cation produced would have structure **16**, which possesses chemically equivalent, charge-bearing CH_2 and CD_2 groups. Therefore the intermediacy of methallyl cation (either free or in an ion–molecule complex) ought to yield products in which deuterium and fluorine are attached to the same carbon approximately half the time. From ^{19}F NMR studies of authentic samples, we find that methallyl fluoride with a $-CD_2F$ isotopic label is shifted 1 ppm away from a sample with a $-CH_2F$. A shift of similar magnitude is expected for the related label distributions in **14**. Scrutiny of the NMR of the EBFlow reaction product mixture (both undecoupled and with ^2H-noise decoupling) shows that no other label distributions are seen above base line and that they cannot be more than 8% of **13b** or **14b**. We therefore conclude that the EBFlow data provide the first unambiguous demonstration of an intramolecular fluoride shift.

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Precursors to the Cyclo[*n*]carbons: [4*n* + 2]- and [4*n*]Annulenes with Unusual Stabilities

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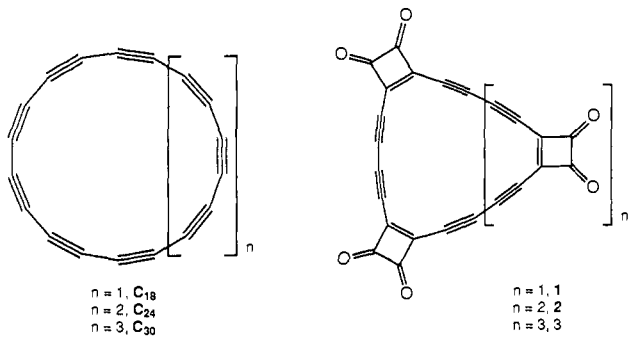
Recently, all-carbon molecules C_n have become the subject of an increasing number of studies.[1] Compounds of sizes ranging from C_2 to C_{200} have been detected in the supersonic beams generated by the laser vaporization of graphite. Theoretical investigations have been useful in assigning structures to these all-carbon molecules.[2] For the unambiguous determination of the structure of a single-sized all-carbon molecule, however, its total chemical synthesis from a well-characterized precursor is required.[3] We describe here the unusual properties of cyclobutenoannulenes, precursors to cyclic C_{18}, C_{24}, and C_{30}. These all-carbon molecules are members of the class of the *cyclo[n]carbons* in which *n* carbon atoms are connected to form monocyclic ring structures. A special relative stability has been predicted for the larger closed-shell cycles ($n \geq 10$) with $4n + 2$ atoms, e.g., cyclo[18]carbon.[4]

Our strategy to the cyclo[*n*]carbons C_{18}, C_{24}, and C_{30} involves the preparation of the dehydro[*n*]annulenes **1–3** fused to 3-cyclobutene-1,2-diones. Starting from **1–3**, the residual acetylenic bonds should be formed by irradiation or flash vacuum pyrolysis under carbon monoxide extrusion.[5,6]

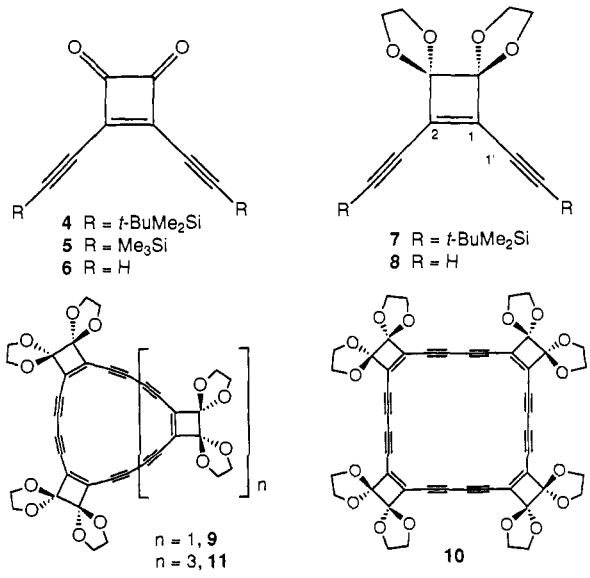
For the synthesis of the 1,2-dione **6**, a direct precursor to **1–3**, the soluble copper(I) acetylide of *tert*-butyldimethylsilylacetylene was reacted with 3,4-dichloro-3-cyclobutene-1,2-dione (THF, 20 °C, 15 min) to afford **4** in 57% yield.[7,8] Similarly, the 1,2-dione **5** was prepared in 27% yield from trimethylsilylacetylene. Unfortunately, all attempts to deprotect **4** or **5** to give **6** led exclusively to polymeric material. Therefore, a route to **1–3** via carbonyl-protected derivatives of **6** was pursued.

