Eye Witness Accounts

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From Small Carbocyclic Rings to Porphyrins: A Personal Account of 50 Years of Research

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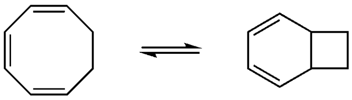
cyclooctatetraene · porphyrins · small-ring systems · valence isomerization

In memory of Rudolf Criegee

1. Introduction

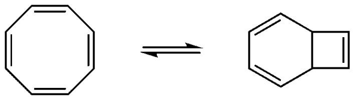
Among the numerous molecular rearrangements, which have been observed in the domain of three- and four-membered carbocyclic rings, the reaction type "valence isomerization"[1] has attracted special attention in modern times. The driving force of these usually thermally induced processes is the release of strain from small or medium-sized rings. It is a characteristic mechanistic feature of valence isomerizations that neither radical nor ionic intermediates can be detected in their course, and that the structural change rests exclusively on a concerted reorganization of the σ- and π-electrons of their molecular skeleton, associated with corresponding changes of bond lengths and angles. When a dynamic equilibrium is established between the components of such a rearrangement it is termed valence tautomerism.

Valence isomerizations and valence tautomerism of systems containing small carbocyclic rings entered the stage in 1952 with the spectacular discovery of A. C. Cope that cycloocta-1,3,5-triene (**1**) and bicyclo[4.2.0]octa-2,4-diene (**2**) are connected by a reversible dynamic equilibrium at temperatures between 80–100 °C; formally this isomerization is, according to the Woodward–Hoffmann rules, an electrocyclic process occurring in disrotatory fashion.



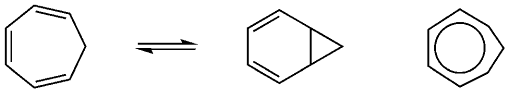
1 **2**

Several years later R. Huisgen demonstrated by high-level kinetic studies of the Diels–Alder reaction of cyclooctatetraene (**3**) with selected dienophiles, that **3**—as had been suspected earlier already—participates in an equilibrium with its bicyclic isomer bicyclo[4.2.0]octa-2,4,7-triene (**4**). As expected, the equilibrium concentration of **4** is extremely small: only 0.01 % and hence below the detection limit of most spectroscopic methods.



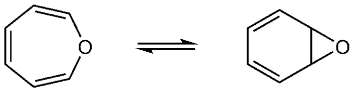
3 **4**

Whereas the equilibria of the valence tautomers **1**$\rightleftharpoons$**2** and **3**$\rightleftharpoons$**4** may be regarded as mechanistically resolved, the tautomeric properties of the related cycloheptatriene (**5**), that is, Willstätter's tropylidene, and norcaradiene (**6**) were subject to controversy until recently. Interestingly W. von E. Doering temporarily regarded **5** and **6** as resonance structures of the hybrid **7**, while H. Meerwein was convinced that he had confirmed the existence of norcaradiene. The Doering–Meerwein dissonance convinced our Cologne research group that the cycloheptatriene–norcaradiene valence tautomerism[2] possesses a considerable synthetic potential, and that it should—in combination with Birch reductions—open the way to numerous novel organic compounds of theoretical and biological interest.



5 **6** **7**

We were encouraged to intensify our efforts in this field by the parallel investigation of H. Günther of the oxepin–benzene oxide valence tautomerism (**8**$\rightleftharpoons$**9**) by low-temperature NMR spectroscopy, one of the first examples of this type, that could be studied successfully by this spectroscopic method.



8 **9**

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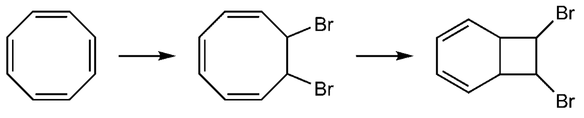
[†] E. Vogel died on March 30, 2011, shortly after completing this manuscript. Correspondence can be sent to Christiane Vogel (at the same address).

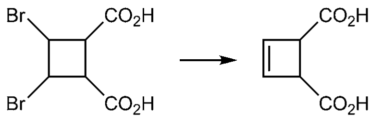
2. New Aspects of Cyclooctatetraene Chemistry: Their Link to the Woodward–Hoffmann Rules

Deeply interlaced with the topic of this account is the chemistry of cyclooctatetraene (**3**), about which W. Reppe and his team at the BASF company had reported earlier in a series of fascinating publications. As an Eldorado of diverse kinds of isomerizations, including valence isomerizations, this eight-membered-ring hydrocarbon exerted a magic attraction on numerous research groups.

