parison with suitable derivatives in which carboxyl group participation is not possible. Bifunctional catalysis by two suitably placed carboxyl groups has not been observed, even though in the case of methoxymethoxyisophthalic acid[46] and the disalicyl acetals **18** and **19** the conditions for demonstration of electrostatic stabilization of a developing carbonium ion appear to be optimal.

Lysozyme. The foregoing information on the chemical hydrolysis of simple acetals can be applied to the mechanism of action of glycosidic enzymes and, in particular, lysozyme. If it is assumed that glutamic acid-35 is involved in the catalytic action of lysozyme and that the enzyme acts in accord with the principles established in the chemical model studies, then two points are clear.

(1) The key problem of general acid catalysis in the enzymatic reaction is explainable if the substrate is distorted during the binding process and if the resulting strain is relieved during the hydrolytic reaction, thereby making C–O bond breaking more facile, in analogy to hydrolysis of the benzaldehyde di-*tert*-butyl acetals. Since with natural substrates for lysozyme the leaving group is poor and the intermediate carbonium ion is relatively unstable, the bond-breaking process *must* be sufficiently enhanced for general acid catalysis to take place. As noted previously, relief of ground-state strain produced by distortion of the substrate has been an integral feature of postulated mechanisms for lysozyme,[7–9] although there is no conclusive evidence that it occurs.

(2) From the lack of bifunctional catalysis in the hydrolysis of dicarboxyl-substituted acetals, regardless of the stability of the intermediate carbonium ion, it is possible that aspartic acid-52 may not be directly involved in the catalytic process in the lysozyme reaction. The bell-shaped pH–rate profile for lysozyme[50] most likely indicates that ionization of two groups is important, but this does not necessarily imply direct involvement of aspartic acid-52 in the reaction. A possibility is that this group is important in stabilizing a particular conformation of the enzyme. A bell-shaped pH–rate constant profile is also obtained with disalicyl acetals such as **19** where participation by one carboxyl group causes most of the observed rate enhancement which is of the magnitude observed in enzyme-catalyzed reactions. Consequently it is not necessary to involve bifunctional catalysis to explain the kinetic behavior of lysozyme. The chemical studies on acetal hydrolysis have therefore set forth the possibilities by which lysozyme exerts its catalytic effect and have led to explanations of the problem of general acid catalysis.

It is hoped that the continuation of such physical-organic work in conjunction with studies of the enzyme itself will finally give a clear picture of how lysozyme is exerting its catalytic effect.

I wish to thank all my coworkers for their contributions to this work. I am particularly grateful to Dr. Edwin Anderson for many stimulating discussions. This work was supported by research grants from the National Institutes of Health and the National Science Foundation.

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(50) J. A. Rupley, *Proc. Roy. Soc., Ser. B*, **167**, 416 (1967); J. A. Rupley and V. Gates, *Proc. Nat. Acad. Sci. U. S.*, **57**, 496 (1967); T. Osawa and Y. Nakasawa, *Biochim. Biophys. Acta*, **130**, 56 (1966).

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[10]Annulenes and Other $(CH)_{10}$ Hydrocarbons

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A limited number of organic compounds expressable in terms of simple molecular formulas have attracted the interest of organic chemists almost since the inception of this science. The annulene series could probably be described in this way. These are fully conjugated, monocyclic polyenes; the number of CH moieties in the ring is indicated by an arabic numeral in brackets.

Aromatic chemistry, guided by the simple "$(4n + 2)$ rule" of Hückel,[2] developed along an interesting course;[3] [6]annulene (benzene) was well known, and [8]annulene (cyclooctatetraene) yielded to synthesis in 1911.[4] However, the next major breakthrough in annulene chemistry was not the isolation of the next higher homolog, [10]annulene, but rather the synthesis of [18]annulene, by Sondheimer in 1959.[5] This was largely due to the discovery that macrocyclic polyacetylenes

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Nicholas Darby is a doctoral candidate working with Professor Masamune on planar ten-π-electron systems.

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(1) F. Sondheimer and R. Wolovsky, *J. Amer. Chem. Soc.*, **84**, 260 (1962).

(2) E. Hückel, *Z. Phys.*, **70**, 204 (1931).

(3) Omitted from this Account are charged species [*e.g.*, cyclopropenyl cation: (a) R. Breslow, J. T. Groves and G. Ryan, *J. Amer. Chem. Soc.*, **89**, 5048 (1967); (b) D. G. Farnum, G. Mehta, and R. G. Silberman, *ibid.*, **89**, 5048 (1967); cyclononatetraenide: (c) T. J. Katz and P. J. Garratt, *ibid.*, **86**, 5194 (1964); (d) E. A. LaLancette and R. E. Benson, *ibid.*, **87**, 1941 (1965)], bridged annulenes [*e.g.*, (e) E. Vogel, *Proc. Robert A. Welch Found. Conf. Chem. Res.*, **12**, 215 (1968)], and derivatives of annulenes.

(4) R. Willstätter and E. Wase, *Ber.*, **44**, 3423 (1911).

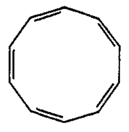
are formed in the oxidative coupling of linear α,ω-diacetylenes. [12]-, [14]-, [16]-, [20]-, [22]-, and [24]-annulenes rapidly followed,[6] so that until recently, despite numerous synthetic attempts in the past, only two members of this series remained unknown: [4]-annulene[7] (cyclobutadiene) and [10]annulene (cyclodecapentaene).

In 1965, Pettit prepared the iron tricarbonyl-[4]-annulene complex and reported the generation of the free hydrocarbon species.[8] The half-life of [4]annulene at ambient temperatures is only a few milliseconds;[9] several derivatives of this compound have been isolated in the lattice at liquid nitrogen temperatures.[10]

The history of the [10]annulenes is long and rich. Although these compounds were postulated as intermediates in several reactions[11] and their trapping in a reaction mixture was reported,[12] only recently, in our laboratories, were these compounds prepared in *crystalline* form and their products of reaction *via* ground and excited states determined.[13] This Account summarizes our work on the chemistry of the intriguing [10]annulenes.[14]

Analysis of the Problem

From early attempts to synthesize [10]annulenes,[11] it was obvious that these compounds are very reactive, whichever of the geometrical isomers (**1**, **2**, or **3**)[15] were purportedly involved in the syntheses or reactions. This seems somewhat surprising in view of Hückel's[2,16] prediction of aromaticity for the planar (cis)[5] isomer **1**, and also in consideration of the stability exhibited by the cyclononatetraenide anion.[3c,d] However, departure from coplanarity in **1** relieves the strain associated with a (hypothetical) planar structure, and thus the energy barrier for thermally allowed transannular reactions leading to bicyclic systems would be very low, even if the molecule gains some stability from the cyclic ten-π-electron system. In the case of the cyclononatetraenide anion, however, deviation from planarity implies a localization of the charge and subsequent destabilization of the species, which lowers the tendency toward transannular reactions.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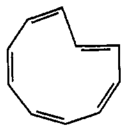
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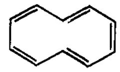
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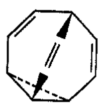
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It is apparent, then, that the final synthetic step to [10]annulenes, including work-up, must be carried out under extremely mild conditions. In 1964 our work directed at the nitrogen-containing ten-π-electron system[17] convinced us of the need to develop low-temperature techniques for separation and purification. We were also aware that such techniques would prove useful in the elucidation of certain reaction mechanisms, such as photochemical reactions involving thermally labile products. We have now developed practical and workable techniques that enable compounds to be handled comfortably below −50° throughout entire reaction processes. It is thus possible to isolate compounds if they are surrounded by a minimum energy barrier of approximately 15 kcal. Some of these low-temperature techniques have been reported;[18] full details will be published elsewhere.

