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Generation of hexahydroazulenes

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ABSTRACT

(*Z*)-Cyclodec-1-en-6-yne (**3**) generates three conjugated hexahydroazulenes **3**→**1k**→**1c**, **1ℓ** under FVP conditions, whereas flash vacuum pyrolysis (FVP) of cyclodecyne (**2**) leads to 1,2,9-decatriene (**9**). We attribute the different thermal behavior of **2** (ring opening) and **3** (ring closure) to different transannular interactions. Altogether 22 constitutional isomers of hexahydroazulene should exist; three new isomers (**1k**, **1ℓ**, and **1m**) are presented here, ten were described earlier, but the reinvestigation of the dehydration route of bicyclic alcohol **11** showed that one of the ten structures has to be revised.

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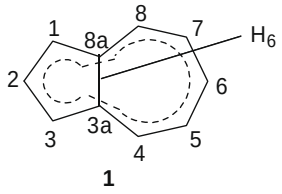
Partly hydrogenated azulenes (bicyclo [5.3.0]decenes, -decadienes, -decatrienes, etc.) are interesting starting compounds for the synthesis of polycycles. However, the majority of hydroazulenes are still unknown. Thus, for example, 22 hexahydroazulenes **1** should exist as constitutional isomers and, moreover, 16 of them should show stereoisomerism. Scheme 1 summarizes the 9 hexahydroazulenes **1a**–**i**, which are, to the best of our knowledge, presently known.[1–11]

Ten-membered carbocycles should be favorable precursors for the generation of hydroazulenes, because these medium-sized ring systems exhibit strong transannular interactions. In the previous years several oxidative transannular ring closures on the basis of cyclodecyne have been published.[12–16] The high energy content of triple bonds makes cycloalkynes as interesting sources for thermal isomerization routes.[17] We present here the reactivity of cyclodecyne (**2**) and (*Z*)-cyclodec-1-en-6-yne (**3**) under flash vacuum pyrolysis (FVP) conditions.

Cyclodecyne (**2**) was prepared by oxidation of 1,2-cyclodecanedione bis-hydrazone.[18–20] Scheme 2 summarizes the preparation of (*Z*)-cyclodec-1-en-6-yne (**3**). 6-Hydroxycyclodecanone (**4**), which exists in a tautomeric equilibrium with its hemiacetal **4′**,[21,22] was transformed to the semicarbazone **5**[23], whose bicyclic form is in DMSO below the NMR detection limit of 5%. Reaction with SeO_2 yielded selenadiazole **6**,[24] which was dehydrated with $POCl_3$/pyridine or $(PhO)_3PCH_3^+$ I^-/hexamethylphosphoramide[25] to yield **7**.[26] Both the processes are regio- and stereoselective. Among the possible products, **7** is the structure with the lowest strain.[27] Fragmentation of **7** on Cu powder gave the target compound **3**.[28]

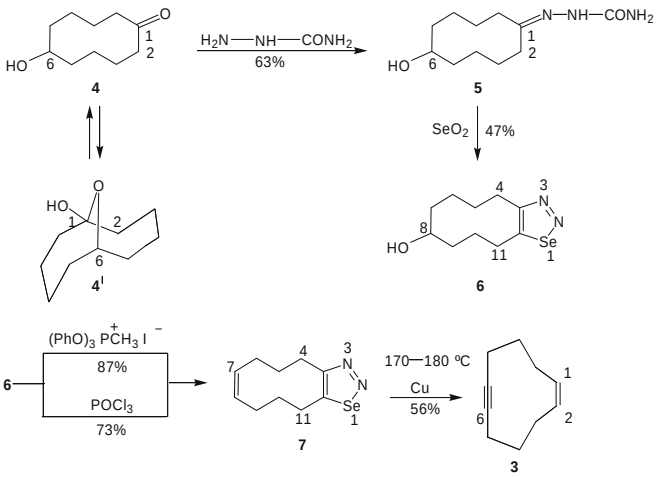
Cyclodecyne (**2**) does not give octahydroazulene **8**[29] under FVP conditions. It is selectively transformed at 600–650 °C and 10^{-4} kPa into 1,2,9-decatriene (**9**).[30] A presumably non-concerted