One of the most remarkable reactions of **3** is, without doubt, its bromination, which takes place with four-membered-ring formation and provides *trans*-7,8-dibromobicyclo[4.2.0]octa-2,4-diene (**11**). According to R. Huisgen—and in contrast to earlier rationalizations—this transformation proceeds by a 1,2-bromine addition to **10** followed by an electrocylization to **11**.

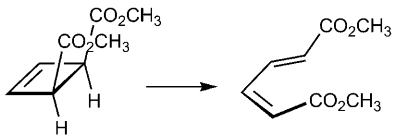


3 **10** **11**



12 **13**

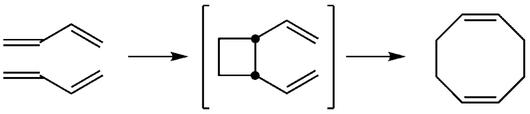
It was the relatively easy access to *cis*-1,2-bis(methoxycarbonyl)cyclobut-3-ene (**14**) via **12** and **13**, that turned our attention to the opening of cyclobutenes to 1,4-disubstituted buta-1,3-dienes, an opening of the cyclobutene ring that until then had only been studied cursorily. As expected, the two electron-withdrawing methoxycarbonyl groups of **14** caused a pronounced reduction of the temperature of isomerization to 120 °C, compared to the 200 °C of the parent cyclobutene. Completely surprising was, however, the observation, that **14** isomerizes stereospecifically with formation of *cis,trans*-1,4-bis(methoxycarbonyl)-buta-1,3-diene (**15**). Although this stereospecificity was regarded as a laboratory curiosity at the time, it soon gained—together with similar observations of R. Criegee and E. Havinga—high significance as one of the experimental pillars of the Woodward–Hoffmann rules.[3]



14 **15**

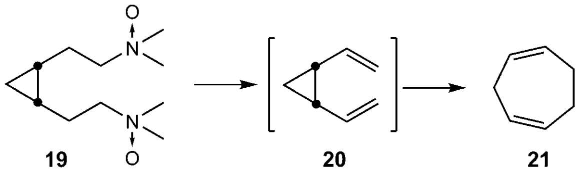
3. Cope Rearrangement of Small Carbocyclic Rings

Undreamt of consequences should result from the study of the thermal behavior of small-ring *cis*- and *trans*-1,2-divinylcycloalkanes. Contemplating the mechanism of the thermal dimerization of the butadiene (**16**) to *cis,cis*-cycloocta-1,5-diene (**18**), first described by K. Ziegler, convinced me that this process should not take place as a [4+4]-cycloaddition, but as a Cope-type, four-center valence isomerization of initially generated *cis*-1,2-divinylcyclobutane (**17**). Indeed, independently prepared **17** isomerizes smoothly at 80 °C to **18**, whereas the already known *trans*-1,2-divinylcyclobutane is stable at these temperatures.



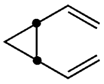
16 **17** **18**

The rearrangement **17**→**18** and the *cis*-1,2-divinylcyclopropane to cyclohepta-1,4-diene (**20**→**21**) isomerizations (subsequently realized by thermolysis of **19**) strikingly underlined the fact, that strain release from an energy-rich small ring provides a significant driving force for the Cope rearrangement.



19 **20** **21**

It was these isomerizations, that induced a dramatic renaissance of the Cope rearrangement, which up to this point had largely remained unnoticed, culminating in Doering's brilliant concept of bullvalene (**24**), with homotropilidene (**23**) preparing the way, and making the Cope process one of the most important rearrangements in organic chemistry.



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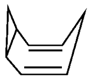

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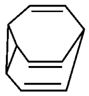
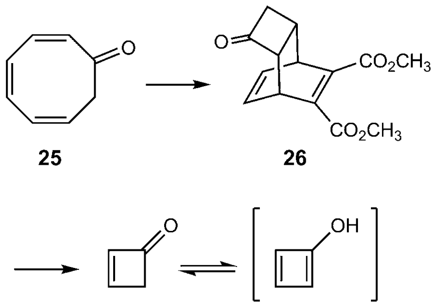


24

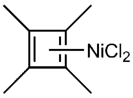
Today the *cis*-1,2-divinylcyclopropane isomerization finds increasing use as the method of choice for the synthesis of carbocyclic seven-membered rings in natural products. That this isomerization is biologically relevant has been shown by L. Jaenicke who demonstrated that various naturally occurring *cis*-1,2-divinylcylopropanes and their corresponding cyclohepta-1,4-diene isomers serve as pheromones of brown algae.

