-rene, the interception products 53 and 47 of 1,2,4-cyclo-hexatriene (44) and its benzo derivative 43, respectively, are formed in good yields.

INTRODUCTION

The short-lived intermediate 1,2-cyclohexadiene (2) was generated for the first time by Wittig and Fritze.[1] They utilized a β-elimination pathway and trapped 2 by [4+2]-cycloaddition with 1,3-diphenylisobenzofuran. Moore and Moser[2] discovered a more convenient method for the genera-tion of 2, i. e. the reaction of 6,6-dibromobicyclo[3.1.0]-hexane with methyllithium. Under these conditions, 2 can be

intercepted by activated olefins. Styrene gives a diastereo-
meric pair of [2+2]-cycloadducts (1).[3] [2+2]-Cycloadducts,
e. g. 3, are also the major products formed from 1,3-buta-
diene[4] and its methyl derivatives[4,5] but small quantities
of [4+2]-cycloadducts, e. g. 15, are observed too, which
apparently arise directly from 2 and the diene and not via
the thermal rearrangement of the [2+2]-cycloadducts (see
below).[4] 1,3-Cyclopentadiene, furan, and 2-methylfuran give
[4+2]-cycloadducts exclusively, whereas 1,3-cyclohexadiene
produces a mixture of [4+2]- and [2+2]-cycloadducts.[5]
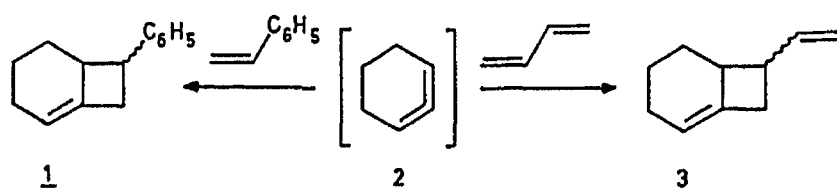
Our lead-in to the chemistry of 1,2-cyclohexadiene and
its derivatives was the reaction of dibromocarbene with
benzvalene giving rise to the dibromocyclopropane 4.[6,7]
Treatment of 4 with methyllithium in the presence of acti-
vated olefins of the kind mentioned above affords a series
of products, e. g. 6 - 9, formed by interception of tricy-
clo[4.1.0.0^{2,7}]hepta-3,4-diene (5).[8]
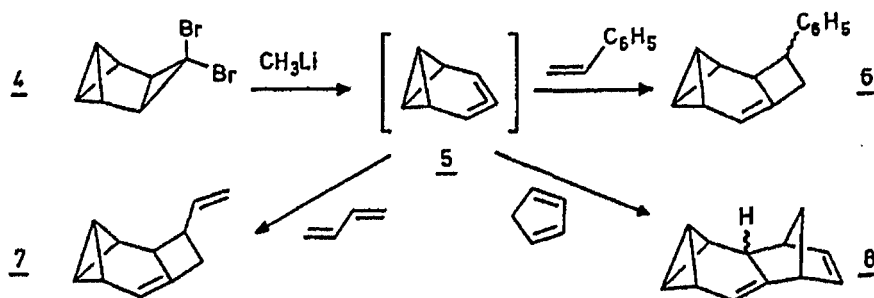
Compounds 6 - 8 behave very differently on thermolysis.
Whereas both the diastereomers 8 rearrange to the bicyclo-
[3.2.0]hepta-2,6-diene derivatives 11 as expected for homo-
benzvalenes,[9] 6 and 7 are converted into the cyclohepta-
trienes 9 and 10, respectively, at unusually low tempera-
tures without the intermediacy of compounds of type 11.[10]