There are two important aspects of [10]annulene chemistry that were vaguely realized by us and later fully documented by others. First, the recognition that [10]annulenes are members of the $(CH)_{10}$ class of compounds became increasingly significant. Second, this relationship was clarified by the concept of the conservation of orbital symmetry as outlined by Woodward and Hoffmann.[19] Balaban's tabulation on the basis of graph theory of all possible $(CH)_{10}$ isomers (and his demonstration of relationships between them),[20] coupled with the orbital symmetry selection rules, aided enormously in the design of a synthetic scheme for [10]annulenes based on sound theoretical principles, rather than on naive or intuitive reasoning.

Several interesting compounds stand out in Balaban's table. One is bullvalene (**4**), the intriguing properties of which were predicted by Doering[21] and subsequently confirmed by the syntheses of Schröder[22] and of Doering

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(5) F. Sondheimer and R. Wolovsky, *Tetrahedron Lett.*, **No. 3**, 3 (1959); F. Sondheimer, R. Wolovsky, and Y. Amiel, *J. Amer. Chem. Soc.*, **84**, 274 (1962).

(6) The chemistry, up to 1966, of these larger annulenes has been summarized by F. Sondheimer, I. C. Calder, J. A. Elix, U. Gaoni, P. J. Garrett, K. Grohmann, G. diMaio, J. Mayer, M. V. Sargent, and R. Wolovsky, *Chem. Soc., Spec. Publ.*, **No. 21**, 75 (1967); for further developments see F. Sondheimer, *Proc. Robert A. Welch Found. Conf. Chem. Res.*, **12**, 125 (1968), and a plenary lecture delivered by F. Sondheimer before the IUPAC (nonbenzenoid aromatics) in Aug 1970, to be printed soon.

(7) M. P. Cava and M. J. Mitchell "Cyclobutadiene and Related Compounds," Academic Press, New York, N. Y., 1967.

(8) L. Watts, J. D. Fitzpatrick, and R. Pettit, *J. Amer. Chem. Soc.*, **87**, 3253 (1965).

(9) W. J. R. Tyerman, M. Kato, P. Kebarle, S. Masamune, O. P. Strausz, and H. E. Gunning, *Chem. Commun.*, 497 (1967); E. Hedeya, R. D. Miller, D. W. McNeil, P. F. D'Angelo, and P. Schissel, *J. Amer. Chem. Soc.*, **91**, 1875 (1969).

(10) M. G. Maier, U. Mende, and G. Fritschi, *Angew. Chem., Int. Ed. Engl.*, **8**, 912 (1969).

(11) A history up to 1968 is summarized by T. L. Burkoth and E. E. van Tamelen in "Nonbenzenoid Aromatics," J. P. Snyder, Ed., Academic Press, New York, N. Y., 1969, Chapter 3, and its duplication is minimized in this Account.

(12) E. E. van Tamelen and T. L. Burkoth, *J. Amer. Chem. Soc.*, **89**, 151 (1967).

(13) S. Masamune, K. Hojo, K. Hojo, G. Bigam, and D. L. Rabenstein, *ibid.*, **93**, 4966 (1971). See also S. Masamune and R. T. Seidner, *Chem. Commun.*, 542 (1969).

(14) For the chemistry of planar dehydro[10]annulenes, see N. Darby, C. U. Kim, J. A. Salaün, K. W. Shelton, S. Takada, and S. Masamune, *ibid.*, 1516 (1971).

(15) Of eight possible geometrical arrangements of the cis and trans double bonds, only **1**, **2** and **3** are structurally possible for [10]annulenes.

(16) For recent calculations, see M. J. S. Dewar and G. J. Gleicher, *J. Amer. Chem. Soc.*, **87**, 685 (1965).

(17) S. Masamune and N. T. Castellucci, *Angew. Chem., Int. Ed. Engl.*, **3**, 582 (1964).

(18) K. Hojo, R. T. Seidner, and S. Masamune, *J. Amer. Chem. Soc.*, **92**, 6641 (1970).

(19) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Verlag Chemie, Weinheim/Bergstr., Germany, and Academic Press, New York, N. Y., 1970.

(20) A. T. Balaban, *Rev. Rom. Chim.*, **11**, 1097 (1966). We had access to a table developed by Professor J. Lederberg, which was equivalent to that of Balaban, through the courtesy of Professor Hoffmann.

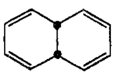
(21) W. von E. Doering, *Zh. Vses Khim. Obshchest.*, **7**, 308 (1962); W. von E. Doering and W. R. Roth, *Angew. Chem., Int. Ed. Engl.*, **2**, 115 (1963).

and his coworkers.[23] The efforts directed toward the syntheses of bullvalene (**4**) and the [10]annulenes formed the core for the development of $(CH)_{10}$ hydrocarbon chemistry. It is now known that these two theoretically important compounds are connected on an energy surface with other $(CH)_{10}$ isomers. Indeed, the two compounds themselves are interrelated.

Synthetic Approach

Valence bond isomerizations among several $(CH)_{10}$ isomers were evident at an early date.[24] Considering this (and the apparent thermal instability of [10]annulenes), *cis*-9,10-dihydronaphthalene (**5**), *trans*-9,10-dihydronaphthalene (**6**), and bicyclo[6.2.0]deca-2,4,6,9-tetraene (**7**) were attractive candidates as immediate precursors in a synthetic sequence leading to the annulenes. Compound **5** was already known at the start of our work[25] but its reported synthesis involved many steps and appeared to afford a meager overall yield of final product. We then turned our attention to compounds **6** and **7**, of which the latter was particularly attractive for two reasons: (i) the strain inherent in the fused cyclobutene ring was expected to be a favorable factor for the desired isomerization and (ii) it was possible to envisage thermal and photochemical rearrangements of this compound that would lead to other intriguing $(CH)_{10}$ isomers.

The synthesis of **7** was achieved relatively easily, from readily available starting materials (reaction 1).[26]



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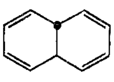

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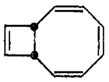

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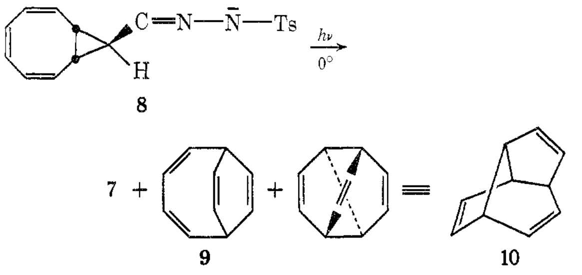


(1)

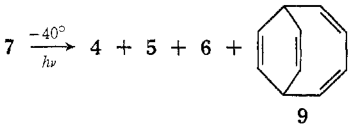
$$7 \xrightarrow{\Delta} [2] \longrightarrow 6$$

$$\Delta H^{\ddagger} = 25 \text{ kcal/mol}$$
$$\Delta S^{\ddagger} = 0 \text{ eu}$$

Photolysis (Pyrex-filtered uv) of the sodium salt of the tosylhydrazone of bicyclo[6.1.0]nona-2,4,6-triene-9-carboxaldehyde (**8**) at 0° gave a reasonable yield of the desired **7**, in addition to bicyclo[4.2.2]deca-2,4,7,9-tetraene (**9**)[27] and tricyclo[$5.3.0.0^{4,8}$]deca-2,5,9-triene (**10**).[28,29] Interestingly enough, compound **7** underwent a quantitative thermal rearrangement to **6**.[12,27] It was proposed that this reaction occurs through the intermediacy of [10]annulene (**2**),[26] and this speculation later received experimental support (*vide infra*).

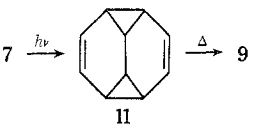
At almost the same time, Doering and coworkers reported an efficient conversion of bullvalene (**4**) into **5**.[23] This provided a practical route to **5**, which made all three of the proposed [10]annulene precursors readily available.