As far as research on the chemical relationship between eight- and the four-membered ring systems, inspired by the chemistry of cyclooctatetraene, is concerned, the transformation of the cyclooctatrienone **25** to cyclobutenone (**27**) is a


25 **26** **27** **28**

further instructive example. Compound **27** is remarkable in that it may be regarded as the tautomer of the fictional hydroxycyclobutadiene **28**.

At this point it is worth taking a look at cyclobutadiene itself and its metal complexes. R. Criegee and G. Schröder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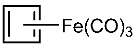
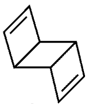

30

prepared the first tetramethylcyclobutadiene nickel complex, **29**, a pioneering act of the highest order and all the more significant because H. C. Longuet-Higgins and L. E. Orgel had predicted, by quantum chemical calculations, that cyclobutadiene metal complexes should be stable. A few years later the iron tricarbonyl complex of the unsubstituted cyclobutadiene, **30**, was prepared by R. Pettit and co-workers starting from dichlorocyclobutene which itself was obtained from cyclooctatetraene.

Attempts to liberate the respective cyclobutadienes from their metal complexes, largely yielded mixtures of the stereoisomeric cyclobutadiene dimers **31** and **32**, respectively.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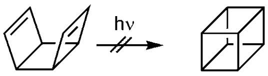
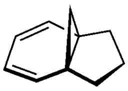


32 **33**

Contrary to expectation, no bridge could be established between the cyclobutadiene and the cubane system **33**: on photolysis of **32** the anticipated ring closure to **33** did not take place.

4. The Discovery of the 10π-Electron Hückel Aromatic Hydrocarbon 1,6-Methano-[10]annulene

Because of various uncertainties concerning the cycloheptatriene–norcaradiene valence tautomerism, I decided to address the equilibrium problem with the help of the authentic norcaradiene derivative **34**. In this hydrocarbon the molecular skeleton is arrested by way of a trimethylene bridge which functions as a molecular clamp. Although this concept did not reveal new structural features, it would turn out to be very fertile.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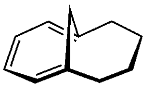
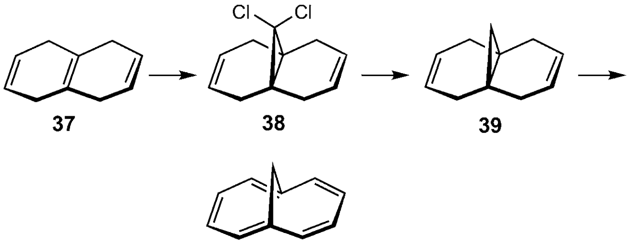

35

The extension of the bridge from three to four methylene units caused practically a total change from the norcaradiene structure to the cycloheptatriene form, **35**, with a ten-membered carbon ring system as the periphery. Formally, all that was required now was the introduction of two additional double bonds into **35**, to arrive at the hitherto not considered 1,6-methano[10]annulene hydrocarbon (**36**).

As a suitable route to **36** the reaction sequence **37**→**39** was developed, with the dichlorocarbene adduct **38** serving as an indispensable synthetic intermediate.