To elucidate the mechanisms of these rearrangements we
have studied the thermolyses of the model compounds 1 and 3.
The equilibrium between the diastereomers 1a and 1b is
established above 140 °C.[11] In this process, diradical 12
is the most likely intermediate, which should also play the
key role in the formation of 1 from 2 and styrene. In
accordance with the latter hypothesis is the finding that on
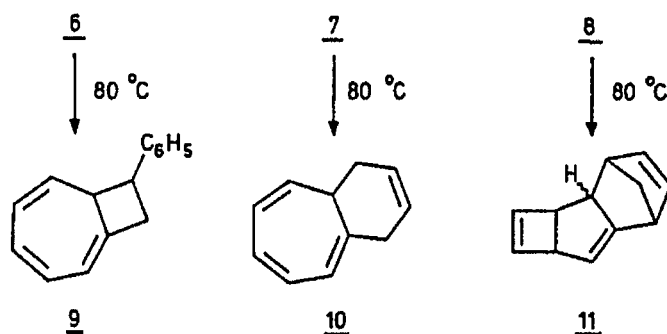
utilization of (Z)-deuteriostyrene the label in **1a** as well as **1b** was determined to be evenly distributed over both the 8-positions.[11,12] Thus, a one-step pathway for the reaction of **2** and styrene is ruled out.
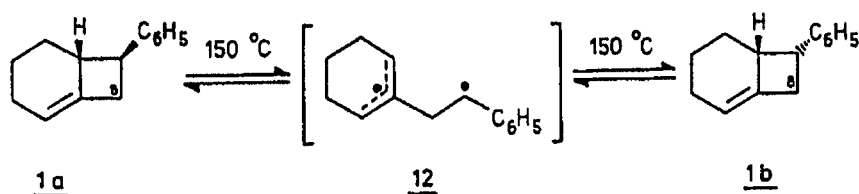

The thermolysis of **3** proceeds in a more complex manner. The interconversion of **3a** and **3b** does take place, most probably via the diradical **13** having an (E)-substituted exocyclic allyl moiety, but the equilibrium composition is arrived at only very incompletely since there is a leak leading to the formation of the more stable isomer **15**. We presume that this vinylcyclobutane-cyclohexene-rearrangement requires diradical **14** as intermediate with a (Z)-substituted exocyclic allyl subunit.[4].
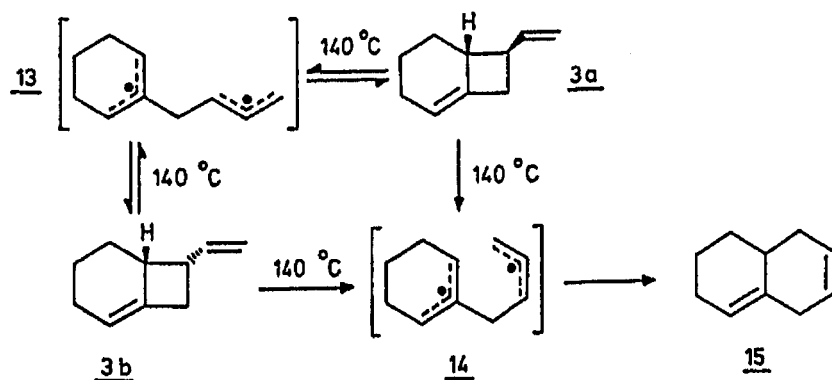
On the basis of these results, mechanisms can be proposed for the rearrangements of **6** to **9** and of **7** to **10**. Thermal activation could transform **6** to diradical **16**, the homobenzvalenyl radical moiety of which could rearrange to the tropylium radical subunit. Thus generated, the diradical **17**