1

Scheme 1. Hexahydroazulenes **1**: 1,2,3,3a,4,8a- (**1a**)[1], 1,2,3,3a,6,8a- (**1b**)[1], 1,2,6,7,8,8a- (**1c**)[2,3], 1,3a,4,6,8a- (**1d**)[4], 1,3a,6,7,8,8a- (**1e**)[5], 1,4,5,6,7,8- (**1f**)[6], 1,5,6,7,8,8a- (**1g**)[7], 2,4,5,6,7,8- (**1h**)[8,9], 3a,4,5,6,7,8- (**1i**).[10,11]

[6e] process **2**→**9** is favored in comparison to the [4*e*] process **2**→**8** (Scheme 3).



Scheme 2. Preparation of (*Z*)-cyclodec-1-en-6-yne (**3**).

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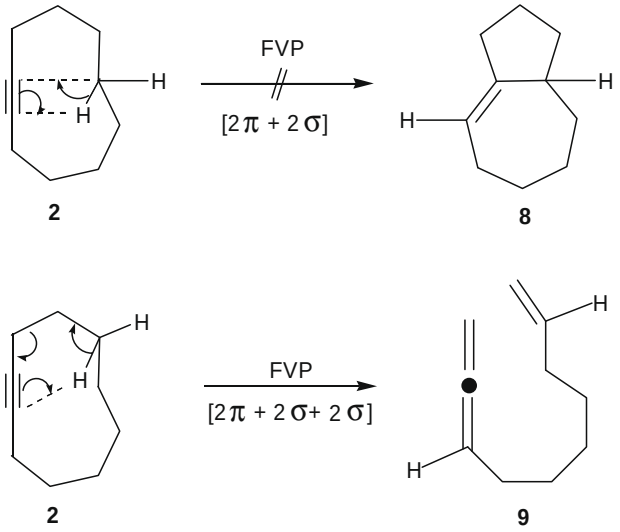
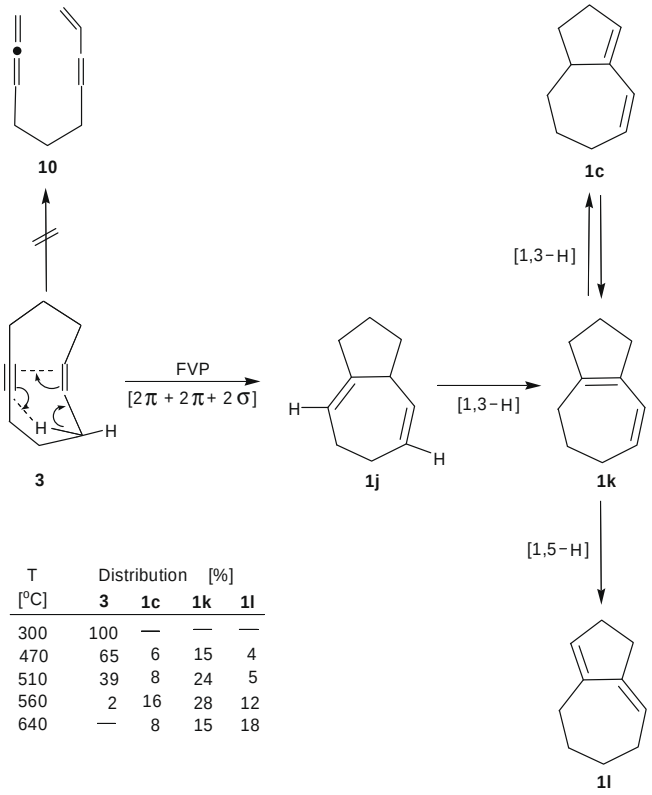


Scheme 3. Thermal isomerization of cyclodecyne (**2**). Related to the consumption of **2**, the open-chain triene **9** is formed in a quantitative process.