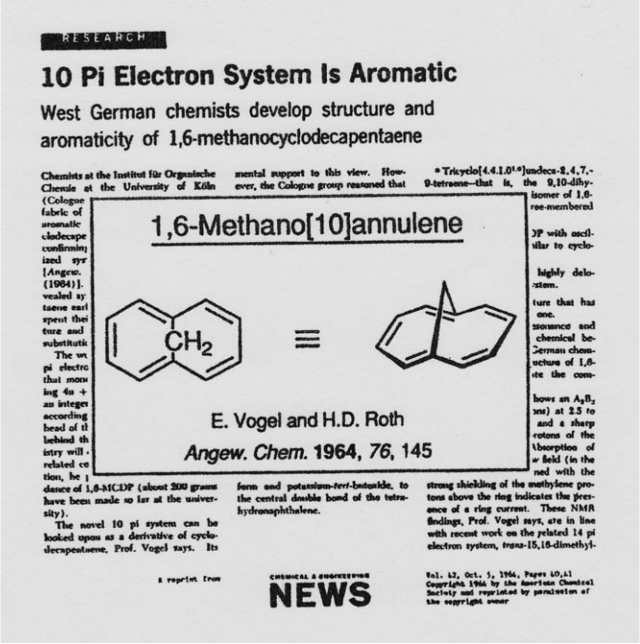
37 **38** **39** **36**

1,6-Methano[10]annulene (**36**) is a relatively stable, pale yellow hydrocarbon with a melting point of 28–29 °C; its C_{10}-perimeter departs only slightly from planarity. According to spectral data and structural analysis it has an aromatic, cyclically-conjugated 10π-electron system and hence is a Hückel aromatic compound.[4] As the first neutral 10π-system it impressively confirms Hückel's rule, rapidly attracted the attention of the scientific community, and was soon incorporated into the textbooks and journals of organic chemistry (as, for example, demonstrated by an article in *Chemical and Engineering News*).[5]

From **36** a host of substitution products may be derived by the action of electrophilic reagents (usually by a sequence of addition and elimination steps) or by independent synthesis.

In quick succession the 1,6-methano[10]annulene analogues 1,6-oxido- and 1,6-imino-[10]annulene (**40** and **41**) followed. Furthermore, 2,7- and 3,8-methanoaza[10]annulene, **42** and **43**, were synthesized and shown to be homologues of pyridine.

Among the additional 1,6-methano[10]annulene variants, to me the stable bicyclo[5.4.1]undecapentaenylium tetrafluoroborate (**46**), is particularly noteworthy. The 10π-cation **46**—although bridged—stands in a harmonious row with its



RESEARCH

10 Pi Electron System Is Aromatic

West German chemists develop structure and aromaticity of 1,6-methanocyclodecapentaene

Chemists at the Institut für Organische Chemie at the University of Köln (Cologne
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dance of 1,6-MCDP (about 200 grams have been made so far at the university).

The novel 10 pi system can be looked upon as a derivative of cyclodecapentaene, Prof. Vogel says. Its

mental support to this view. However, the Cologne group reasoned that

form and potassium-*tert*-butoxide, to the central double bond of the tetrahydronaphthalene.

* Tricyclo[4.4.1.0^{1,6}]undeca-2,4,7,-9-tetraene—that is, the 9,10-dihy-
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strong shielding of the methylene protons above the ring indicates the presence of a ring current. These NMR findings, Prof. Vogel says, are in line with recent work on the related 14 pi electron system, *trans*-15,16-dimethyl-

1,6-Methano[10]annulene

E. Vogel and H.D. Roth

Angew. Chem. **1964**, *76*, 145

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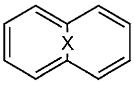
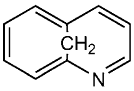


X = O **40**
X = NH **41**



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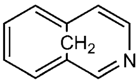
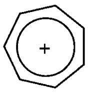


43

preceding aromatic ions cyclopropenium (**44**) and tropylium cation (**45**).

44



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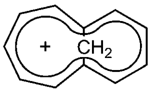
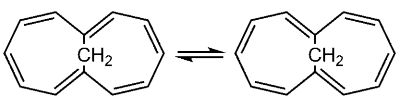


46

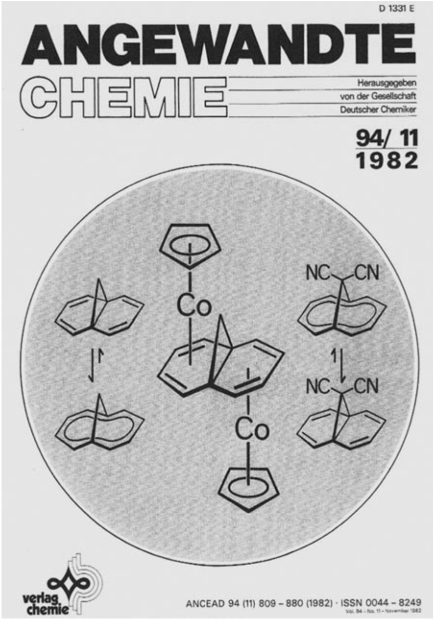
For the development of the 1,6-methano[10]annulene chemistry it was extremely useful to have access to a large-scale, technical laboratory—a generous gift of the Bayer company. Over the years a total of approximately 12 kg of the annulene were prepared in this fashion.



