kcal·mol^{-1})[16] is slightly less stable than **3** (ΔH_f° = 74.6 kcal·mol^{-1})[16] but certainly much more stable than **4** (ΔH_f° = 102.7 kcal·mol^{-1}). We consider it likely that **1c** is indeed formed on irradiation of **3** but that the photostationary state is even more unfavorable than in the case of **2b** where 6–7% of **2b** are in photoequilibrium with its Dewar isomer.[5]

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Tricyclo[5.3.0.0^{2,8}]deca-3,5,9-triene

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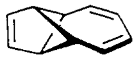
The inherent capability of cyclobutane σ bonds to interact electronically with neighboring π systems was first demonstrated by us in the case of bicyclo[4.1.1]octa-2,4-diene (β = 1.9 eV).[2] This observation led to a theoretical analysis of the extent to which two mutually perpendicular π systems might effectively interact through the Walsh "relay" orbitals of a four-membered ring.[3] Particular attention was given to the three closed-shell polyolefins **1–3**. Whereas the basis orbital energies calculated for **1** and **3** predict that destabilization would be manifested, those present in **2** were deemed to be marginally stabilizing. Tricyclo[3.3.0.0^{2,6}]cota-3,7-diene (**1**) had been earlier synthesized and shown to rearrange rapidly to semibullvalene at 20 °C.[4] More recently, access has been gained to **3**.[5] At 80 °C, this tetraene undergoes formal [1,3]-sigmatropic rearrangement with a half-life of 7 h.


1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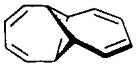
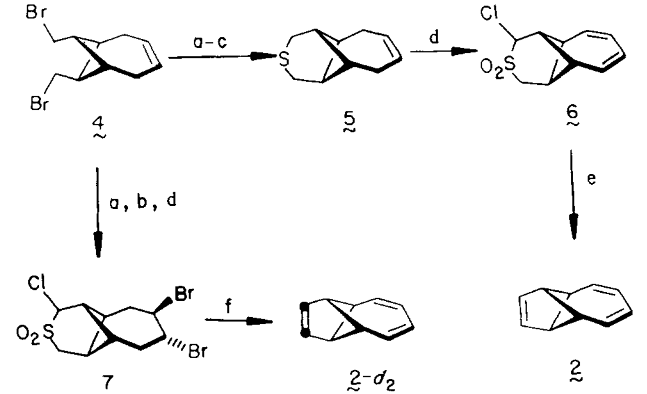

3

To the extent that through-bond interaction governs the reactivity of these systems, the title compound (**2**) should, on the basis of Gleiter's prediction,[3] prove still more stable than **3**. On the other hand, its strain energy lies intermediate between that of **1** and **3** and the relative importance of this property requires clarification. We report here a synthesis of this (CH)$_{10}$ hydrocarbon and demonstrate its particular sensitivity to structural isomerization by a process very probably involving *biradicaloid* intermediates. This behavior contrasts markedly with the formally *concerted* rearrangement pathway followed by **3**.

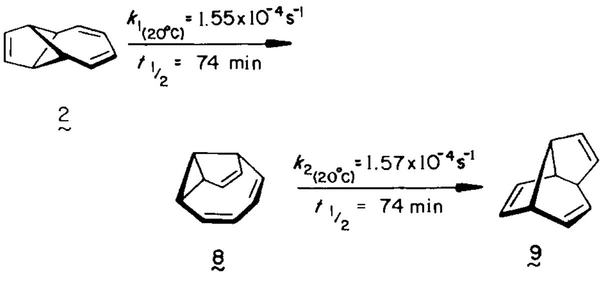
The known dibromide **4**[5] appeared to be an ideal advanced intermediate for the elaboration of **2**. We envisioned that Ramberg–Bäcklund rearrangement of a derived α-chloro sulfone might be performed under conditions sufficiently mild[6] to preserve the structural integrity of the product. The preliminary three-step conversion to **5** proceeded smoothly (84% overall, Scheme I). Due to competing epoxidation, this sulfide was transformed less efficiently (45%) into **6**. When **6** was treated with excess KO-*t*-Bu in THF at 0 °C,[7] desulfonylative ring contraction was seen to be complete within 1 h to give pure **2**, the spectral properties of which[8] are in complete agreement with the structural assignment.

