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1,2-DIMETHYLSPIRO[2.3]HEX-1-ENE BY ADDITION OF CYCLOBUTYLIDENE TO 2-BUTYNE

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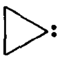
*The first addition of a cyclobutylidene (carbenoid) to an alkyne is reported. By C_4+C_2-coupling the spiro[2.3]hex-1-ene system **8** is constructed. Furthermore, cyclobutylidene adds to methylenecyclopropane, its intramolecular reaction product, to give the novel dispiro[2.1.3.0]octane **11**.*

The formation of cyclopropane and cyclopropene rings by the addition of carbene(oid)s to alkenes and alkynes is well documented.2a) In contrast, only few examples have been reported for the construction of spiro[2.n]alkanes and spiro[2.n]alk-1-enes (n = 2,3) by reactions of small ring carbenes with C-C-double and triple bonds.



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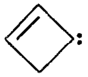

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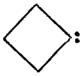

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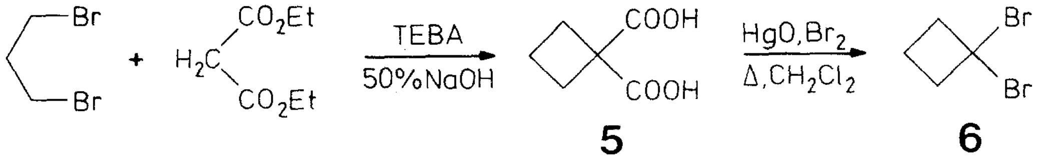
Thus, cyclopropylidenes (**1**) add intermolecularly to olefins only, when highly strained products (allenes, tricyclic compounds etc.)3) would result from intramolecular reaction pathways. – Cyclopropenylidenes (**2**) cannot stabilize themselves intramolecularly and, therefore, being nucleophilic carbenes, undergo additions to electron deficient double bonds.4)

Cyclobutenylidene (**3**)5) contains a vinylcarbene as a structural subunit and thus can be regarded as a stabilized carbene when compared with cyclobutylidene (**4**). In contrast to **4** which undergoes intramolecular rearrangements to methylenecyclopropane und cyclobutene,6,7) in cyclobutenylidene (**3**) the corresponding reactions leading to strained methylenecyclopropene and antiaromatic 1,3-cyclobutadiene have not been observed.5a) Because intramolecular reactions are impeded, perchloro-substituted **3** adds intermolecularly to olefins and 2-butyne to give spiro[2.3]hex-4-enes and spiro[2.3]hexa-1,4-dienes, respectively, in yields of 35-40%.5b) Here again, intermolecular reactions compete with intramolecular ones if the latter are thermodynamically unfavorable.

We have recently shown8) that cyclobutylidene (carbenoid) (**4**) adds to different substituted styrenes and to *cis*- and *trans*-2-butene stereospecifically to afford spiro[2.3]hexanes in yields between 57 and 27%.

Herein, we report the first addition of cyclobutylidene (**4**) to an alkyne, whereby the spiro[2.3]hex-1-ene ring system is constructed in one step through a C_4+C_2-coupling.

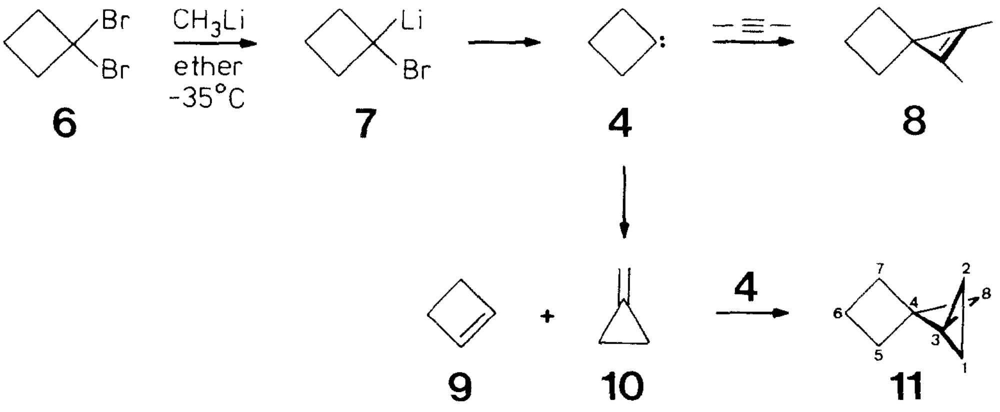
Cyclobutylidene (**4**), the C_4-building block, is easily generated from 1,1-dibromocyclobutane (**6**) by action of alkyllithium.[7] **6** can be obtained in three steps from cyclobutene[7,8] or more conveniently by a two step synthesis developed by *Paquette*.[9] Treatment of 1,3-dibromopropane with diethyl malonate in aqueous sodium hydroxide solution with triethylbenzylammonium chloride (TEBA) yields 1,1-cyclobutanedicarboxylic acid (**5**)[10,11] which is converted to **6** by a double Hunsdiecker degradation.[9]



1,1-Dibromocyclobutane (**6**) was treated with methyl-lithium in ether at -35°C in the presence of a tenfold excess of 2-butyne. Methylenecyclopropane (**10**) and cyclobutene (**9**), the characteristic intramolecular products of cyclobutylidene (**4**)[6,7,12] where formed by ring contraction reaction and competitive 1,2-hydrogen migration in yields of 30 and 4.5%[13], respectively.