could collapse to 9. The formation of 10 from 7 should
proceed analogously via the diradicals 18 and 19, with the
allyl moiety in the (Z)-configuration required for the ex-
pansion of the four- to the six-membered ring. In agreement
with the assumed ease of the rearrangements of 16 to 17 and
of 18 to 19, it has been shown recently that the unsubsti-
tuted homobenzvalenyl radical transforms to the tropylium
radical with an activation energy of 13.4 kcal/mol.[13]
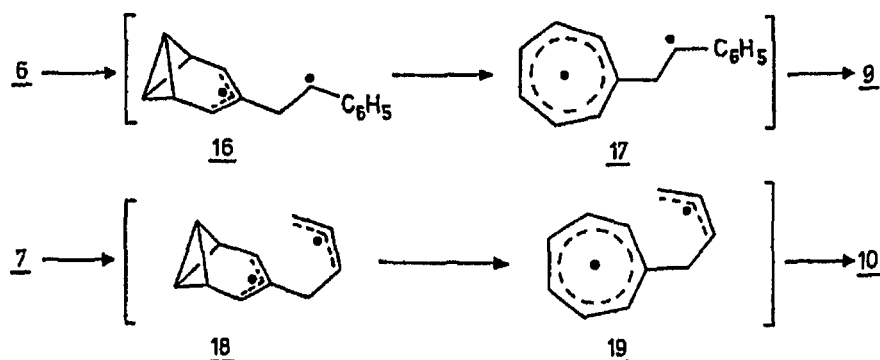
The intermediacy of several further 1,2-cyclohexadiene
derivatives, namely bicyclo[3.2.1]octa-2,3-diene,[14] bicy-
clo[3.2.1]-octa-2,3,6-triene,[15] and a benzanellated deriva-
tive of the latter,[16] has been proved by trapping
reactions. The properties of these strained allenes and
theoretical investigations on them have been summarized.[17]
We have generated 1-methyl-1,2-cyclohexadiene from 6,6-
dibromo-1-methylbicyclo[3.1.0]hexane and trapped it with
styrene[11] and 1,3-butadiene.[4] Until recently, very little
was known, however, about hetero derivatives of 2,[17] which
is why we undertook to investigate the existence of both the
possible oxa derivatives 20 and 21.

1-Oxa-3,4-cyclohexadiene is smoothly generated from 6,6-
dibromo- and 6,6-dichloro-3-oxabicyclo[3.1.0]hexane (22)
with methyllithium and n-butyllithium, respectively.[18] The
interception of 20 succeeded with styrene, 1,3-butadiene,
methyl derivatives of the latter, and furan. Styrene pro-
vides the diastereomeric [2+2]-cycloadducts 23, whereas 1,3-
butadiene and its methyl derivatives give rise to [2+2]-cy-
cloadducts and small amounts of [4+2]-cycloadducts such as
24 and 25, respectively. In contrast, furan affords the endo
[4+2]-cycloadduct exclusively. The vinylmethylene-cyclo-

butane derivatives of type 24 rearrange to isochromenes of
type 25 on heating at 165 °C.
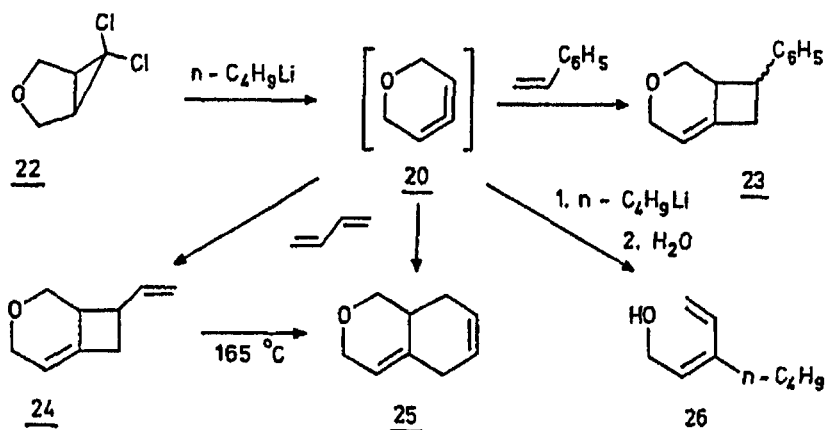
A new type of process was discovered when 20 was genera-
ted in the absence of a sufficiently active olefin. The
central carbon atom of the allene moiety is then attacked by
the organolithium reagent causing the ring opening in an
S_N2'-type substitution with the oxygen atom serving as lea-
ving group. We have obtained 3-substituted 2,4-pentadien-1-
ols analogous to 26 with a methyl, ethyl, n-propyl, neo-
pentyl, phenyl, 2-methoxyphenyl, 2-thienyl, or a 3-thienyl
group.