For the preparation of bis(ketal) **7**, compound **4** was heated in 1,2-bis(trimethylsilyloxy)ethane in the presence of 1 equiv of trimethylsilyltriflate (80 °C, 6 h, 76%).[9] Deprotection of the acetylenic groups in **7** (catalytic tetrabutylammonium fluoride, THF, H_2O, 20 °C, 30 min, 95%) gave the ene-diyne **8** as a stable solid. While the coupling of **8** under Eglinton–Glaser conditions[10] produced only polymers, Hay coupling[11] (O_2, CuCl·*N*,*N*,*N*′,*N*′-tetramethyl-1,2-ethylenediamine, acetone, 20 °C, [**8**] = 0.01 M) gave three cyclic products, the pale yellow trimer **9** (3.8%), the orange-red tetramer **10** (5.1%), and the bright yellow pentamer **11** (0.8%). While the hexadehydro[18]annulene **12**[12,13] and the

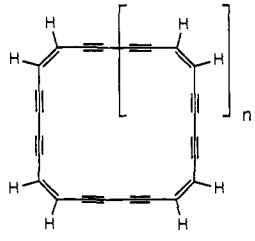
Scheme I



Scheme II



Scheme III



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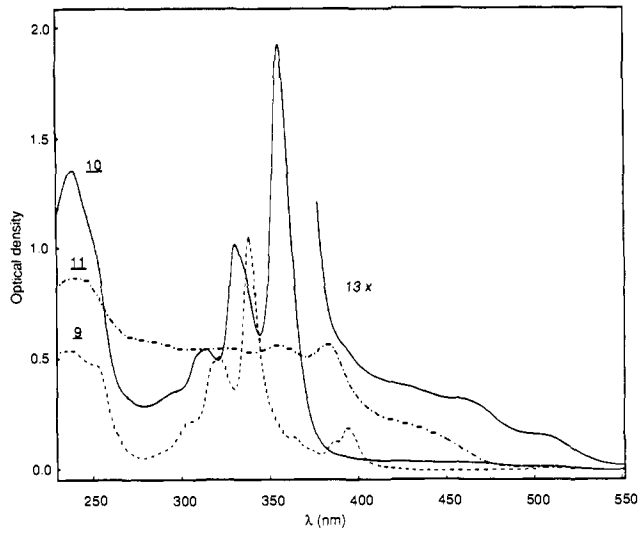

Figure 1. Electronic absorption spectra of **9-11** recorded in CH_2Cl_2, T = 293 K, d = 1 cm; $c = 1.4 \times 10^{-5}$ M for the complete spectra of **9** (– –), **10** (—), and **11** (–·–); $c = 1.7 \times 10^{-4}$ M for the long wavelength absorptions of **10** (—).

octadehydro[24]annulene **13**[14] are very unstable in the solid state, the crystalline compounds **9**, **11**, and, especially, **10** are kinetically quite stable and can be kept for weeks at room temperature and ambient atmosphere without noticeable decomposition.