In general, it has been found that the ratio of **10** and **9** always is in favor of **10** (2-6:1).[6,7] independent of the method applied for the generation of cyclobutylidene (**4**). The ratio **10**:**9** (6.7:1) determined in the reaction of **6** in the presence of 2-butyne corresponds well with the value obtained at the same temperature under similar conditions, however, without any trapping reagent present (**10**:**9** = 6:1).[7]

The possibility exists that after its intramolecular formation from **4**, methylenecyclopropane (**10**) is attacked intermolecularly by cyclobutylidene (**4**) to give the strained hitherto unknown dispirane **11**. Indeed, after vpc separation (Fractonitril, 65°C) of the higher boiling fraction containing the intermolecular products of the reaction of **6**, ca. 6% of the novel dispiro[2.1.3.0]octane (**11**)[14] could be isolated. Furthermore, **11** was synthesized independently by reacting **6** with methylenecyclopropane (**10**) under the conditions comparable to those when 2-butyne was used. Besides ca. 1% of 1-bromo-1-methylcyclobutane[15] the C_8H_{12}-hydrocarbon **11**[14] was isolated in an unoptimized yield of 18%.



As the main component of the intermolecular products, however, the expected 1,2-dimethylspiro[2.3]hex-1-ene (**8**)[14] resulting from addition of **4** to the triple bond of 2-butyne was obtained after vpc separation in a yield of 21%. Clearly, cyclobutylidene (carbenoid) (**4**) represents a „stabilized" carbene, where therefore intermolecular reactions to **8** and **11** compete efficiently with intramolecular ones to **9** and **10**.

Besides the hydrocarbons **8**, **9**, **10**, and **11**, three[16] compounds containing a bromine atom could be detected in the reaction mixture. While bromocyclobutane[18] was formed only in trace amounts, 1-bromo-1-methylcyclobutane[15] could be isolated in 12% yield. These compounds are thought to result from protonation and methylation, respectively, of the intermediate organolithio compound **7**, formed after halogen-metal exchange in **6**.

In conclusion, our synthetic strategy of applying a C_4+C_2-coupling for the construction of the spiro[2.3]hex-1-ene system offers, although the yield thus far obtained has been only moderate, exceptional brevity [only two steps from commercially available 1,1-cyclobutanedicarboxylic acid (**5**)], making it superior to other known approaches to this interesting class of compounds.[2b,19]

In comparison to the plethora of compounds known comprising spiro-connected three-membered rings, far fewer examples of polyspiranes containing cyclobutanes have been reported.[2b] This discrepancy obviously stems from the fact that, in general, more efficient methods are available for the synthesis of cyclopropanes. The use of cyclobutylidene (**4**) as a reactive C_4-spiroalkylation reagent might, therefore, offer new perspectives for the construction of polyspiranes containing four-membered rings.

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13) Determined with 1,3-butadiene as external standard.
14) **8**: ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 1.71 ("quint."; 2H, 5-H); 1.95 (s; 6H, CH_3); 2.04 (t; 4H, 4/6-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 8.5 (q; 2C, CH_3); 14.5 (1C, C-5); 27.7 (s; 1C, C-3); 32.6 (t; 2C, C-4, C-6); 119.0 (s; 2C, C-1, C-2);
11: ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.64-0.73 (AA'BB'-system; 4H, 1-H, 2-H); 0.75 (s; 2H, 8-H); 1.75-1.84 (m; 1H, 6-H); 1.91-2.07 (m; 3H, 5-H, 6-H, 7-H); 2.08-2.18 (m; 2H, 5-H, 7-H); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 5.0 (t; C-1, C-2); 16.8 (t; C-6); 18.6 (t; C-8); 19.2 (s; C-3); 24.8 (s; C-4); 28.8 (t; C-5, C-7).
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16) The third compound which was formed in ca. 1% yield proved to be bromocyclobutylmethane.[17]
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19) For example, spiro[2.3]hex-1-ene has been synthesized from methylenecyclobutane. Dibromocarbene addition afforded 1,1-dibromospiro[2.3]hexane (yield: 55%) which after reduction to the monobromo compound (87%) was dehydrohalogenated to the cyclopropene (43%).[20] Naturally, by this method 1,2-disubstituted spiro[2.3]hex-1-enes are not available.
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