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6-Methyltetracyclo[4.2.0.0^{1,7}.0^{5,7}]octane - a Bridged [3.3.3]Fenestrane

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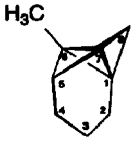
Abstract: The reaction of 1-bromo-2-chloromethyl-7-methyltricyclo[4.1.0.0^{2,7}]heptane with methyllithium leads to either 2-methyl-3-methylenetricyclo[4.1.0.0^{2,7}]heptane or 7-bromo-1,7-dimethyl-2-methylenebicyclo[4.1.0]heptane depending on the methyllithium reagent used. Both products suggest that 6-methyltetracyclo[4.2.0.0^{1,7}.0^{5,7}]octane was formed as an intermediate.

Tricyclo[2.1.0.0^{1,3}]pentane **1**[2] ([3.3.3]fenestrane[3]), first synthesized by Wiberg and McClusky, is one of the most highly strained hydrocarbons. One signal of its ^{13}C NMR spectrum has been observed at -55 °C. At -50 °C, however, **1** rearranged in a concerted but nonsynchronous process under cleavage of the two central bonds (C-1-C-3 and C-1-C-4) of **1** to give cyclopentenylidene **2**, which was stabilized by hydrogen migration to afford cyclopentadiene.

1,3-Bridged derivatives of **1** such as **3** (6-methyltetracyclo[4.2.0.0^{1,7}.0^{5,7}]octane) would be expected to have a lower propensity to cleave the bicyclobutane central bonds (C-1-C-7 and C-6-C-7) leading to carbene **4**, because the CC double bond in **4** is placed at a bridgehead position. Therefore, this energetically less favorable ring opening of **3** might enhance its lifetime and allow a full spectroscopic characterization and perhaps its isolation. 1-Bromo-2-chloromethyl-7-methyltricyclo[4.1.0.0^{2,7}]heptane (**5a**)[4a, b] was regarded as a suitable precursor for **3**. Its synthesis was achieved from cyclohexene in seven steps.

1

2



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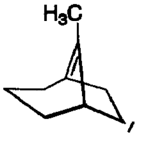

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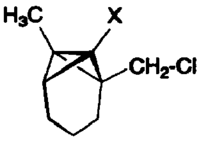
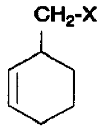


5

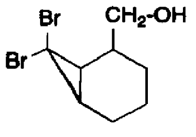
5	X
a:	Br
b:	Li
c:	H

Cyclohexene was lithiated at the allylic position as reported by Schlosser by use of potassium *tert*-

butoxide and *n*-butyllithium,[5a] followed by workup with *para*-formaldehyde affording (2-cyclohexenyl)methanol (**6a**)[5b] in 65% yield. **6a** was O-protected to give **6b** by treatment with 3,4-dihydro-2H-pyran/pyridinium p-toluenesulfonate (PPTS).[6] Addition of dibromocarbene (CHBr$_3$/NaOH, NBu$_3$)[7] to the tetrahydropyranyl ether **6b** followed by cleavage of the protecting group gave a 63 % yield of (7,7-dibromobicyclo[4.1.0]hept-2-yl)methanol **7** as a 3.5 : 1 mixture of *trans* and *cis* isomers. Treatment of this mixture with 2.0 equiv. of MeLi gave a 9:1 mixture of tricycloheptanes **8a** and **9** in a total yield of 42%. Methylation of **8a** at its bridgehead position was achieved with 2 equiv. of BuLi in ether followed by addition of potassium *tert*-butoxide and addition of methyl iodide producing a 73 % yield of **8b**.[8] Lithiation of **8b** at the second bicyclo[1.1.0]butane bridgehead with 2 equiv. of BuLi and reaction of the organometallic intermediate with tosyl bromide produced a 55 % yield of **8c** which could be converted into **5a** in 63 % yield by use of tris(dimethylamino)phosphine/tetrachloromethane.[9]



6a: X = O-H
6b: X = O-THP



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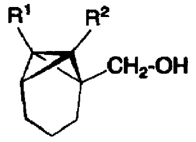
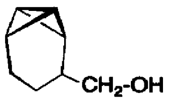