RESULTS AND DISCUSSION

The conversion of 22 into 20 and the trapping of the lat-
ter encouraged us to treat the known 6,6-dichloro-2-oxa-bi-
cyclo[3.1.0]hexane (27)[19] with n-butyllithium in the pre-
sence of styrene. Indeed, two diastereomers of 28, seemingly
[2+2]-cycloadducts of 1-oxa-2,3-cyclohexadiene (21), were
formed, but the yield was only 7%. The product mixture
consisted mainly of polystyrene and 1-chloro-1-phenylhexane
(29). It is well known that n-butyllithium polymerizes sty-
rene.[20] The initial step produces 1-phenylhex-1-yllithium,
which sequentially attacks further styrene molecules but in
the presence of 27 undergoes a competing reaction, namely
the lithium-chlorine-exchange leading to 29 and the car-
benoid precursor of 21. Obviously, the desired reaction of
27 with n-butyllithium, generating 21, proceeds consider-
ably more slowly than that of 22 producing 20.

Hence, we searched for another source of 21. The dibromo
compound analogous to 27, from which 21 could be liberated
with the less nucleophilic methyllithium, cannot be isolated
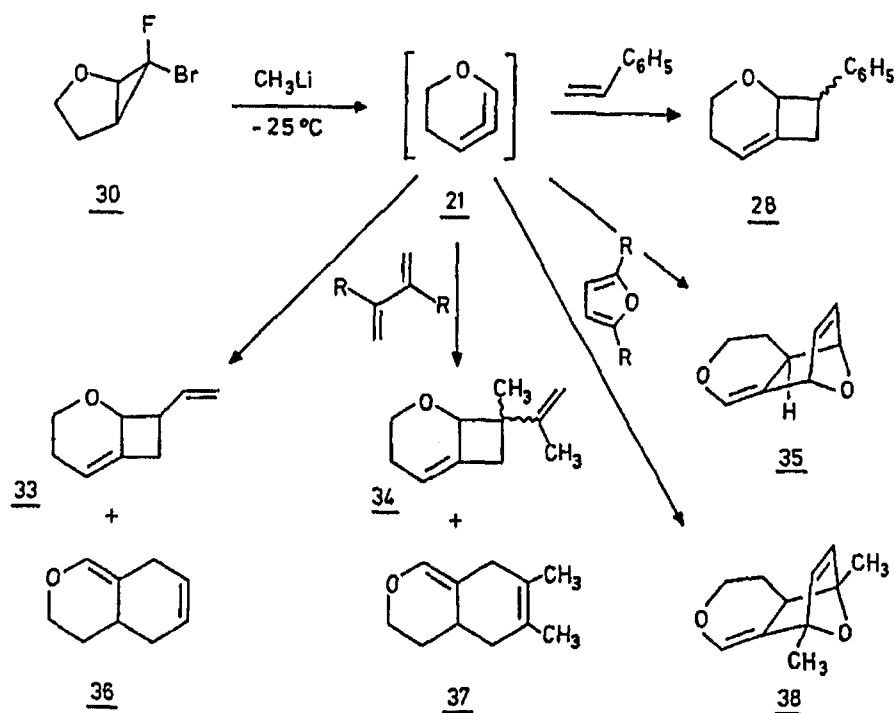due to rapid rearrangement.[19] However, the fluoride ion is

27   28   29
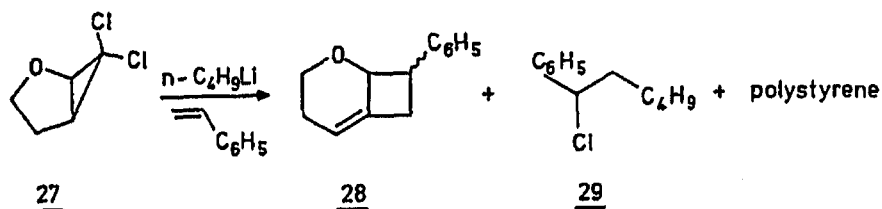
a less favorable leaving group. Thus, we treated 2,3-dihy-drofuran with dibromofluoromethane and sodium hydroxide in the presence of triethylbenzylammonium chloride. After hy-drolytic work-up we isolated the desired exo-6-bromo-endo-6-fluoro-2-oxabicyclo[3.1.0]hexane (30) in 25% yield and the acetal 32, which also results from the reaction of chloro-fluorocarbene with 2,3-dihydrofuran.[19] Apparently, the dia-stereomer 31 is formed in addition to 30 and converted into 32 by sequential rearrangement and hydrolysis.