47

The nature of 1,6-methano[10]annulene (**36**) as a 10π-Hückel aromatic compound is underlined by the synthesis and the properties of its 12π-analogue, 1,7-methano[12]annulene (**47**). Since the bridged [12]annulene, according to X-ray structural analysis, also has an approximately planar carbon perimeter, the pair **36** and **47** is a good model for a comparison of a $[4n+2]\pi$ system and a $[4n]\pi$ system. Indeed, as expected, 1,7-methano[12]annulene differs drastically from its aromatic analogue by displaying fluctuating π-bonds and showing contrasting NMR spectroscopic characteristics (diatropic vs. paratropic behavior).

The boundaries for the existence of 1,6-methano[10]annulene is reached (as shown in a cover picture from *Angewandte Chemie* in 1982), when metal complexation or suitable substitution of a bridging carbon atom forces a valence isomerization from 1,6-methano[10]annulene to a "bisnorcaradiene" system.



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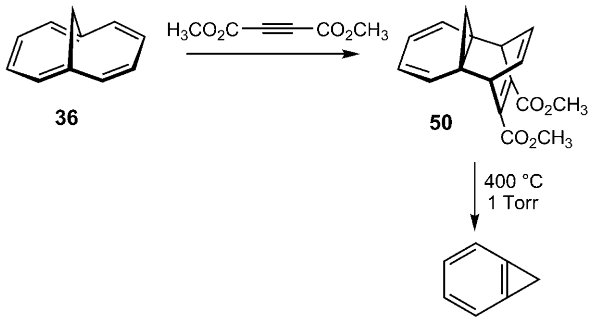
In the case of 1,6-methano[10]annulenes, the resonance stabilization of the aromatic system is so large that the valence isomers in equilibrium cannot be detected directly, whereas the 11,11-dicyano derivative, according to crystallographic analysis, is only present in the bisnorcaradiene form. A simple explanation of this situation was provided, according to H. Günther, by the Walsh MO orbital model of the cyclopropane rings. This model showed that for the norcaradiene—cycloheptatriene equilibrium, substituents with acceptor character in the bridge stabilized the norcaradiene form, because they decrease the anitbonding component of the occupied orbitals of the basal bond of the three-membered ring. The bisnorcaradiene form of the parent system can only be fixed when the diene unit is used as a ligand in transition-metal complexes, as shown in the biscobalt complex in the cover picture image.

5. Cyclopropabenzene (Benzocyclopropene)

A fascinating extension of the chemistry of 1,6-methano[10]annulene (**36**) was promised by the preparation of the highly strained hydrocarbon cyclopropabenzene (**51**), from which—prior to our synthesis—only derivatives had been described. The annulene **36** reacts with dimethyl acetylenedicarboxylate with formation of a Diels–Alder adduct **50**. When **50** is subjected to pyrolysis at 400 °C under 1 Torr, the expected hydrocarbon **51** is produced by an Alder–Rickert cleavage as a colorless liquid. Although the hydrocarbon is very reactive, its spectroscopic data reveal that it is an aromatic compound.

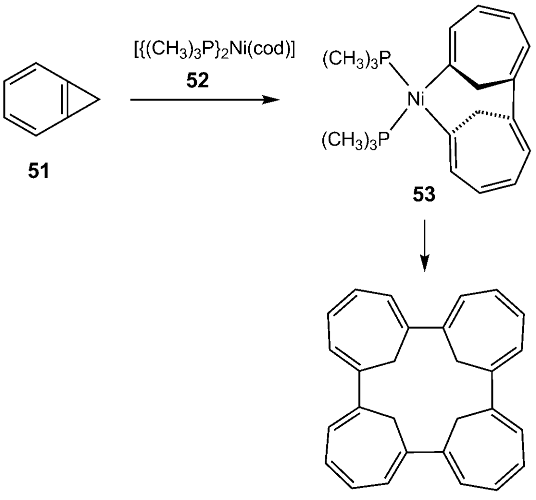


36 **50** **51**

The synthesis of **51** by W. Grimme and S. Korte unfortunately did not turn out to be a source of joy alone. Cyclopropabenzene is characterized by an extremely unpleasant odor, which rapidly permeated through the whole Cologne Chemistry Institute. It was bound to happen: Demoralized by countless complaints, the university administration simply barred us from further work with this hydrocarbon and we were forced to let others fathom the suspected chemical potential of cyclopropabenzene.