8

8	R^1	R^2
a:	H	H
b:	CH$_3$	H
c:	CH$_3$	Br



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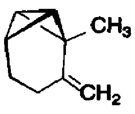

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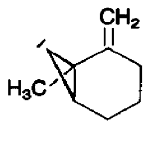


11

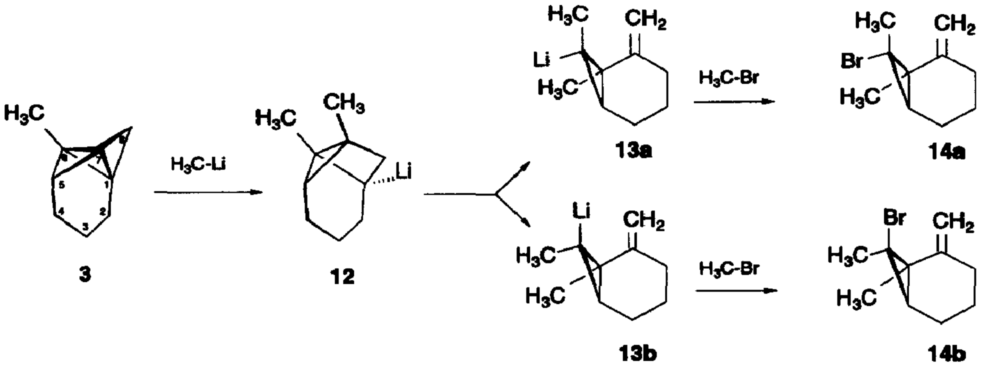
Reaction of **5a** with BuLi in THF at -90 °C gave **5b** which did not cyclize to **3** at this temperature. Warming this solution under ^{13}C NMR control to 0 °C in temperature intervals of 10 °C did not lead to new NMR signals which could be assigned to **3**. Quenching of **5b** with methanol in the range of -90 to -78 °C gave chloride **5c** together with non-identified olefinic material.

Neither the MeLi/LiBr complex nor halide-free MeLi were able to induce the Li/Br exchange of **5a** in THF at -78 °C. However, when the mixture of MeLi/LiBr and **5a** was allowed to warm to room temperature, 2-methyl-3-methylenetricyclo[4.1.0.0^{2,7}]heptane (**10**) was formed in 45% yield. The structure of this compound rests on the spectral data of **10**, specifically on its ^{13}C NMR spectra. The structure of **10**, which is isomeric to **3**, shows that massive bond reorganization has taken place. A rational course of the formation of **10** proceeds via retrocarbene ring opening of intermediate **3**. In accordance with our initial working hypothesis, carbene **4** is not involved in the isomerization process. The extra strain energy of the bridgehead

CC double bond in **4** is circumvented by an alternate fission of CC bonds in **3**: cleavage of the bonds C-1-C-7 and C-7-C-8 leads to carbene **11**. As a bicyclo[4.1.0]hept-7-ylidene, **11** is expected to stabilize by a CH-insertion reaction leading to tricyclo[4.1.0.0^{2,7}]heptane **10**.[10]

A somewhat different reaction course was observed when halide-free MeLi was used as a base. After mixing MeLi and **5a** in THF at -78 °C and warming the solution to room temperature aqueous workup afforded a 30% yield of a 2.5:1 mixture of (2-methylene)bicyclo[4.1.0]heptanes **14a** and **b**. An obvious route for the formation of **14** could be the addition of MeLi to carbene **11**, followed by Li/Br exchange of the corresponding adduct and methyl bromide, present in the reaction mixture by the intial formation of **5b**. This reaction path, however, seems rather unlikely, because a considerable number of bicyclo[4.1.0]hept-7-ylidenes have been generated in the presence of MeLi or other organolithium reagents without the observation of an RLi adduct to the carbenic center. A preliminary reasonable mechanism of the formation of **14** is depicted in Scheme 1:

Scheme 1:



In the first step of Scheme 1, halide-free MeLi adds to the most highly strained carbon atom to give **12**. In the second step **12** is isomerized to the cyclopropyl derivative **13a** or **b** in a rarely observed, but not unprecedented ring opening of a cyclobutyllithium derivative.[11] The observed products **14a/b** are generated by Li/Br exchange. Details of this mechanism are under further investigation.