Scheme I

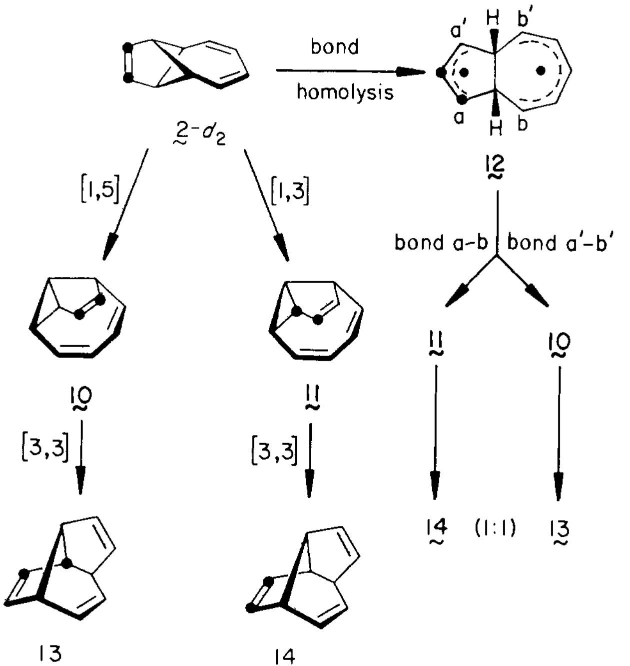


^{a}(a) Na$_2$S, HMPA, 110 °C, 2.75 h; (b) PyH$^+$Br$_3^-$, CCl$_4$–HOAc (1:1), room temperature; (c) KO-*t*-Bu, THF, room temperature; (d) NCS, CCl$_4$, 90 °C, MCPBA; (e) KO-*t*-Bu, THF, 0 °C, 1 h; (f) KO-*t*-Bu (24 equiv), D$_2$O (12 equiv), THF, –70 to 0 °C during 1 h, 0 °C for 1 h.

Scheme II



Scheme III



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(8) ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.28 (t, J = 2.3 Hz, 2 H), 6.34–6.24 (m, 2 H), 6.24–6.15 (m, 2 H), 3.56–3.49 (m, 2 H), 1.17 (t, J = 2.3 Hz, 2 H); ^{13}C NMR (75 MHz, CDCl$_3$) 149.36, 136.26, 126.69, 78.37, 29.61 ppm.

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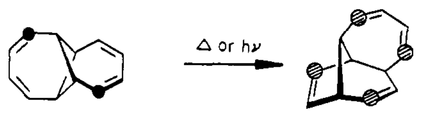
In order to assess the reactivity of **2**, solutions were prepared in $CDCl_3$ and monitored at frequent time intervals by 300-MHz ^1H NMR spectroscopy at 20 °C. Isomerization occurred quickly to give isobullvalene (**8**) and somewhat more slowly to give lumibullvalene (**9**, Scheme II).[9,10] Thus, **2** is a relatively frangible molecule.[11]

Three mechanistic options have been considered for this isomerization (Scheme III): (1) a concerted, thermally allowed [1,5]-carbon shift across the diene bridge (**2** → **10**); (2) a concerted, thermally forbidden [1,3]-carbon shift across the ethylene bridge (**2** → **11**);[12] (3) a stepwise diradical process involving homolysis of any of the four symmetry-equivalent cyclobutane σ bonds (**2** → **12**).[13] Since the pure [3,3] sigmatropy associated with the **8** → **9** process[9b] permits reliable accounting of the fate of the individual carbon atoms at this stage (e.g., **10** → **13** and **11** → **14**), suitable isotopic labeling of tricyclo[5.3.0.0^{2,8}]deca-3,5,9-triene can in principle distinguish between the three hypothetical pathways.