To our gratification cyclopropabenzene, which thus had become fair game, found the interest of the research group of R. Mynott, R. Neidlein, H. Schwager, and G. Wilke at the Max Planck-Institute for Coal Research. This group recognized that metal organic catalysts are necessary to unveil the chemistry of cyclopropabenzene.

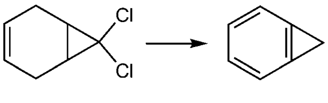
As a first success, a very unusual two-step synthesis of a tetrabismethano[24]annulene (**54**) was announced by formal cyclotetramerization of **51** via a metallacyclic intermediate. When **51** was treated with cycloocta-1,5-diene bis(trimethyl)phosphine nickel(0) (**52**), it readily furnished the bismethano nickelacyclotridecahexaene (**53**). Subsequent exposure of **53**, an intermediate that itself possesses a rich chemistry, to trimethylphosphine induces the reductive elimination to **54**, the four rings of which are present in their cycloheptatriene form.



51 **53** **54**

A stir was also caused by the preparation of various nickel complexes with propellane structure, generated by the reaction of difluorocyclopropabenzene with nickel(0) complexes.

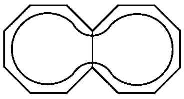
The essential contributions to cyclopropabenzene chemistry of the group of R. Neidlein and G. Wilke would not have been possible, if W. E. Billups had not opened up an easy preparative access to **51** by dehydrochlorination of the dichloride **55**.



55 **51**

6. Synthesis and Properties of Octalene

As an example for the usefulness of small carbocyclic ring systems in combination with valence isomerizations, I present the synthesis of the 14π-electron system octalene (**56**–**58**), a classical representative from the area of non-benzenoid aromatic compounds. Octalene, an air-sensitive, yellow liquid of boiling point 50–52 °C/1 Torr and melting point −5 to −4 °C, is a ring system formally constructed of two *ortho*-fused cyclooctatetraene moieties; it can thus be regarded as an eight-membered-ring analogue of naphthalene.



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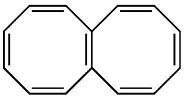

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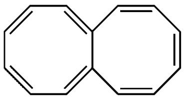

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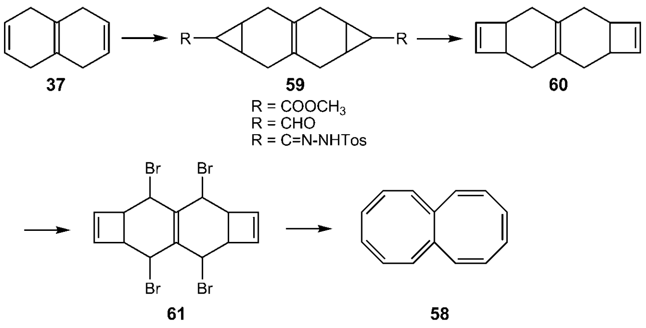
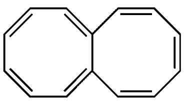
As far as the electronic nature of octalene is concerned, the question may be raised whether it is an aromatic compound, as in **56**, or one of the two olefinic isomers which differ by the position of their double bonds or a mixture of both isomers (**57** and **58**). Since all experiments, to obtain octalene from suitable eight-membered-ring precursors failed, we considered a strategy change mandatory. Indeed, a way to the target molecule was opened up when instead of eight-membered-ring precursors a sequence using cyclopropane and cyclobutane derivatives, and including valence-isomerization steps, was employed, on the lines of the sequence **37**→**58**.