We then began investigating the photochemistry of **7** at low temperatures, because of its thermal instability. Irradiation for 5 min at −40°, followed by work-up at room temperature, gave **4**, **5**, **6** and **9** in a ratio of 8:25:24:48 (reaction 2). Prolonging the photolysis at this temperature, again followed by a room temperature work-up, did not significantly alter the product distribution. The fact that **9** was photochemically labile under the conditions employed indicated that there must have been an intermediate in this reaction that was photochemically inert, but thermally labile. This was verified by recording the nmr spectrum of the cold photolysate before and after warming.



(2)

Purification of this unknown precursor of **9** was subsequently achieved by alumina chromatography at −80°, providing colorless needles. The structure of this compound was proven to be tetracyclo[$4.4.0.0^{2,10}.0^{5,7}$]deca-3,8-diene (**11**), and its facile thermal conversion into **9** was confirmed (reaction 3).[30] Compound **11** turned out to be an oft-cited (but unisolated) key intermediate in some interconversions of $(CH)_{10}$ isomers. This was our first success at isolating and characterizing elusive, thermally unstable $(CH)_{10}$ hydrocarbons.



(3)

The most intriguing question at this point, however, was the mechanism by which **11** was formed photochemically from **7**. To our surprise, we soon discovered that compounds **5**, **6**, and **7** all reached, upon irradiation at −110°, a photostationary state consisting of **5**, **6**, and **11** and a small amount of **4** (reaction 4).[30] This suggested that [10]annulene(s) were involved as intermediates. However, careful monitoring of the photolysis of 0.05–0.5 *M* solutions of **5**, **6** or **7** from the beginning to the stationary state did *not* provide

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[22] G. Schröder, *Angew. Chem. Int. Ed. Engl.*, **2**, 481 (1963); G. Schröder, *Chem. Ber.*, **97**, 3140 (1964).

[23] W. von E. Doering, B. M. Ferrier, E. T. Fossel, J. H. Hartenstein, M. Jones, G. Klumpp, R. M. Rubin, and M. Saunders, *Tetrahedron*, **23**, 3943 (1967).

[24] C. D. Nenitzescu, M. Auram, J. J. Pogany, G. D. Mateescu, and M. Farcasin, *Stud. Cercet. Chim.*, **11**, 7 (1963).

[25] E. E. van Tamelen and B. Pappas, *J. Amer. Chem. Soc.*, **85**, 3296 (1963).

[26] S. Masamune, C. G. Chin, K. Hojo, and R. T. Seidner, *ibid.*, **89**, 4804 (1967).

[27] M. Jones, Jr., and L. T. Scott, *ibid.*, **89**, 150 (1967).

[28] M. Jones, Jr., *ibid.*, **89**, 4236 (1967).

[29] For a definite structural proof of **10**, see S. Masamune, H. Zenda, M. Wiesel, N. Nakatsuka, and G. Bigam, *ibid.*, **90**, 2727 (1968), footnote 9.

[30] S. Masamune, R. T. Seidner, H. Zenda, M. Wiesel, N. Nakatsuka, and G. Bigam, *ibid.*, **90**, 5286 (1968).

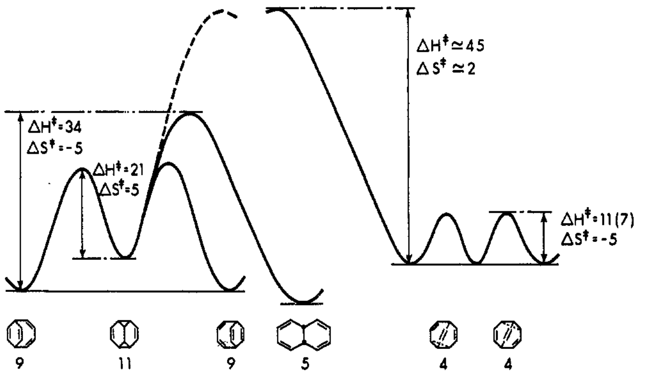
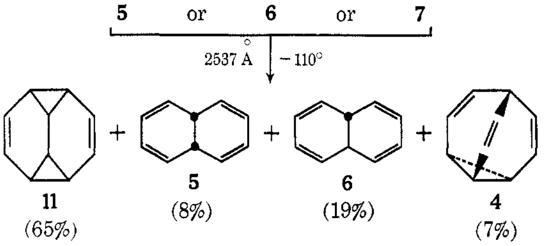


Figure 1.



(4)

(photostationary composition)

evidence for any compounds other than those mentioned, despite an earlier report that a [10]annulene had been trapped.[12] Before elaborating on this important question (*vide infra*), we summarize briefly some of our work on $(CH)_{10}$ hydrocarbons that centered on thermally unstable intermediates other than [10]annulenes.

A Digression

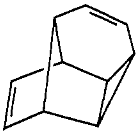
Compound 11. The isolation of thermally unstable species and the study of their chemistry provide strong evidence of reaction mechanism. The chemistry of **11** implicated it as being involved in the degenerate isomerization of compound **9**; this conclusion was substantiated by labeling experiments and temperature-dependent nmr studies.[31-33] Furthermore, the isomerization of **9** to **5** involves **11** (Figure 1). This reaction needs somewhat more energy because it is regarded as thermally disallowed.

Compound **11** was first proposed by Schröder[22] as the initial thermolysis product of bullvalene (**4**), which ultimately provided naphthalene through the intermediacy of **5**.[23] This process (**4** → **5**) is also thermally disallowed, and therefore needs energy as high as 45 kcal. This high energy barrier, in addition to problems involved in specific deuterium labeling of **4**, renders Schröder's proposal difficult to prove.

Photochemistry at room temperature is often complicated if the initial photoproducts are thermally unstable. The products observed are not only those from thermolysis of unstable intermediates, but also their secondary photoproducts. Our studies of the photochemistry of $(CH)_{10}$ hydrocarbons at low temperatures (below the temperature at which thermal reactions are essentially quenched) are much simpler to interpret. Thus the room temperature photolysis of bullvalene (**4**) gives at least five $(CH)_{10}$ isomers, one of which is **9**, and the product distribution varies with the duration of irradiation.[28,34] On the other hand, photolysis of **9** gives a good yield of **4** if the reaction is terminated at an early stage.[27,35] In contrast, photolyses of both **4** and **9** at −100° within 90 min reach a photostationary mixture, consisting of **11** (37–40%), **4** (25%), and several other minor products, as shown in Table I.[18,36] The composition of the photostationary mixture changes only slightly with prolonged irradiation (6 hr). A comparison of the photolyses at room temperature and at −100° therefore indicates that the formation of **9** in room-temperature photolyses of **4** is a result of the thermolysis of **11** (reaction 5). Also, examination of the low-temperature photolysis of **9** at an early stage shows that the major products (>90%) are **4** and **11** and, because the starting material (**9**) is the thermolysis product of **11** at room temperature, the photochemical reaction is clean.

Table I
Product Distribution of Photolysis of 4 and 9 at −100°

Start. material	Product, %						
	11	5	6	4	12	13	14
4	40	4	12	24	6	9	2
9	37	6	9	25	7	10	3



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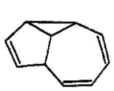

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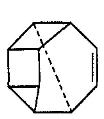

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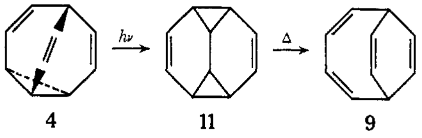

(5)

Another interesting aspect of this photochemistry is the similarity of the product distributions from **4** and **9** with those from compounds **5**, **6**, and **7** (*vide supra*). It is difficult to prove the exact sequence of the photoconversions, but the general observation is that the photolysis of certain $(CH)_{10}$ hydrocarbons reaches a photostationary state with a similar distribution of products and that prolonged irradiation affects only a slow leakage from this photochemical pool.

