or that the elimination is followed by inactivation in the first few turnovers. The concentration of enzyme was not great enough to allow an initial burst to be seen.

Compound **2** behaves as though it were an irreversible inhibitor since it shows time-dependent inactivation[14] with a rate constant of 7.6×10^2 M^{-1} s^{-1}, as shown in Figure 2. The percent inhibition of aldolase reactivity, measured by standard assay techniques,[15] depends on both the concentration of **2** and the length of time with which it is incubated with enzyme. The reaction may in fact be reversible under appropriate experimental conditions even though the equilibrium constant for formation of inhibited enzyme is quite large.[14] As is also shown in Figure 2, the enzyme is protected from inhibition by the natural substrate, dihydroxyacetone phosphate, DHAP. The K_m for DHAP computed from these data, 1.5×10^{-6} M, is smaller than the K_m measured by fluorescence,[16] 4.5×10^{-6} M. Since the literature value was determined in the presence of Cl^-, a known reversible inhibitor of aldolase, these values are not inconsistent. The disappearance of inhibitory ability in solutions of **2** kept at 25 °C and pH 7.0 parallels the slow conversion of **2** to **4b** as followed spectrophotometrically. In contrast to **2**, methyl vinyl ketone exhibits a much slower inactivation of aldolase and that inactivation is not completely prevented by high concentrations of DHAP. A possible mechanism for the inactivation of aldolase by **2** is that shown in Scheme I.

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(4) To a solution of 5.2 g (2.46×10^{-2} mol) 3a in 300 mL of benzene at 60 °C was added 4.2 mL of oxalyl chloride (4.92×10^{-2} mol) and the mixture was refluxed for 90 min to yield a solution of **3b**: ^{1}H NMR (CDCl$_3$) δ 3.40 (t, 2 H), 4.33 (t, 2 H), 6.88 (d, 2 H), 8.05 (d, 2 H).
(5) The overall yield from **3a** to **3c** is 75%. Compound **3c**: mp 94–95 °C; ^{1}H NMR (CDCl$_3$) δ 2.83 (t, 2 H), 4.40 (t, 2 H), 5.40 (s, 1 H), 6.95 (d, 2 H), 7.84 (d, 2 H); IR 1740, 2130 cm^{-1}; analysis satisfactory.
(6) Compound **1**: mp 84–86 °C; ^{1}H NMR (D$_2$O, pD 1.6) δ 3.11 (t, 2 H), 4.44 (t, 2 H), 4.65 (d, J = 7.93 Hz, 2 H, CH$_2$OP), 7.09 (d, 2 H), 8.23 (d, 2 H); IR (KBr) 1730 cm^{-1}.
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(9) Compound **2**: ^{1}H NMR (D$_2$O, pD 7.1) δ 4.49 (d, 2 H, J = 6.35 Hz, CH$_2$OP), 5.94–6.68 (m, 3 H).
(10) Compound **4a**: ^{1}H NMR (D$_2$O, pD 7.1) δ 3.86 (s, 2 H, CH$_2$OD), 4.49 (d, 2 H, J = 6.35 Hz, CH$_2$OP).
(11) Compound **4b**: ^{1}H NMR (D$_2$O, pD 7) δ 2.78 (t, 2 H), 3.85 (t, 2 H), 4.48 (d, 2 H, J = 6.25 Hz, CH$_2$OP).
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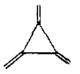
Hexaradialene

Sir:

Of the parent radialenes[1] only [3]-[2] and [4]radialene[3] (**1** and **2**) have been isolated as air-sensitive, reactive hydrocarbons. Several stable, substituted radialenes are known[4] including hexaalkylated hexaradialenes.[1,5] The latter appear to minimize nonbonded interactions by adopting a nonplanar cyclohexane chair-type conformation[6] devoid of 6π-electronic delocalization. The parent hexaradialene (hexamethylenecyclohexane) (**3**) is of considerable theoretical[7] and synthetic interest because of its potentially stabilizing benzenoid topology, its potential as a synthon for the construction of polycyclic nuclei, and as a possible precursor to the strained tricyclobutabenzene **4**[8] and the elusive cyclophane **5**, respectively.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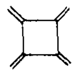
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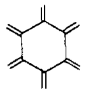
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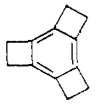
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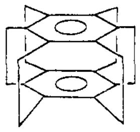
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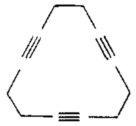

6

Recently we reported that 1,5,9-cyclododecatriyne (**6**)[9] reacted with dimethyl maleate at 230 °C to give a triadduct formally derived from **4** via sequential four-ring opening or, alternatively, from **3** via threefold cycloaddition.[10] Since in the absence of trapping agent extensive polymerization occurred we decided to investigate the gas phase thermochemistry of **6**.

Sublimation of **6** through a hot quartz tube (650 °C (10^{-3} Torr)) and collection of the pyrolysate at −196 °C gave a colorless brittle solid which turned dark on warming. Vacuum transfer of solvent (toluene-d_8) onto the pyrolysis product or, alternatively, collection of the pyrolysate on a frozen solvent covered glass surface allowed on warming the rapid extraction of nonpolymerized materials and transfer into an NMR tube which was vacuum sealed. In addition to starting material (τ 7.62, toluene-d_8) a new sharp singlet was observed in the *olefinic* region (τ 4.69). This signal disappeared after several hours at room temperature or instantly on exposure of the sample to air with concomitant deposition of a brown flocculent precipitate. No new absorptions appeared in the NMR spectrum. Gas phase pyrolysis of **6** at 850 °C led to complete disappearance of starting material (NMR). A mass spectrum of this product gave a parent ion at *m/e* 156.

Hydrogenation of the pyrolysate prepared at 650 °C (Pd/C, ether, −65 °C to room temperature) gave[11] nearly equal amounts of naphthalene,[12] hexamethylbenzene,[12] and cyclododecane,[12] in addition to several unidentified products. Analysis[11] of the air-oxidized crude pyrolysate of **6** (generated at 650 °C) indicated a multitude of products including starting material and naphthalene, but no hexamethylbenzene. Deuteration of the pyrolysis product gave hexakis(deuteriomethyl)benzene.[11]

Gas phase pyrolysis of **6** at temperatures above 850 °C gave rise to increasing amounts of volatile but stable butatriene, identified by its singlet NMR singlet at τ 4.65 and by comparison with authentic material.[13,14] Pyrolysis of butatriene[3] under the above conditions gave recovered starting material.

The observed experimental data are most easily accommodated by the assumption that cyclododecatriyne **6** undergoes pyrolytic conversion to hexaradialene (**3**), a highly reactive compound seemingly devoid of any stabilizing "aromatic" features and comparable in its properties with the other known radialenes **1** and **2**.[15] If one invokes **4** as a likely intermediate in this transformation, then the reported data lead to the somewhat surprising conclusion that radialene **3** enjoys higher thermal stability than benzene **4**. Thermochemical calculations[16,17] (Figure 1) seem to support this view. Thus, even a hypothetical, fully "aromatic" **4** ($\Delta H_f° = 93$ kcal/mol) is estimated to be at least 11 kcal/mol higher in energy than (nonplanar) **3**.[18]