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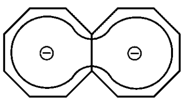

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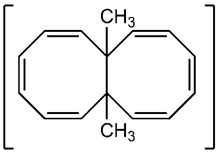

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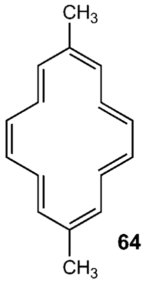

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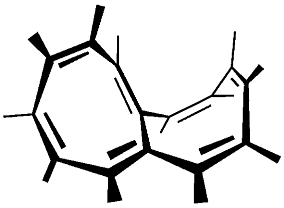
As demonstrated by recent calculations, the resonance stabilization of a planar octalene does not suffice to compensate—there is a deficit of approximately 50 kcal mol^{-1}—the strain that is built up on planarization of the two eight-membered rings. Correspondingly, the ^{1}H NMR spectrum of **58** displays only signals for olefinic protons. According to line-shape analysis of the temperature-dependent ^{13}C NMR spectrum, performed by K. Müllen and J. F. M. Oth, octalene has a nonplanar structure **58**, superimposed by conformational processes.



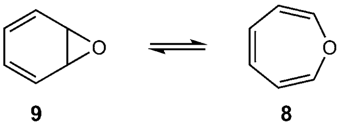
58

The chemical behavior of octalene is dominated by its capability to accept four electrons, whether these are provided by lithium or electrochemically. In a sequence passing through the radical anion, the dianion (diamagnetic), and the radical trianion, the tetraanion is finally reached (which is diamagnetic as is its dianion precursor). Monitoring the reaction by NMR and ESR spectroscopy allows the reduction to be stopped at the stage of the dianion **62**. If the solution containing the dianion is quenched with dimethylsulfate, *cis*- and/or *trans*-1,8-dimethyl[14]annulene (**64**) is produced. Its formation by methylation of the quaternary carbon atoms (see intermediate **63**) followed by a valence isomerization step was predicted by MO calculations. The transformation of **3** to **64** is also of interest since it connects octalene chemistry and the chemistry of the annulenes as developed by F. Sondheimer.

7. Arene Oxides and Oxepins

The discovery of benzene oxide (**9**), and other arene oxides and of oxepines—just in 1965, the year of the centenary of the discovery of the benzene structure by A. Kekule (1865)—is another highlight in our investigations,[6] especially since these oxygenated hydrocarbons play an important role in biochemistry.

Again Hückel theory inspired our research because the original goal of our investigations in this area was the 8π-system oxepine (**8**), for which an olefinic nature had been predicted, rather than the aromatic one for its homologue, furan.

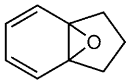


The benzene oxide **9** was to be prepared as a precursor to **8**. The synthesis was in principle simple, involving the dehydrohalogeation the known 4,5-dibromo-1,2-epoxycyclohexane with a suitable base. The effect of quinolin on the dibromide, at higher temperatures however was too drastic and defined products could not be isolated.

Success came when my colleague Dr. W. Böll (a student of G. Wittig) carried out the reaction under mild conditions (sodium ethylate in boiling diethyl ether) and obtained in 80 % yield a yellow, product, initially thought to be oxepine. As demonstrated by temperature-dependent NMR spectroscopy (H. Günther)—and to the surprise of many—Böll's oxepine, was a valence-tautomeric mix of oxepine and benzene oxide (**9**), an equilibrium in which both partners are present in about equal amounts. That the nature of this rapid valence isomerization could be brought to light was aided by the availability of 8,9-indane oxide (**65**) and 2,7-dimethyloxepine (**66**), which served as isomer-free benzene oxide and oxepine reference compounds, respectively.

According to the energy profile the benzene oxide is surprisingly almost 2 kcal more stable than oxepine (Figure 1), however for entropic reasons the oxepine remains in equilibrium.

The real significance of **9** and arene oxides in general soon became apparent in a biochemical research group. Knowledge of the spectroscopic and chemical properties of benzene oxide and other arene oxides synthesized in the Cologne laboratory, especially the 1,2-naphthaline oxide (**69**; NBS =



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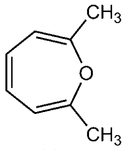

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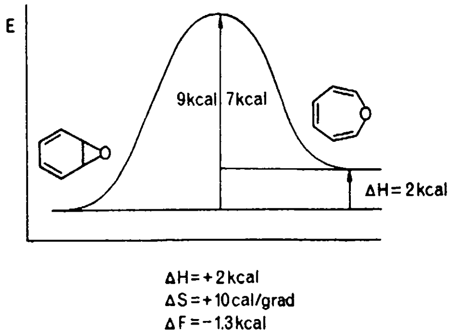
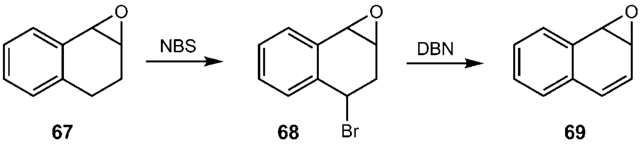