30   31   32
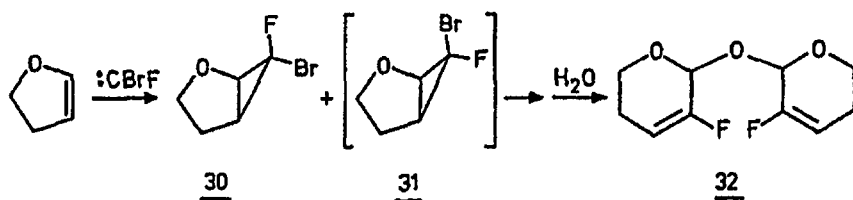
Fluorocompound 30 proved to be an efficient precursor of 1-oxa-2,3-cyclohexadiene (21), which could be generated smoothly by reaction of 30 at -25 °C with methyllithium in ether. In the presence of the trapping reagents styrene, 1,3-butadiene, 2,3-dimethyl-1,3-butadiene, furan and 2,5-dimethylfuran, products with the expected structures 28 and 33 - 38 were formed. The ratio of the diastereomeric styrene adducts 28 (54% yield) was determined to be close to 1 : 1, whereas the ratio of the corresponding adducts of 2 was about 3.5 : 1 in favor of the exo-isomer 1a in the reaction at -25 °C.[11] 1,3-Butadiene afforded a 2 : 1-mixture (80% yield) of the [2+2]-cycloadduct 33 consisting largely of one stereoisomer, probably the exo-compound, and the [4+2]-cy-cloadduct 36. 2,3-Dimethyl-1,3-butadiene yielded a 7 : 1 : 1-mixture (57%) of the two diastereomeric [2+2]-cyclo-adducts 34 and the [4+2]-cycloadduct 37. Furan and 2,5-dimethylfuran took up 21 to form the [4+2]-cycloadducts 35 (31%) and 38 (37%), respectively.

It is interesting to note that [2+2]- and [4+2]-cycload-ditions of 21 proceed with a different chemoselectivity. While the former take place at the enol ether double bond, in the case of the latter the double bond more remote from the oxygen reacts exclusively. We take these results as evi-

F

O   Br

CH₃Li
-25 °C

$$\underline{30}$$

$$\underline{21}$$

C₆H₅

O   C₆H₅

$$\underline{28}$$

R

R

O

R

R

$$\underline{35}$$

H

O

$$\underline{33}$$

+

O

$$\underline{34}$$

CH₃

CH₃

+

R

CH₃

O

CH₃

$$\underline{38}$$

O

$$\underline{36}$$

O   CH₃

CH₃

$$\underline{37}$$

dence for different mechanisms. If the [4+2]-cycloadditions were one-step processes, i. e . true Diels-Alder reactions, on the basis of the frontier orbital concept, the more electron-rich enol ether double bond would be the less active one toward the electron-rich diene in agreement with experiment. According to the above discussion, we consider the [2+2]-cycloadditions as two-step processes with the diradicals 40 as intermediates. Whether the collapse of 40 occurs involving positions 2 or 4 to give 39 and 41, respectively, is a matter of relative reaction rates, since the equilibrium between 39 and 41 should not be mobile under the reaction and work-up conditions. Due to the radical-stabilizing property of an alkoxy substituent,[21] the spin density within the allyl radical subunit of 40 should be larger in position 2 than in position 4 favoring the ring closure in position 2 and giving rise to 39.