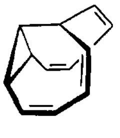
By exposure of **7** to an excess of KO-*t*-Bu in cold (−70 °C) THF containing D_2O and gradual warming of this mixture to 0 °C, it proved possible to deuteriate **2** exclusively on the olefinic bridge (0.46 D incorporation). Although the triene was likely not equivalently deuteriated at both sites, this issue is unimportant since the C_{2v} symmetry of **2** does not allow independent distinction of these positions. The species is therefore assigned as **2**-d_2 for simplicity. The smooth rearrangement to lumibullvalene-d_2 at 20 °C was monitored by ^2H NMR spectroscopy (CCl_4, 77 MHz). By means of this technique, three different types of deuterium were seen to appear (δ 6.63, 5.58, and 3.18) and in a ratio of 1:2:1.[14]

It is improbable that the 1:1 distribution of **13** and **14** arises because of entirely similar rates of [1,5] and [1,3] sigmatropy in **2**. On the other hand, formation of diradical **12** is fully compatible with our observations. Since this intermediate possesses a mirror plane, identical (save for the isotope effects) ring closure rate constants (k_{ab} and $k_{a'b'}$) explain the equal proportion of **13** and **14**. Importantly, the a priori possibility that symmetrization might originate by interconversion of **10** and **11** via a forbidden [3,5] sigmatropic rearrangement has previously been ruled out by Katz in a monodeuteriated derivative.[9b]

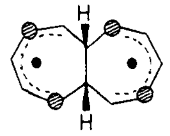
Force-field calculations (MMP2) give heats of formation for **2** (95.44 kcal mol^{-1}), **8** (83.70 kcal mol^{-1}), and **9** (73.63 kcal mol^{-1}) that are in good agreement with the experimental observations. In the $(CH)_{12}$ valence isomer series to which **3** ($\Delta H_f^\circ = 90.50$ kcal mol^{-1}) belongs, however, the semibullvalene-like structure **15** is of ***higher*** energy (102.35 kcal mol^{-1}) and therefore not attainable from **3** by thermal activation. The energetically feasible conversion to **16** (79.63 kcal mol^{-1}) has previously been shown to occur.[5] Following more recent preparation of the d_2 derivative,[15] the labeled tetraene has now been separately heated to 110–115 °C in CCl_4 (sealed tube) and irradiated at 366 nm in CH_2Cl_2 solution. Under both sets of circumstances, only four of the 12 possible positions in **16** showed deuterium incorporation, all with the same intensity (^2H NMR). Full symmetrization via **17**-d_2, which would have distributed the isotopic label over eight sites, clearly does not obtain. Thus, the ground- and excited-state reactivity of **3** appears limited to a formally concerted [1,3]-C migration.[12]



3-d_2 **16**-d_2



15



17-d_2

Finally, photoelectron spectroscopic measurements to be made on **2** are expected to reflect a very different electronic situation than that present in **3**. The possible relationship of through-bond interaction or the lack of it to the widely variant half-lives of **2** and **3** and their adoption of different mechanistic channels for rearrangement is the subject of continued study.[16]

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(16) The authors acknowledge with thanks the financial support of the National Science Foundation (Grant CHE-8317954) that made this research possible.

δ-(L-α-Aminoadipyl)-L-cysteinyl-D-valine Synthetase (ACV Synthetase): A Multifunctional Enzyme with Broad Substrate Specificity for the Synthesis of Penicillin and Cephalosporin Precursors

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The biosynthesis of penicillins and cephalosporins is a linear process in both eukaryotic and prokaryotic organisms.[1,2] The process begins, at the amino acid oxidation level, with the coupling of L-α-aminoadipic acid, L-cysteine, and L-valine to form the tripeptide δ-(L-α-aminoadipyl)-L-cysteinyl-D-valine (LLD-ACV, **1**).[3] This peptide is then converted sequentially into isopenicillin N (**2**),[4] penicillin N (**3**),[5] desacetoxycephalosporin C (**4**),[6] desacetylcephalosporin C (**5**),[7] and cephalosporin C (**6**)[8] or carba-

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