An alternative approach to rationalize the observed data

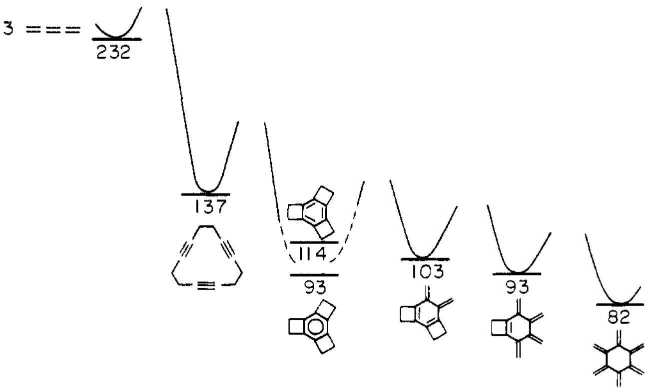
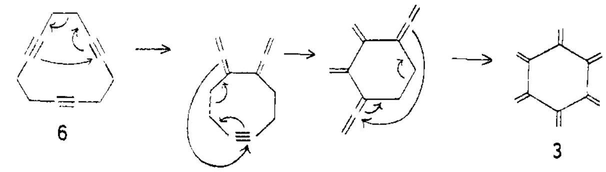


Figure 1. Calculated heats of formation (kilocalories/mole) of $C_{12}H_{12}$ isomers and butatriene using group equivalent techniques. Estimates for the xylylenes and hexaradialene do not include cis-butadienoid H-H repulsions and residual aromaticity.

Scheme I



invokes a direct pathway from **6** to **3** and cannot be ruled out. Thus, a series of sequential Cope rearrangements or their equivalent as depicted in Scheme I could provide the mechanistic connection between **6** and **3**.

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(18) If one views the **4** → **3** interconversion as essentially a threefold 1,2-dimethylcyclobutene → 2,3-dimethylbutadiene process ($\Delta H° = 3 \times -8.8 = -26.4$ kcal/mol),[19] then the maximum "aromaticity" of 4 would be expected to amount to ~23 kcal/mol.

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β Helices Formed in Cyclohexane Solution by Oligomeric Chains of Alternating D- and L-Valine Residues. Relationship between Sequence and Prevailing Helical Sense

Sir:

Some Boc- and MeO-protected, DL-alternating oligopeptides derived from L-isoleucine and D-alloisoleucine, and having D-aIle as the C-terminal residue, have been reported[1,2] to favor in solution, independently of chain length, β-helical conformations[3] with the same prevailing sense of twist. In principle, this conformational preference might be determined by the chiral side chains of identical configuration (*S*) which characterize these oligopeptides, or by the sequence pattern. In this communication we present experimental evidence from the study of similarly protected DL-alternating oligopeptides derived from valine that demonstrates that the sequence of residues in these oligomers per se can preferentially stabilize one sense of twist over the other. In addition, a correlation between the sequence pattern and the preferred handedness of the β-helical conformation is proposed.

Boc-D-Val-(L-Val-D-Val)$_3$-OMe (I) and Boc-(L-Val-D-Val)$_4$-OMe (II) were prepared using racemization-free synthetic procedures. In cyclohexane solution (25 °C) these two oligopeptides exhibit IR, NMR,[4] and CD (Figure 1) properties similar to those observed[1] for Boc-D-aIle-(L-Ile-D-aIle)$_3$-OMe (III) and Boc-(L-Ile-D-aIle)$_4$-OMe (IV) under the same conditions indicating that the conformational equilibria of these four oligomers in cyclohexane are analogous. In particular, since the signs of the dichroic bands (Figure 1) are identical, the handedness of the predominant β-helical conformations must be the same for all four oligopeptides. There is[2] some indication that the β helices formed by III and IV have ~4.4 residues per turn. If this, as expected, is the case also for the β helices formed by the valine oligomers, then the general arrangement of the interturn hydrogen bonds in the oligopeptides can be depicted as in Scheme I. As indicated, if the sense of twist is left-handed, the urethane NH of the octapeptides contributes to an interturn hydrogen bond, whereas that of the heptapeptides does not. The reverse is true, if the sense of twist is right-handed. The NMR spectra (360 MHz) of cyclohexane solutions of II and IV[1] show no apparent NH resonance below 6.5 ppm, while that of III[4] shows one of the NH doublets at a substantially higher field (5.3 ppm), hinting[5]