(*Z*)-Cyclodec-1-en-6-yne (**3**) behaves different to **2**. It does not form tetraene **10**, its FVP yields hexahydroazulenes with conjugated double bonds. The transannular CC bond formation should first lead to **1j**[31], but **1j** was not present in the product mixture in sufficient quantity to be identified. Fast secondary isomerizations (formal, presumably non-concerted [1,3-*H*] and [1,5-*H*] hydrogen shifts) furnished **1c**, **1k**, and **1ℓ**. The optimum reaction temperature was around 560 °C at 10^{-4} kPa (Scheme 4). At lower temperatures, the conversion is too low, at higher temperatures too much decomposition occurs—solely the absolute yield of **1ℓ** increases (Scheme 4). Figure 1 shows the gas chromatogram of the reaction mixture obtained at 560 °C. The connected ion trap indicated correct *m*/*z* values 134 for all three peaks.



T [°C]	Distribution [%] 3	1c	1k	1l
300	100	—	—	—
470	65	6	15	4
510	39	8	24	5
560	2	16	28	12
640	—	8	15	18

Scheme 4. Thermal isomerization of (*Z*)-cyclodec-1-en-6-yne (**3**) to hexahydroazulenes.

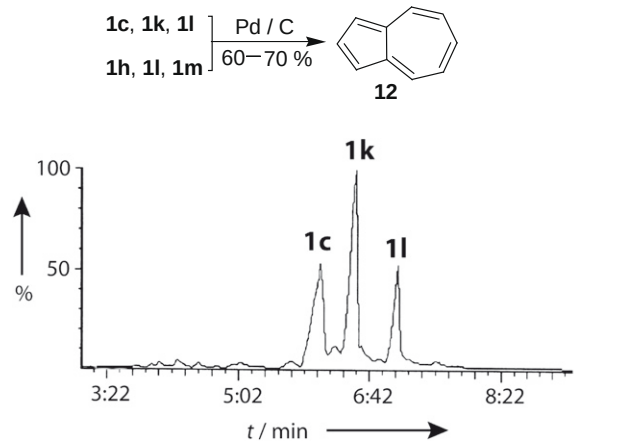
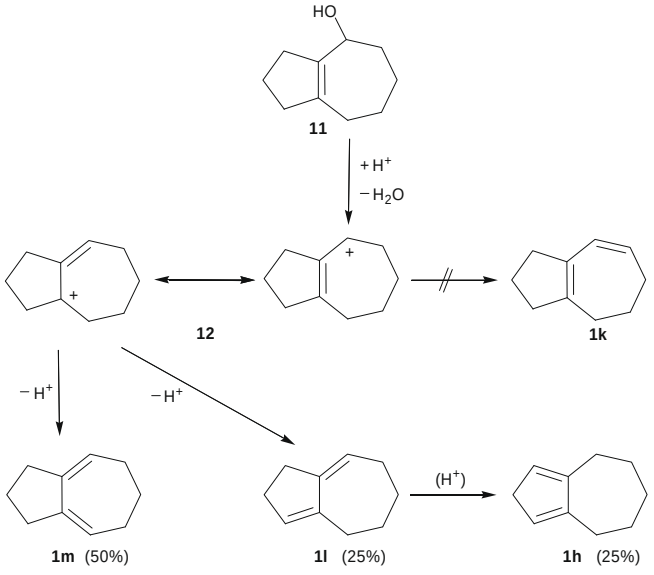


Figure 1. GC of FVP of **3** at 560 °C (Carlo Erba HRGC 5160, column MN 3314-1).