O   R

$$\underline{39}$$

O

R

$$\underline{40}$$

O

R $$\underline{41}$$
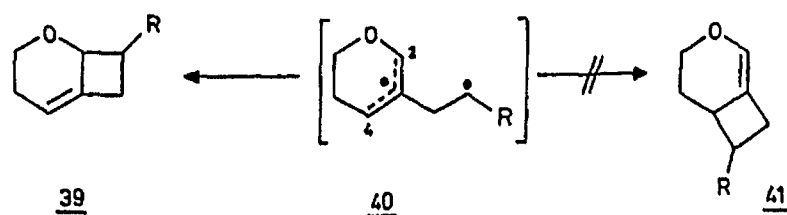
The kinetic stability of 30 encouraged us to investigate whether additional derivatives of 2 could exist. In 1987, Miller and Shi[22] reported the generation of the allenic

isomer **42** of the dimethylnaphthalenes by a β-elimination route and the interception of **42** with 1,3-diphenylisobenzofuran. We were interested whether the geminal methyl groups in **42** would be a necessary condition for a sufficiently long lifetime to allow trapping reactions. After all, in the case of the unsubstituted analogue **43** of **42**, a rapid base-induced isomerization to naphthalene is conceivable since the methylene group is doubly activated for deprotonation due to its allylic and benzylic position. In the benzene isomer **44**, the methylene group has doubly allylic character and thus should be similarly acidic as 1,4-cyclohexadiene, which is readily deprotonated with potassium amide in liquid ammonia.[23)]

CH₃ CH₃   H H   H H

42   **43**   **44**
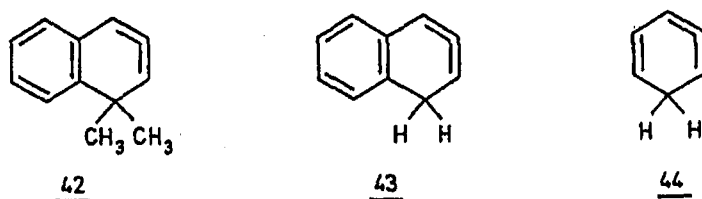
It follows from the above discussions that dihalocarbene adducts of indene and 1,3-cyclopentadiene should be appropriate precursors of **43** and **44**. The dichlorocarbene adducts of indene[24)] and 1,3-cyclopentadiene[25)] are known, but they convert into 2-chloronaphthalene and chlorobenzene readily. Since n-butyllithium is required to generate allenes from dichlorocyclopropanes but attacks the favorable trapping reagent styrene,[20)] we again applied the fluorine trick. From the reaction of indene with bromofluorocarbene we obtained the **exo**-bromo-**endo**-fluoro compound **45**, albeit in 8% yield. To a considerable extent 2-fluoronaphthalene was formed originating from the **endo**-bromo-**exo**-fluoro isomer **46**. Treatment of **45** with methyllithium in the presence of sty-

F

Br +   Br   F

45   **46**

CH₃Li,-20°C

C₆H₅   C₆H₅

C₆H₅

170 °C

C₆H₅

**43**   **47**   **48**
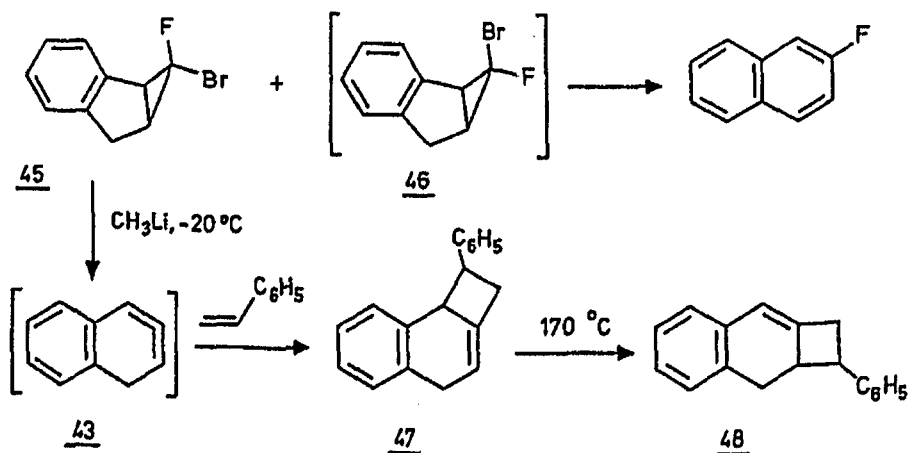
rene afforded a 63% yield of the [2+2]-cycloadduct **47** of the allenic naphthalene isomer **43**. On heating at 170 °C for one hour, **47** rearranged to the alternative [2+2]-cycloadduct **48**.