The electronic absorption spectra of **9-11** (Figure 1) provide valuable information on the geometries of the cyclobutenoannulenes. The spectrum of **9** closely resembles the spectra of **12**[12] and a new hexadehydro[18]annulene for which the planar annulene perimeter was shown by X-ray analysis.[3,15] The strong absorptions at λ_{max}(nm) = 314 (ϵ 41 000), 332 (75 600), 356 (142 200) in the spectrum of **10** show bathochromic shifts as compared to **9**. In addition, weaker absorptions (ϵ between 3500 and 6500) are visible at λ = 400-550 nm which account for the orange-red color of **10**. From the shape similarity of the absorptions of **9** and **10** in the region between λ = 300 and 400 nm, we conclude that **10** also possesses a planar, conformationally rather rigid annulene perimeter.[16] The spectrum of **10** differs strikingly from the one described for **13**.[14] The longest wavelength absorption of **13** is reported at λ_{max} = 352 nm (ϵ = 45 100), and all bands have extinction coefficients below ϵ = 50 000. On the basis of its electronic absorption spectrum and the absence of paratropicity in the ^{1}H NMR spectrum, a nonplanar, cyclooctatetraene-like structure was postulated for **13**. The spectrum of pentamer **11** resembles in its shape the one reported for the tetramer **13**. We take the low extinction coefficients, the considerably reduced vibrational structure, and the lack of long wavelength transitions as strong evidence for a nonplanar, conformationally flexible chromophore in **11**.

Although the ethylene ketal protons in **9-11** are at a remote distance of the π-systems, their ^{1}H NMR resonances provide additional evidence for planar annulene perimeters in **9** and **10**. The comparison of the centers of the AA'BB' multiplets for the ethylene ketal protons in the spectra of **8** (δ 4.04), **9** (δ 4.27), **10** (δ 3.95), and **11** (δ 4.07) indicates that **9** has a diatropic and **10** a paratropic character.

Preliminary computational studies (AM1)[17] show that the peculiar stereochemistry of the 1,2-diethynyl-1-cyclobutene unit defines the unique properties of the cyclobutenoannulenes.[18] The monomer *cis*-3-hexene-1,5-diyne with a C(2)-C(3)-C(4) angle of 125.4° is preferentially incorporated into the planar trimer **12**. The accommodation into a planar tetramer **13** generates angle strain, and a cyclooctatetraene-like conformation is preferred. At 136.3°, the C(1')-C(1)-C(2) angle in **8** is considerably larger. The incorporation of **8** into the planar trimer **9** generates angle strain. On the other hand, **8** can be accommodated in a nearly strain-free way into the planar tetramer **10**, which is of lower energy than a nonplanar, cyclooctatetraene-like conformer.

The use of the cyclobutenoannulenes **9-11** for the generation of ketones **1-3** and the corresponding cyclo[*n*]carbons is now under way.

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Conformational Changes in the Inactivation of β-Lactamase by Penicillin Sulfones

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Mechanism-based inhibitors of enzyme are a source of potential new drugs. We wish to point out that even though there may be a good *chemical* rationale for inhibition in such cases, physical (conformational) processes may play a critical role, especially if the inhibitor or enzyme are conformationally mobile. For example, the inactivation of β-lactamase by penicillin sulfones with large hydrophobic side chains (Type A substrates[1]) is accompanied by significant change in the protein conformation, as determined by circular dichroism (CD), whereas no such change is observed with penicillanic acid sulfone, which lacks the C6 side chain. We believe it is the conformational change which is responsible for the observed irreversible inhibition at high pH.

The sulfones of several penicillins have been shown to be inhibitors[3-12] of β-lactamases; the inhibition appears to be a form of suicide inactivation in which the lability of the C-S bond results in the formation of a transient imine acyl-enzyme intermediate (**1a**) which tautomerizes to the more stable enamine form (**1b**),[8] a β-aminoacrylate of reduced hydrolytic sensitivity. The inhibitory reaction has been studied in the most detail with penicillanic acid sulfone (**2**), especially by Knowles and co-workers[5-8] using the TEM β-lactamase. They conclude that the acyl-enzyme can undergo three fates: hydrolysis leading to turnover, conversion to the enamine leading to transient inhibition, and transimination by a suitably positioned lysine residue in the active site leading

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