In order to check the structure of the major product **1k**, we repeated an early study of Anderson[32] and dehydrated the bicyclic

Table 1
^{13}C NMR data of hexahydroazulenes in $CDCl_3$

Compound	sp^2–C CH	C_q	sp^3–C CH_2	CH
1c	130.9 129.7 125.9	146.8	34.8, 33.6 31.2, 30.9 27.4	48.6
1h	126.4	149.9	39.1, 32.5 31.1, 25.0	
1k	126.5 122.3	140.4 134.3	33.0, 32.8 31.1, 25.9 23.4, 23.3	
1ℓ	131.1 125.0	141.1 137.8	40.0, 38.7 32.5, 30.7 24.5, 22.3	
1m	124.1	139.7	36.7, 31.4 29.9, 24.6	
1n[31]	133.8 131.3 129.1 126.6		39.1, 30.4 26.8, 22.9	47.8 41.0



Scheme 5. Dehydration of the bicyclic alcohol **11**.

alcohol **11** with *p*-toluenesulfonic acid. It turned out that the reported product **1k** was not formed at all. We got a 2:1:1-mixture of **1m**, **1ℓ**, and **1h** in a quantitative process (Scheme 5).

The ^{13}C NMR data permit the unambiguous differentiation between the obtained hexahydroazulenes by symmetry, multiplicity, and chemical shift criteria (Table 1).

A preparative GC separation of the two mixtures **1c**/**1k**/**1ℓ** and **1h**/**1ℓ**/**1m** seems to be easily feasible (Fig. 1); however, both mixtures can be directly transformed on Pd/charcoal to azulene (**12**).