Isobullvalene[37] **[Tricyclo[5.3.0.0^{2,10}]deca-3,5,8-triene (13)].** Because of the clever entry into the field of

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[31] W. Grimme, H. J. Riebel, and E. Vogel, *Angew. Chem., Int. Ed. Engl.*, **7**, 823 (1968).

[32] M. Jones, Jr., and B. Fairless, *Tetrahedron Lett.*, 4881 (1968).

[33] R. T. Seidner, N. Nakatsuka, and S. Masamune, *Can. J. Chem.*, **48**, 187 (1970). This note was originally submitted on July 15, 1968.

[34] M. Jones, Jr., S. D. Reich, and L. T. Scott, *J. Amer. Chem. Soc.*, **92**, 3118 (1970).

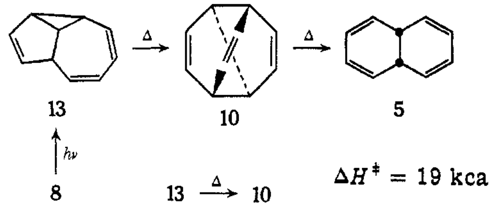
[35] W. von E. Doering and J. W. Rosenthal, *Tetrahedron Lett.*, 349 (1967).

[36] S. Masamune and K. Hojo, unpublished.

[37] Isobullvalene is suggested as a name for this hydrocarbon by L. A. Paquette and J. R. Malpass, *J. Amer. Chem. Soc.*, **90**, 7151 (1968).

$(CH)_{10}$ hydrocarbons executed by Katz and coworkers,[38] and because of the mechanistic importance of this work to $(CH)_{10}$ isomerizations, we became interested in **13**, which was subsequently isolated.[18,39] Compound **13** undergoes a facile thermal Cope rearrangement to **10**, which is further converted into **5**, presumably through an intermediate, *cis*^{5}-[10]annulene (**1**) (reaction 6). Thus is **13** interrelated with other compounds previously discussed.

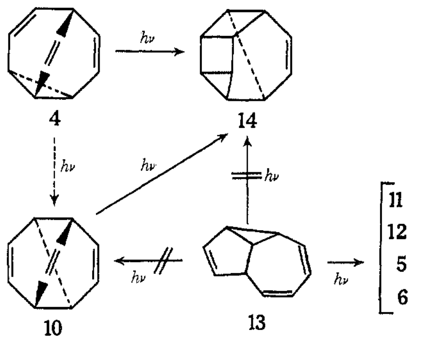
Armed with knowledge of the thermal behavior of **13**, we could easily test the hypothesis[38] that **13** is an intermediate in some transformations of $(CH)_{10}$ hydrocarbons. That the formation of **10** from **8** occurred through the intermediacy of **13** (at least as a major course of this reaction) was soon confirmed (reaction 6).



(6)

$13 \xrightarrow{\Delta} 10$ $\Delta H^{\ddagger} = 19$ kcal/mol

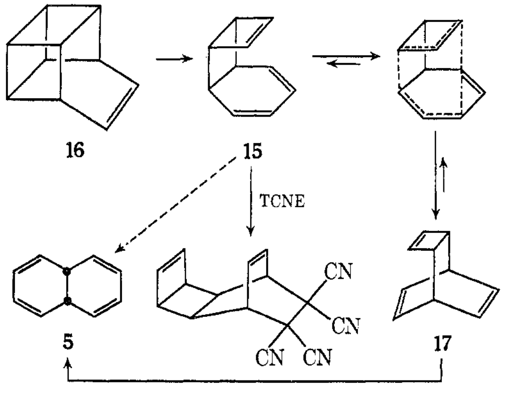
$\Delta S^{\ddagger} = -10$ eu



(7)

The suggestion that the appearance of **10** in the photolysis of **4** is due to the thermolysis of **13** may in fact be valid at ambient temperatures. However, evidence was secured for the *direct* formation of **10** from **4**, again through a low-temperature (−100°) photochemical study. At this temperature, the thermolysis of **13** was completely quenched, and the photolysis of **13** did not yield either **10** or **14**. As indicated in Table I, **14** existed in the photolysate of bullvalene (**4**) (−100°). Since **10** was readily converted into **14**, it is likely that a direct transformation from **4** to **10** (as indicated by the dotted line in eq 7) was operative, and that the photoreaction (**4** → **10**) did not proceed through **13** at −100°.

Tricyclo[4.4.0.0^{2,5}]deca-3,7,9-triene (15). Our first $(CH)_{10}$ hydrocarbon was pentacyclo[4.4.0.0^{2,5}.0^{3,8}.0^{4,7}]-dec-9-ene (**16**), more commonly known as basketene,[40,41] which underwent a thermal rearrangement (at *ca.* 100°) to the so-called Nenitzescu's hydrocarbon (**17**).[24,41,42] That this transformation was not a simple ${}_{\sigma}2_s + {}_{\sigma}2_s$ cleavage but rather a reaction involving intermediate **15** was proven by deuterium labeling, kinetic studies, and trapping experiments (reaction 8).[43,44] Compound **17** was thermolyzed (at 250 to 300°) to **5**[24,45] after equilibration with **15** (deuterium labeling experiments).[43] In this way, basketene was linked with other $(CH)_{10}$ hydrocarbons. Recently Vedejs isolated the unstable intermediate **15**,[46] providing additional support for the mechanism that we proposed earlier.[43] Compound **15** isomerizes into **17** very readily (E_a = 23.5 kcal). Incidentally, one of our initial synthetic approaches to compound **7** involved the ring opening of **15**[47] but was abandoned half-way because of the successful synthesis outlined above. (See the Addendum for other instances of $(CH)_{10}$ hydrocarbon isomerizations.)



(8)

Photochemistry Involving [10]Annulenes

As mentioned previously, we had failed to detect a [10]annulene in the photolyses of compounds **5**, **6**, and **7**, in spite of its probable involvement as an intermediate. Because we already had some familiarity with *cis*^{4}-cyclononatetraene (**18**) we undertook a study of C_9H_{10} photochemistry to gain insight into the mechanisms of $(CH)_{10}$ phototransformations.

In 1965, Vogel and coworkers reported photoinduced isomerizations of *cis*-8,9-dihydroindene (**19**) and *cis*-bicyclo[6.1.0]nonatriene (**20**) by irradiation with a low-pressure mercury lamp at −20°.[48,49] Obviously, this report suggested the involvement of then unknown, thermally labile hydrocarbons.

When we carried out the low-temperature photolysis of several C_9H_{10} hydrocarbons, **18**, **19**, **20**, *trans*-8,9-dihydroindene (**21**), and *trans*-bicyclo[6.1.0]nonatriene (**22**), we found that all of them except **21** (which rearranged to **23**) provided a similar product distribution (eq 9), suggesting that a photostationary state was established, insofar as the situation was similar to what we observed for $(CH)_{10}$ compounds.[50] The

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[38] T. J. Katz and J. J. Cheung, *J. Amer. Chem. Soc.*, **91**, 7772 (1969).

[39] T. J. Katz, J. J. Cheung, and N. Acton, *J. Amer. Chem. Soc.*, **92**, 6643 (1970).

[40] S. Masamune, H. Cuts, and M. G. Hogben, *Tetrahedron Lett.*, 1017 (1966).

[41] W. G. Dauben and D. L. Whalen, *ibid.*, 3743 (1966).

[42] E. N. Cain, R. Vukov, and S. Masamune, *Chem. Commun.*, 98 (1969).

[43] H. H. Westburg, E. N. Cain, and S. Masamune, *J. Amer. Chem. Soc.*, **91**, 7512 (1969); **92**, 5291 (1970).

[44] E. Legoff and S. Oka, *ibid.*, **91**, 5665 (1969).