Most probably, **43** takes up styrene to give diradical **49**, which collapses kinetically affording **47** due to the higher spin density in position 1 of **49** relative to position 3. At higher temperatures, the bond making in **49** to give **47** becomes reversible, and the kinetically unfavorable but more exergonic ring closure involving position 3 of **49** leads to **48**.
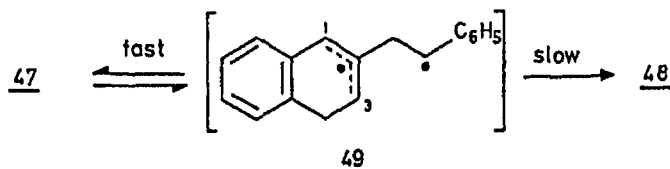
Analogous to the synthesis of **45**, we prepared exo-bromo-endo-fluorobicyclo[3.1.0]hex-2-ene (**50**) (13% yield) by treatment of 1,3-cyclopentadiene with dibromofluoromethane and sodium hydroxide in the presence of triethylbenzylammonium chloride. The reason for the low yield is in part the formation of the endo-bromo-exo-fluoro compound **51**, which is converted rapidly into fluorobenzene. Reaction of **50** dissolved in styrene with methyllithium afforded the dihydrophenylcyclobutabenzene **53** in 66% yield. We propose that at first 1,2,4-cyclohexatriene is generated, which attacks styrene to produce diradical **52** containing a pentadienyl radical subunit. Interestingly, **52** is not subject to an intramolecular hydrogen transfer, which would yield 1,2-diphenylethane, but collapses via the position 3, where the spin density of the pentadienyl radical moiety is higher than in position 1.
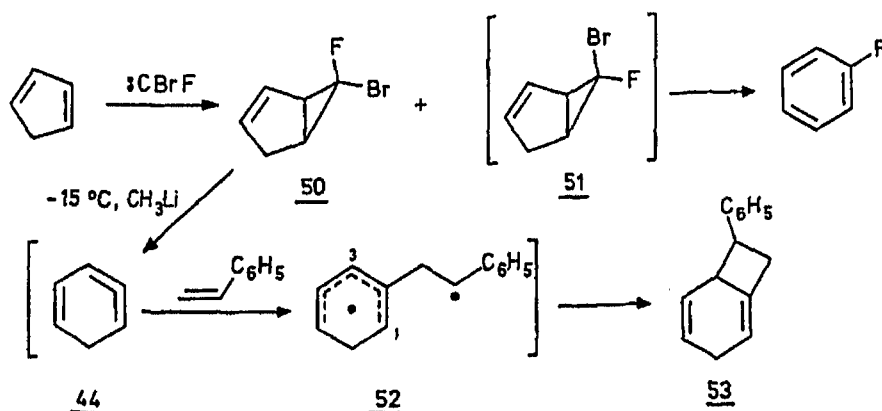
In summary, we have shown that the properties of geminal bromofluorocyclopropane derivatives are unique in providing synthetic access to certain 1,2-cyclohexadienes. First, by addition of bromofluorocarbene to the corresponding cyclopentenes exo-bromo-endo-fluorobicyclo[3.1.0]hexane derivatives are formed. These do not readily rearrange at room temperature because of the strength of the carbon-fluorine bond, which prevents the dissociation into a fluoride ion and a carbocation. Second, the bromine atom is replaced smoothly by a lithium atom under mild conditions, i. e. on treatment with methyllithium, which is followed by the α-elimination of lithium fluoride to give the cyclopropylidene and then, by ring enlargement, the cyclic allene. This methodology allows the generation of 1-oxa-2,3-cyclohexadiene (21) and its trapping by several activated olefins. Also, the benzene isomer 1,2,4-cyclohexatriene (44) and its benzo derivative 43, which is an isomer of naphthalene, do not aromatize under these conditiones and can be intercepted by [2+2]-cycloadditions with styrene.

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