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20. *Cyclodecane-1,2-dione bishydrazone*: ^{1}H NMR ($CDCl_3$): (*E*,*E*)-isomer (87%) δ 5.30 (br s, 4H, NH_2), 2.53 (m, 4H, α-CH_2), 1.67 (m, 4H, CH_2), 1.32 (m, 4H, CH_2), 1.16 (m, 4H, CH_2); (*E*,*Z*)-isomer (13%) δ 5.55 (br s, 2H, NH_2), 5.30 (br s, 2H, NH_2), 2.67 (m, 4H, α-CH_2), 1.67 (m, 4H, CH_2), 1.32 (m, 4H, CH_2), 1.16 (m, 4H, CH_2); ^{13}C NMR ($CDCl_3$): (*E*,*E*)-isomer δ 152.6 (CN), 25.5, 24.3, 23.5, 20.9; (*E*,*Z*)-isomer δ 164.5, 151.5 (CN), 27.2, 25.8, 25.4, 24.6, 24.2, 23.6, 22.7, 21.1.
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22. The ratio **4**/**4′** amounts to about 50:50 in $CDCl_3$ and to 78: 22 in CD_3OD. Compound **4**: ^{1}H NMR (CD_3OD): δ 4.90 (br s,1H, OH), 3.83 (m, 1H, 6-H), 2.76 (d,d,d, ^2J = 15.7 Hz, ^3J = 9.2 Hz, $^3J'$ = 3.7 Hz, 2H, 2-H, 10-H), 2.40 (d,d,d, ^2J = 15.7 Hz, ^3J = 8.3 Hz, $^3J'$ = 3.9 Hz, 2H, 2-H, 10-H), 2.10–1.45 (m, 12H, 3,4,5,7,8,9-H); ^{13}C NMR (CD_3OD): δ 217.5 (C-1), 69.9 (C-6), 42.8 (C-2, C-10), 34.5, 24.3, 23.9 (C-3,4,5, 7,8,9). Compound **4′**: ^{1}H NMR (CD_3OD): δ 4.90 (br s, 1H, OH), 4.07 (m, 1H, 6-H), 2.10–1.45 (m, 16H, 2,3,4, 5,7,8,9,10-H); ^{13}C NMR (CD_3OD): δ 103.5 (C-1), 76.6 (C-6), 41.7 (C-2, C-10), 34.6, 24.3, 23.9 (C-3,4,5,7,8,9).
23. Compound **5**: Mp 173–174 °C. ^{1}H NMR (CD_3SOCD_3): δ 9.01 (s, 1H, NH), 6.20 (br s, 2H, NH_2), 4.21 (m, 1H, 6-H), 3.61 (br s, 1H, OH), 2.43–2.07 (m, 4H, 2,10-H), 1.84–1.18 (m,12H, 3,4,5,7,8,9-H); ^{13}C NMR (CD_3SOCD_3): δ 157.3 (CO), 151.1 (C-1), 68.5 (C-6), 33.8, 32.2, 31.6, 29.3, 23.6, 22.1, 22.1, 19.8 (C-2,3,4,5,7,8,9,10).
24. Compound **6**: Mp 101–103 °C. ^{1}H NMR ($CDCl_3$): δ 3.91 (m, 1H, 8-H), 3.20 (m, 3H), 3.05 (m, 1H), 1.95 (m, 1H), 1.89 (m, 2H), 1.63 (m, 2H), 1.48 (m, 1H), 1.38 (m, 1H), 1.33 (m, 1H), 1.15 (m, 1H), 1.02 (m, 1H) [CH_2 groups], 1.48 (br s, 1H, OH). Broadening of the signals indicates that the ring dynamics are becoming slow at room temperature in terms of the NMR time scale; ^{13}C NMR ($CDCl_3$): δ 160.1, 159.5 (C-3a, 11a), 69.8 (C-8), 33.7, 28.3, 27.2, 27.0, 26.1, 24.9, 19.5 (C-4,5,6,7,9,10,11).
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26. Compound **7**: Mp 66 °C. ^{1}H NMR ($CDCl_3$): δ 5.40 (m, 2H, 7,8-H), 3.21 (m, 1H), 3.01 (m, 2H), 2.70 (m, 1H), 2.25 (m, 2H), 2.0–1.7 (m, 6H) [CH_2 groups]; ^{13}C NMR ($CDCl_3$): δ 160.7, 159.8 (C-3a,11a), 130.7, 129.0 (C-7,8), 31.3, 26.8, 25.2, 24.7, 23.8, 23.5 (C-4,5,6,9,10,11). ^{77}Se NMR ($CDCl_3$): δ 203.5.
27. See: Dale, J.; Ekeland, D.; Schaug, J. *Chem. Commun.* **1968**, 1477–1479.
28. Compound **3**: Colorless oil, bp_{12} 110 °C; ^{1}H NMR ($CDCl_3$): δ 5.36 (m, 2H, 1,2-H), 2.28 (m, 4H, 3,10-H), 2.19 (m, 4H, 5,8-H), 1.57 (m, 4H, 4,9-H); ^{13}C NMR ($CDCl_3$): δ 130.3 (C-1,2), 82.1 (C-6,7), 25.3, 23.9 (C-3,4,9,10), 18.1 (C-5,8).
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30. Column chromatography (SiO_2, pentane) enables a simple separation of the mixture of **9** (35%, R_f = 0.90) and **2** (65%, R_f = 0.50). **9**: ^{1}H NMR ($CDCl_3$): δ = 5.68 (ddt, $^3J_{trans}$ = 17.0 Hz, $^3J_{cis}$ = 10.3 Hz, $^3J'$ = 6.7 Hz, 1H, 9-H), 4.97 (m, 1H, 3-H), 4.87 (m, 1H, 10-H), 4.81 (m, 1H, 10-H), 4.52 (m, 2H, 1-H), 2.00–1.85 (m, 4H, 4,8-H), 1.37–1.20 (m, 6H, 5,6,7-H). ^{13}C NMR ($CDCl_3$): δ = 208.6 (C-2), 138.9 (C-9), 114.1 (C-10), 89.9 (C-3), 74.4 (C-1), 33.6 (C-8), 28.9, 28.7, 28.5, 28.1 (C-4,5,6,7).
31. See for example: Snider, B. B.; Killinger, T. A. *J. Org. Chem.* **1978**, *43*, 2161–2164.
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