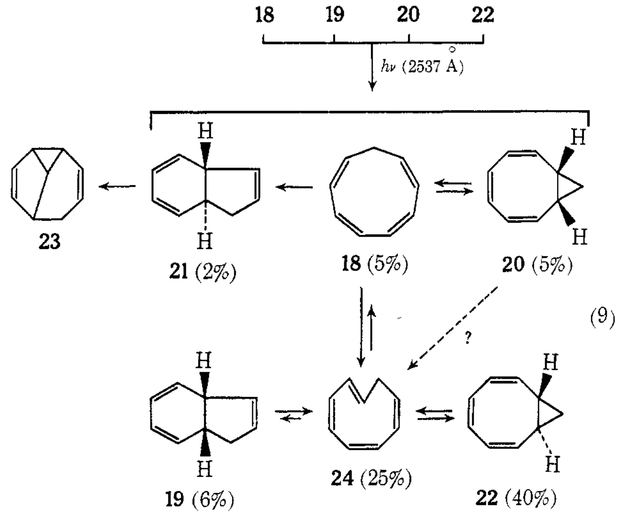
[45] W. von E. Doering and J. W. Rosenthal, *ibid.*, **88**, 2078 (1966).

[46] E. Vedejs, *Chem. Commun.*, 536 (1971).

[47] K. E. Wilson, R. T. Seidner, and S. Masamune, *ibid.*, 213 (1970).

[48] E. Vogel, W. Grimme, and E. Dinne, *Tetrahedron Lett.*, 391 (1965).

[49] G. J. Fonken and W. Moran, *Chem. Ind. (London)*, 1841 (1963).



(9)

23 (photochemically inert)

$\mathbf{18} \xrightarrow{\Delta} \mathbf{19}$, $\Delta H^{\ddagger} = 21.4$ kcal/mol; $\Delta S^{\ddagger} = -4$ eu

$\mathbf{24} \xrightarrow{\Delta} \mathbf{21}$, $\tau_{1/2} \sim 90$ min at $-15°$

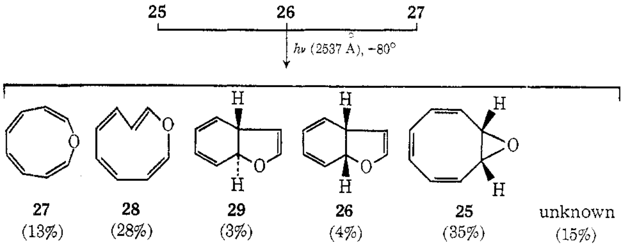
product analysis was mainly based on exhaustive hydrogenation of the photoproduct mixture with Rh catalyst at $-80°$.[13] This is the only catalyst found capable of hydrogenating double bonds as low as $-80°$ without causing complications that may have arisen from the presence of cyclopropane rings.

The existence of two cyclononatetraenes (**18** and **24**), and the distinction between them, was established in the following manner: after **20**, for instance, was photolyzed as described above, the photolysate was kept at $-15°$ and portions were withdrawn at intervals and hydrogenated at $-70°$. Finally the sample was warmed to 50° and treated as above. The product distribution of perhydro compounds demonstrated that one cyclononatetraene was thermally converted into **21** at $-15°$ (first-order kinetics) and that another was rather stable, and isomerized to **19** only after heating to 50°. That the latter was the all-cis isomer was proven by comparison of the kinetics and products of its isomerization with those of authentic *cis*^{4}-cyclononatetraene.[50–53] The thermally more labile compound must therefore be a geometrical isomer of **18**. We proposed, on the basis of the selection rule, that it would very likely possess the structure *trans,cis*^{3}-cyclononatetraene (**24**). These isomers were subsequently isolated in a pure state, which proved our postulate correct.

At $-60°$, the thermal reactions of the C_9H_{10} hydrocarbons involved in the photolyses were virtually stopped. If we are allowed to apply the Woodward–Hoffmann selection rules, we can now set up a reaction scheme for the photochemistry of this set of compounds (eq 9). The three compounds (**21**, **18**, and **20**) in the first row should be photochemically interconnected, as should those in the second row (**19**, **24**, and **22**). Because a similar photostationary state was reached in the photolysis of each of the compounds involved, there must be at least one pathway for the interconversion of compounds in the two subsets. We suggest that the two cyclononatetraenes (**18** and **24**) are the interconverting species; there are numerous precedents for the photoisomerization of cis and trans double bonds.[54]

The exact sequence of the photochemical course of these reactions is too complex to elucidate without detailed kinetic analysis. Nevertheless, the photochemical behavior of each of the compounds involved is compatible with the scheme shown above. The expected interconversion of **18** and **24** (*the transformation of* **18** *into* **24** *is faster than the reverse process*) does occur, and the rates of ring closure of **18** and **24** into bicyclo compounds are comparable to the rates of ring opening of these bicyclo compounds. The obvious consequence is that monocyclo compounds should be major products in the photostationary state, with the *trans,cis*^{3}-cyclononatetraene predominating. Extrapolating from this point to the $(CH)_{10}$ system, our failure to detect [10]annulenes below $-110°$ simply means that photoisomerization of these compounds to bicyclic compounds proceeds faster than formation of the [10]annulenes. *Since there is no way to avoid concurrent photoisomerization of all the compounds involved in the photolysis of one compound*, we had to find those conditions under which the formation of [10]annulenes could complete with their disappearance in order to isolate these elusive species.

With relation to the C_9H_{10} chemistry, it is appropriate to discuss the chemistry of C_8H_8O and C_8H_8NR isomers. We initiated work in this field several years ago,[17] but the studies were not conclusive until we had developed low-temperature techniques. In a manner analogous to that of C_9H_{10} compounds, [8]annulene epoxide (**25**) and *cis*-8,9-dihydrobenzofuran (**26**) on irradiation at $-80°$ soon reached a photostationary state consisting of five C_8H_8O compounds: **25**, **26**, *cis*^{4}-oxonin (**27**), *trans, cis*^{3}-oxonin (**28**), and **29** (reaction 10).[55,56]



$$\mathbf{27} \xrightarrow{30°} \mathbf{26},\ \Delta H^{\ddagger} = 19 \text{ kcal/mol},\ \Delta S^{\ddagger} = -10 \text{ eu} \qquad (10)$$

$$\mathbf{28} \xrightarrow[\tau_{1/2}\ \sim 1 \text{ hr}]{-25°} \mathbf{29}$$

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(50) S. Masamune, P. M. Baker, and K. Hojo, *Chem. Commun.*, 1203 (1969).

(51) G. Boche, H. Bohme, and D. Martens, *Angew. Chem., Int. Ed. Engl.*, **8**, 594 (1969).

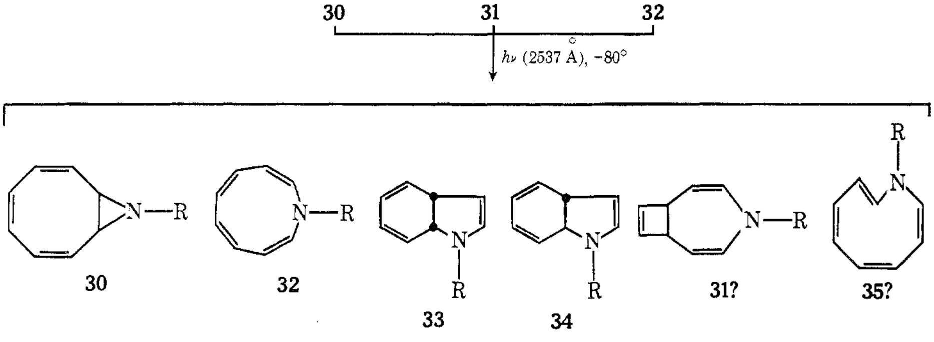
(52) A. G. Anastassiou, V. Orfanos, and J. H. Gebrian, *Tetrahedron Lett.*, 4491 (1969).

(53) P. Radlick and G. Alford, *J. Amer. Chem. Soc.*, **91**, 6529 (1969).