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4. (a) All new compounds were characterized by their NMR and MS spectra and gave correct elemental analyses and/or molecular weights (HRMS). All NMR spectra were recorded in $CDCl_3$ on a Varian 400 MHz spectrometer.

   (b) **5a**: ^{1}H NMR: δ 1.26-1.60 (m, 6 H, 3-H_2, 4-H_2, 5-H_2), 1.49 (s, 3 H, CH_3), 2.40 (t, 1 H, 6-H), 3.49, 3.52 (d, 2 H, CH_2Cl). ^{13}C NMR: δ 8.81 (q, CH_3), 18.59, 20.77, 21.59 (t, C-3, C-4, C-5), 22.09 (s, C-7), 33.38 (s, C-1), 47.15 (t, CH_2Cl), 48.31 (d, C-6), 51.82 (s, C-2). EIMS: m/z (%) 238 (2), 236 (10), 234 (7) [M^+], 210 (1), 208 (5), 206 (4), 201 (10), 199 (11), 157 (15), 155 (37), 91 (100). **5c**: ^{1}H NMR: δ 1.18 - 1.38 (m, 6 H, 3-H_2, 4-H_2, 5-H_2), 1.40 (d, 7-H), 1.57 (s, 3 H, CH_3), 2.10 (dt, 1 H, 6-H), 3.38, 3.53 (d, 2 H, CH_2Cl). ^{13}C NMR: δ 11.39 (q, CH_3), 15.12 (d, $^1J_{CH}$ = 204 Hz, C-7), 18.94 (s, C-1), 19.20, 21.35, 22.29 (t, C-3, C-4, C-5), 40.59 (d, C-6), 48.31 (s, C-2), 48.91 (t, CH_2Cl). EIGC: m/z (%) 158 (14), 156 (47) [M^+], 143 (8), 141 (27), 121 (100), 91 (58). **10**: ^{1}H NMR: δ 1.23 (s, 3 H, CH_3), 1.53 (dt, 2 H, 5-H_2), 1.73 (d, NOE with s at 1.23, 2 H, 1-H, 7-H), 2.08 (tt, 2 H, 4-H_2), 2.42 (quint., 1 H, 6-H), 4.73 (q, 1 H, olefinic *exo*-H), 4.80 (q, NOE with d at1.23, 1 H, olefinic *endo*-H). ^{13}C NMR: δ 13.76 (d, $^1J_{CH}$ = 203 Hz, C-1, C-7), 18.16 (q, CH_3), 22.13 (t, C-5), 30.69 (t, C-4), 38.35 (d, C-6), 48.87 (s, C-2), 105.69 (t, olefinic CH_2), 149.63 (s, C-3). EIGC: m/z (%) 120 (88) [M^+], 105 (100), 91 (80), 79 (38), 77 (32). **14a**: ^{1}H NMR: δ 1.20 (dd, 1 H, 6-H), 1.23-2.10 (m, 6 H, 3-H_2, 4-H_2, 5-H_2), 1.47, 1.49 (s, 6 H, CH_3), 4.99, 5.05 (m, 2 H, olefinic CH_2). ^{13}C NMR: δ 18.37, 22.01 (t, C-4, C-5), 22.21, 24.68 (q, CH_3), 27.57 (s, C-1), 31.63 (t, C-3), 31.78 (d, C-6), 52.48 (s, C-7), 113.32 (t, olefinic CH_2), 146.45 (s, C-2). **14b**: ^{1}H NMR: δ 0.87 (dd, 1 H, 6-H), 1.23 - 2.10 (m, 6 H, 3-H_2, 4-H_2, 5-H_2), 1.31, 1.68 (s, 6 H, CH_3), 4.95, 5.05 (m, 2 H, olefinic CH_2). ^{13}C NMR: δ 20.05, 22.47 (t, C-4, C-5), 22.72, 26.17 (q, CH_3), 26.83 (s, C-1), 31.21 d, C-6), 32.36 (t, C-3), 53.51 (s, C-7), 112.24 (t, olefinic CH_2), 147.91 (s, C-2). **14**: EIGC: m/z (%) 216 (4), 214 (4) [M^+], 135 (100), 107 (28), 91 (35).
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