(54) For instance, see R. S. Liu, *ibid.*, **89**, 112 (1967), and references quoted therein.

(55) S. Masamune, S. Takada, and R. T. Seidner, *J. Amer. Chem. Soc.*, **91**, 7769 (1969).

(56) A. G. Anastassiou and R. P. Cellura, *Chem. Commun.*, 903 (1969).



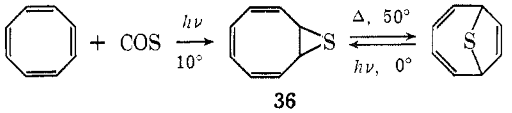
R = COOEt

(11)

$$30 \longrightarrow 31 \xrightarrow[100^\circ]{\tau_{1/2}\ \sim 1\ \text{hr}} 33 \longleftarrow 32$$

$$\Delta H^\ddagger = 24\ \text{kcal/mol}$$

$$\Delta S^\ddagger = -3.5\ \text{eu}$$

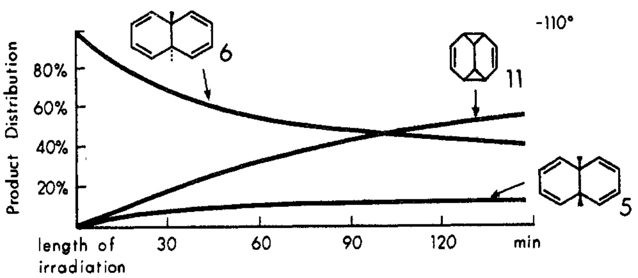


36

(12)

27 also produced the same photochemical pool on irradiation at low temperatures. There was some confusion in the literature concerning the thermal behavior of **27**[56] and the structural assignments for some of its photoproducts.[57] Now they are known to behave as predicted by the Woodward–Hoffmann selection rules,[55,58,59] and their respective geometries have been defined.

The nitrogen analogs behaved thermally and photochemically much as in the C_9H_{10} and C_8H_8O series of compounds. Thus **30** and its thermal product **31**,[17] as well as *N*-carbethoxyazonin (**32**),[60–64] upon irradiation rapidly formed a pseudophotostationary state, consisting of **30**, **32**, **33**, and **34** (reaction 11). Because of experimental difficulty and the rather extensive leakage from this stationary state upon further irradiation, the existence of **31** and an isomer of **32** (**35**) was expected, but not confirmed. Thermolysis of **32** provided **33**. Compound **30** rearranged rapidly at 60° to give **31**, which in turn provided **33** at 100°, presumably through **32**. The sulfur analog of **30** (**36**) was obtained upon irradiation of a mixture of [8]annulene and COS and underwent thermolysis at 50° to the bridged compound, which reverted to **36** upon irradiation (reaction 12).[65] Attempts have been made to obtain thionin, the sulfur analog of **27** or **32**, by photolysis of **36** under a variety of conditions, but our efforts have not been rewarded thus far.



First half-life of **6** (0.3 *M*)

−50°	40 min	THF-d_8
−60°	55 min	THF-d_8
−80°	70 min	THF-d_8
−110°	90 min	THF-d_8
−150°	120 min	THF-d_8–EtOH-d_6
−190°	∞	THF-d_8–EtOH-d_6

Figure 2.

As indicated in eq 4, compounds **5**, **6**, and **7** all provided a similar product distribution on irradiation (2537 Å) at −110°; a photochemical course is shown in Figure 2, using compound **6** as an example. Compounds **5** and **7** behave similarly. In all of these photolyses, we observed a smooth decrease of starting material and a concomitant increase in **11** and either **5** or **6** depending on the starting material use. Another common feature is that the rate of photoconversion is very temperature dependent; the first half-life of the starting material is greatly increased as the temperature is lowered. At this point, applying the sagacity newly won from studies in the C_9H_{10} series, we speculated on the course of photolysis of $(CH)_{10}$ hydrocarbons. Reaction 13 is analogous to that of the C_9 series, and it assumes that the [10]annulenes (**1** and **2**) are involved, although they had thus far eluded detection. Because the concurrent photolysis of all of these compounds cannot be avoided, the production and accumulation of [10]annulenes depend on a means of accomplishing two things: (i) acceleration of the photochemical ring-opening reaction of the bicyclo compounds to [10]annulenes relative to the ring closure reaction of these latter compounds back to the bicyclo material; (ii) choosing the bicyclo compound

(57) J. M. Holovka, P. D. Gardner, C. B. Strow, M. L. Hill, and T. V. van Auken, *J. Amer. Chem. Soc.*, **90**, 5041 (1968).

(58) A. G. Anastassiou and R. P. Cellura, *Chem. Commun.*, 1521 (1969).

(59) J. M. Holovka, R. R. Grabbe, P. D. Gardner, C. B. Strow, M. L. Hill, and T. V. van Auken, *ibid.*, 1522 (1969).

(60) S. Masamune, K. Hojo, and S. Takada, *ibid.*, 1204 (1969).

(61) A. G. Anastassiou and J. H. Gebrian, *J. Amer. Chem. Soc.*, **91**, 4011 (1969).

(62) A. G. Anastassiou and J. H. Gebrian, *Tetrahedron Lett.*, 5239 (1969).

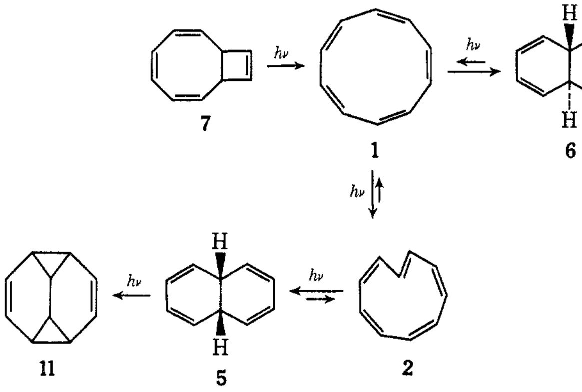
(63) For the nmr spectral behavior of *N*-carbethoxyazonin, see K. Hojo and S. Masamune, *J. Amer. Chem. Soc.*, **92**, 6690 (1970); *cf.* also ref 64.

(64) A. G. Anastassiou, R. P. Cellura, and J. H. Gebrian, *Chem. Commun.*, 375 (1970).

(65) G. O. Spessard and S. Masamune, unpublished results. After this manuscript was submitted, a preparation of **36** using a different method appeared: A. G. Anastassiou and B. T. H. Chao, *Chem. Commun.*, 979 (1971).

that would be most favorable to the accumulation of [10]annulenes in the photo mixture.

We have already mentioned the temperature dependence of the ring-opening reaction. If the ring closure is insensitive to temperature *relative to* the ring opening, then photolysis at the highest temperature at which the thermolysis of [10]annulenes and compound **11** is essentially quenched should lead to the formation of useful amounts of [10]annulenes. This maximal temperature was found to be about −50° (*vide infra*). The choice of starting materials was again based on analogy to the C_9H_{10} series, whereof it was expected that photoconversion of **2** to **1** is slower than the reverse process (**1** to **2**). Therefore, photolysis of **5**, in concentrated solution, should result in a situation in which both [10]annulenes accumulate, if the photolysis is quenched at an early stage (reaction 13); conversely, photolysis of **6** or **7** might lead to the accumulation of **5**, rather than **1** and **2**, because of the initial low concentration of **5**.



(13)

On following this reasoning, we were pleased to see moderately weak, but definitely new, nmr signals in the olefinic region, indicating the formation of new compounds; these signals appeared only when we performed the photolysis of **5** between −50 and −70° (compounds **6** and **7** provided only minor amounts, if any, of the compounds responsible for these new signals at any temperature, with the photoapparatus which we used). The direct spectral observation was soon followed by the separation of the compounds responsible for these signals. Thus, irradiation (2537 Å) of **5** (2 *M*, THF) at −60°, followed by removal of **11** (which crystallized at −80°), provided a [10]annulene-enriched mixture. Chromatography on alumina (Woelm, 1.5% wt H_2O, *n*-pentane–CH_2Cl_2 gradient) at −80° finally ended the long search for these elusive compounds by providing **1** and **2** in crystalline form.[13]

The Properties of [10]Annulenes[13]

The geometry of the isolated [10]annulenes, **1** and **2**, is assigned on the basis of the following data: (i) the symmetry of the molecules as demonstrated by their nmr spectra (both ^{1}H and ^{13}C), (ii) their uv spectra, and (iii) the thermolysis of **1** into **5** ($\Delta H^{\ddagger} = 20$ kcal/mole; $\Delta S^{\ddagger} = -3$ eu) and **2** into **6** ($\Delta H^{\ddagger} = 17$ kcal/mole; $\Delta S^{\ddagger} = -3$ eu). *cis*^{5}-[10]Annulene (**1**) is a nonplanar molecule which readily undergoes conformational change from **1a** to **1b** by pseudorotation of two double bonds around one single bond in the manner depicted above. This process is reminiscent of the interconversion of the twist-boat cyclohexane conformers, and is distinct from the conformational changes of cyclooctatetraene.[66] The nmr spectra (decoupled ^{13}C and ^{1}H) of **1** are sharp singlets at temperatures as low as −160°.

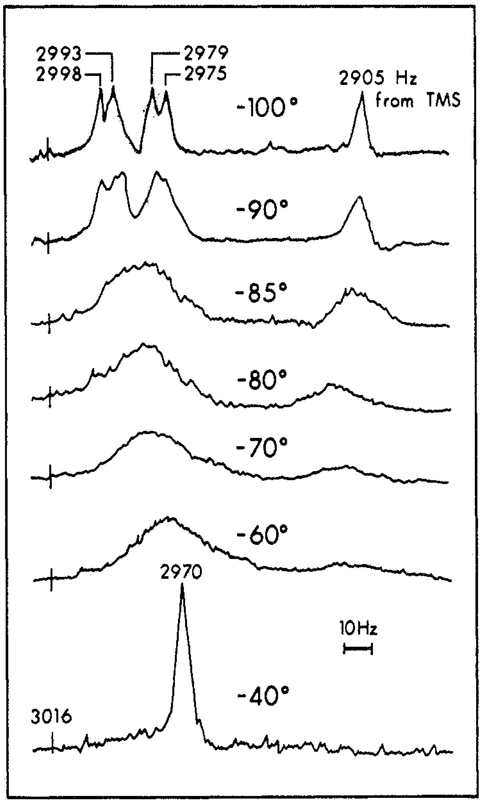
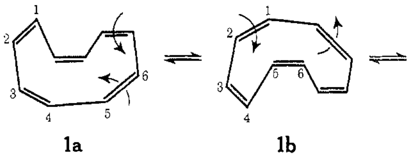


Figure 3. ^{13}C spectra of **2** (22.63 MHz, THF-d_8).



1c ⇌ **1d** ⇌ **1e** ⇌ **1j**

The other [10]annulene, **2**, is now assigned the trans,-cis^4 geometry, after elimination of structure **3** as a possibility. Decoupled ^{13}C nmr spectra of **2** show five signals at −100°, which all merge to a singlet on warming to −40° (Figure 3). Dreiding models indicate that there exists a stable and puckered conformer (**2a**) (C_2), which can be converted into a less stable and nearly coplanar conformer (**2′a** or **2′b**) through rotation a or b. The latter two conformers (**2′a** and **2′b**) provide pathways leading from **2a** to **2b** and **2j**; thus the original 1,2-*trans,cis*^{4}-[10]annulene is converted into 1,10-*trans,cis*^{4}- or 2,3-*trans,cis*^{4}-[10]annulene. Through conformers similar to **2′a** or **2′b** one trans double bond rotates around the ring, all of the nuclei (H or C) of the system ultimately achieving equivalence. Comparison of the ^{13}C spectra with those simulated on a computer on the

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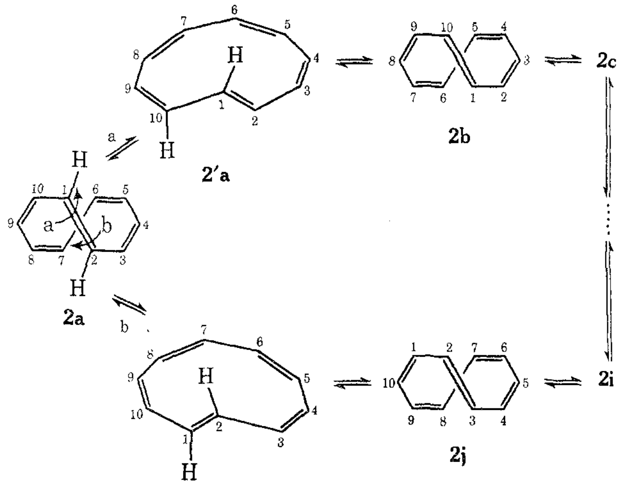
(66) F. A. L. Anet, A. J. R. Bourn, and Y. S. Lin, *J. Amer. Chem. Soc.*, **86**, 3576 (1964).



basis of the above mechanism indicates that only one process (transfer of one double bond to the next position) is responsible for the variation with temperature of the conformation of **2**.

The high reactivity of the [10]annulenes, expected earlier, is now confirmed. However, *only after the isolation and the inspection of the properties* of these compounds is it possible to conclude whether or not they are aromatic. The uv spectra of **1** and **2** are dramatically different from those expected for ten-π aromatic systems,[67] but they closely parallel the spectra of cyclononatetraenes. Similarly, the chemical shift values of the ring protons in the ^{1}H nmr spectra[13] indicate that there is only a minimal if any diamagnetic ring current.

That our reasoning about the relative rates of the thermolyses and photolyses of [10]annulenes and their isomers was essentially correct was born out after **1** and **2** were isolated, and their respective reactivities studied. The kinetic data show that the thermolyses of **1** and **2** are quenched below $-50°$. Rapid photochemical interconversion of **1** and **2** is now verified experimentally and, indeed, the rates are comparable to those of photocyclization of **1** and **2** to give bicyclo compounds such as **5** and **6**. The rates of these cyclizations *relative to those of the (photochemical) ring opening of the bicyclo compounds* are, at minimum, one order of magnitude greater over a wide range of concentrations at $-100°$, and these relative rates decrease as the temperature increases. Therefore, while at $-110°$ or below we observed the formation of [10]annulenes at most in trace amounts (at any stage of the photolysis of the bicyclo compounds), **1** and **2** accumulated substantially at -50 to $-60°$, in the early stages of the photolysis of compound **5**. van Tamelen and Greeley have recently stated[68] that in their *trapping* of [10]annulene, **1** or **3** (not **2**) forms in 14–40% yield based on starting material (**6**, not **5**) consumed when solutions of **6** at low concentrations ($6 \times 10^{-4}\ M$) were employed. However, no consideration has been made of concurrent rapid photoconversion of **1** to **2** and subsequent photocyclization. Their results, in light of the data concerning rates described above, seem somewhat unusual, but matrix (glass) photolysis (77°K) may involve subtle experimental variables such that further photolysis of **1** or **3** was in some way minimized.

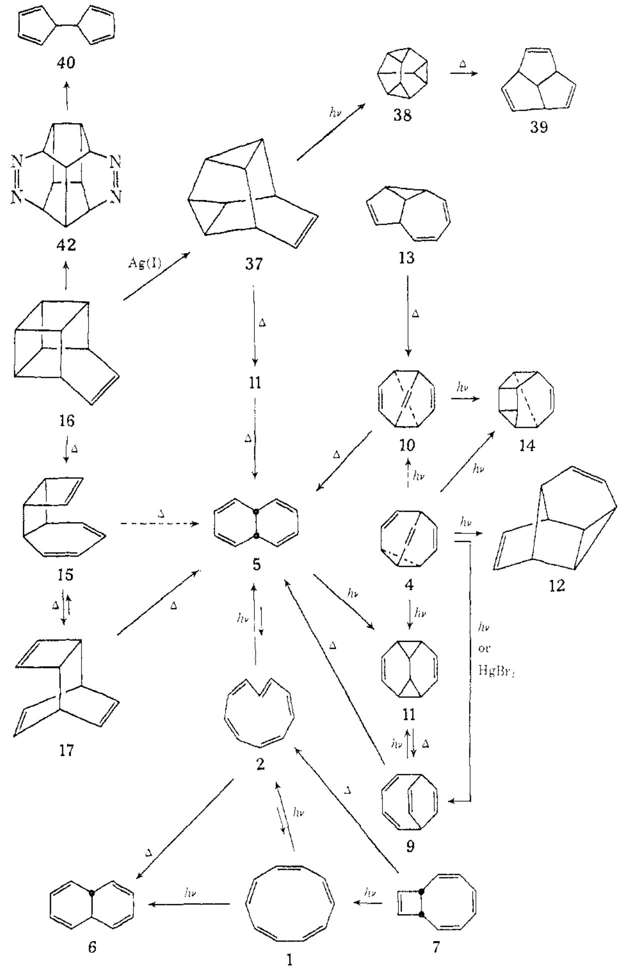


Figure 4.

Addendum

Of the large number of $(CH)_{10}$ hydrocarbon transformations, some of those not mentioned include metal-catalyzed rearrangements and the reactions of the new hydrocarbons that are thus formed. An example is the metal-catalyzed rearrangement of bullvalene (**4**) into **9**,[69–71] and since **9** is readily converted to **5**, this latter compound is now abundantly available. Silver ion catalysis converts basketene (**16**) into **37**[72,73] which provides **5** on thermolysis, presumably through **11**.[74] Photolysis of **37** leads to **38**,[75,76] which in turn is thermolyzed to triquinacene (**39**), first prepared some years

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(67) E. Vogel and H. D. Roth, *Angew. Chem., Int. Ed. Engl.*, **3**, 228 (1964); H. D. Roth, Inaugural-Dissertation, University of Cologne, 1965.

(68) E. E. van Tamelen and R. H. Greeley, *Chem. Commun.*, 601 (1971).

(69) H. P. Loffler and G. Schröder, *Angew. Chem., Int. Ed. Engl.*, **7**, 736 (1968).

(70) E. Vedejs, *J. Amer. Chem. Soc.*, **90**, 4751 (1968); see also ref 71.

(71) G. N. Schrauzer, P. Glockner, and R. Merényi, *Angew. Chem. Int. Ed. Engl.*, **3**, 509 (1964).

(72) W. G. Dauben, M. G. Buzzonlini, C. H. Schalhorn, D. L. Whalen, and K. J. Palmer *Tetrahedron Lett.*, 787 (1970).

(73) L. A. Paquette and J. C. Stowell, *J. Amer. Chem. Soc.*, **92**, 2584 (1970).

(74) L. A. Paquette and J. C. Stowell, *ibid.*, **93**, 2459 (1971).

ago,[77] presumably as a precursor to dodecahedrane. Compound **39** can now be placed on the energy surface connecting other $(CH)_{10}$ isomers. Compound **40** is formed on pyrolysis of nickelocene (**41**)[78] or from the thermolysis of **42**,[79] which in turn is made from **16**.

Figure 4 summarizes thermal and photochemical isomerizations of $(CH)_{10}$ hydrocarbons which have been discussed in this Account. It is amusing to note that virtually all of the compounds known thus far have [8]annulene as their origin.

The senior author is grateful to his collaborators mentioned in the references for their diligent efforts, in particular for their execution of extremely demanding experiments. He also thanks the National Research Council of Canada and the Defense Research Board for financial support of this work.

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(75) A. de Meijere, D. Kaufmann, and O. Schallner, *Angew. Chem., Int. Ed. Engl.*, **10**, 417 (1971).

(76) H. Prinzbach and D. Stusche, *Helv. Chim. Acta*, **54**, 755 (1971).

(77) R. B. Woodward, T. Fukunaga, and R. C. Kelly, *J. Amer. Chem. Soc.*, **86**, 3162 (1964).

(78) E. H. Hedaya, D. W. McNeil, P. Schissel, and D. J. McAdoo, *ibid.*, **90**, 5285 (1968).

(79) K. Shen, *ibid.*, **93**, 3064 (1971).

The Heteronins

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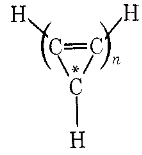
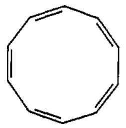
Ever since the original formulation, some 40 years ago, of Hückel's "$4n + 2$" theory of aromaticity,[1] experimentalists have engaged in testing its applicability and its limitations. Over the years the theory has withstood the test remarkably well, and it is now generally agreed that Hückel's prediction of an energetically beneficial electron-delocalization effect within *planar monocyclic* systems containing a total of "$4n + 2$" π electrons has proven entirely correct. Not surprisingly, much of the crucial experimentation in this area was executed quite recently, for only in recent years have adequate isolation and spectral techniques become available.

Perhaps the most striking success of Hückel's theory has been in the area of electrically charged "π" monocycles where the "$4n + 2$" frames of **1a–1d** have been synthesized and were found to be both stable[2] and planar.[3] Further, the requirement of planarity for "π" stabilization within these systems is obvious, inasmuch as the natural propensity of a carbocyclic system the size of **1d** is to assume a puckered arrangement. Actually, **1d** appears to represent an upper size limit for the skeletal strain introduced by a planar all-cis arrangement to be offset by the aromatic stabilization enjoyed by a planar system; the next larger potentially aromatic all-cis carbomonocycle, cyclodecapentaene (**2**), was in fact generated[4] but could not be effectively isolated owing to its pronounced thermal lability.



1a, $n = 1$, * = (+)
b, $n = 2$, * = (−)
c, $n = 3$, * = (+)
d, $n = 4$, * = (−)



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Once the predictive value of Hückel's theory was recognized, application of the $4n + 2$ rule was naturally extended to heterocyclic systems as well. Thus, the long-known stability of the π-excessive heterocycles **3a**, **3b**, and **3c** was reasonably traced to their being iso-π-electronic and skeletally isoatomic with the cyclopentadienyl anion (**1b**). Nonetheless, these heterocycles ought to differ from their carbocyclic analog (**1b**) in terms of overall π delocalization chiefly because of differences in electronegativity between carbon and the respective heteroatoms. Specifically, one would expect π-electron delocalization and thus overall "aromaticity" to increase in the order **3a**, **3b** or **3c**, **1b** since in terms of electronegativity $O > N \sim S > C$. This indeed appears to be the case among the three heterocycles; pyrrole (**3b**) and thiophene (**3c**) are believed to be more

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(1) (a) E. Hückel, *Z. Phys.*, **70**, 204 (1931); (b) *ibid.*, **76**, 628 (1932).

(2) The term denotes *thermodynamic* stability.

(3) For a review, see: P. J. Garratt and M. V. Sargent, *Advan. Org. Chem.*, **6**, 1 (1969).

(4) E. E. van Tamelen and T. L. Burkoth, *J. Amer. Chem. Soc.*, **89**, 151 (1967); S. Masamune and R. T. Seidner, *Chem. Commun.*, 542 (1969); E. E. van Tamelen and R. H. Greeley, *ibid.*, 601 (1971). Very recently the $(CH)_{10}$ monocycle was reportedly isolated at subzero temperatures in two distinct geometric forms: S. Masamune, K. Hojo, K. Hojo, G. Bigam, and D. L. Rabenstein, *J. Amer. Chem. Soc.*, **93**, 4966 (1971).