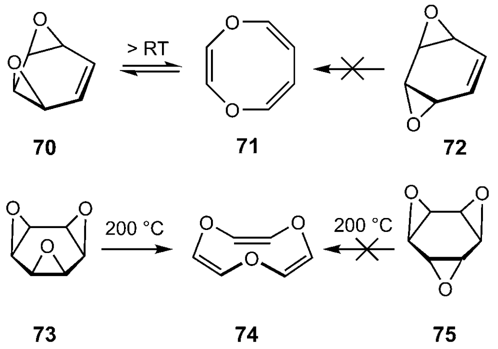
Figure 1. The benzene oxide–oxepine equilibrium.

N-bromosuccinimide, DBN = diazabicyclo[4.3.0]non-5-ene) prepared by F.-G. Klärner, enabled B. Witkop, who had come close to arene oxides already earlier by the discovery of the NIH-shift, to provide the experimental proof that arene oxides are metabolites in the oxidative degradation of aromatic compounds in living organisms. This provided the trigger for a flood of studies on arene oxides (mainly in the US), and made these oxidation products of aromatic hydrocarbons an integral part of biochemical research.



Parallel to this development, H.-J. Altenbach was able to prepare in Cologne the complete series of the higher benzene oxides: *syn*- (**70**) and *anti*-benzene dioxide (**72**), *syn*- (**73**) and *anti*-benzene trioxide (**75**), with **73** being reported simultaneously by H. Prinzbach.

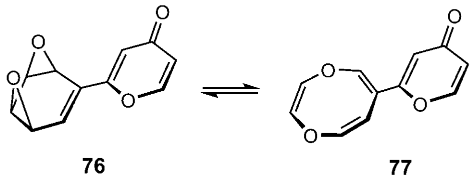
Surprisingly, it was uncovered that *syn*-benzene dioxide **70**—and in contrast to its thermally very stable *trans*-isomer **72**—exists in a balanced equilibrium with its monocyclic valence tautomer, 1,4-dioxocin (**71**). Whereas this equilibration is established slightly above room temperature, *syn*-benzene trioxide **73**, which has also been prepared by H. Prinzbach, only isomerizes at high temperature (200 °C) in an apparently irreversible process to its nine-membered-ring isomer, trioxocin (**74**) and the *anti*-benzene trioxide is stable under these conditions and doesn't decompose even in the gas phase at 400–500 °C



1,4-Dioxocin (**71**) and its nitrogen and sulfur analogues, 1,4-diazocine and 1,4-dithiocine, respectively, are of interest as potential 10π-heteroaromatic compounds. As it turned out, the presumably non-planar **71** is of olefinic nature. In contrast, 1,4-diazocine, which could be prepared from *syn*-benzene dioxide (**70**) via the syn-benzene bisimine derivative by H.-J. Altenbach—a further synthesis was described by H. Prinzbach—is a planar, aromatic molecule. In contrast to the oxygen analogues the rearrangement of the *syn*-benzene imines leads completely to the eight-membered ring system. Derivatives of 1,4-diazocine with electron withdrawing substituents on the nitrogen atoms had no aromatic character.

1,4-dithiocine, should, like the oxygen analogue, be olefinic, the *syn*-benzene bissepisulfide shows no tendency to open to an eight-membered ring. The properties of substituted 1,4-dithiocine discovered later, confirmed this conclusion.

The Cologne studies on arene oxide-oxepines were rounded off harmoniously by the synthesis of the antibiotic LL-Z1220 (**76**, **77**) (with H.-J. Altenbach, 1984), a naturally occurring *syn*-benzene dioxide-1,4-dioxocin system discovered by American authors, the structure of which could, however, only be assigned using the knowledge gathered with the parent system.



8. [4n+2]π-Homologues of 1,6-Methano[10]annulene

The full potential of 1,6-methano[10]annulene emerges only when it was realized that the hydrocarbon can be regarded as the parent molecule of a whole series of [4*n*+2]π-homologues with an acene perimeter. The homologues with *syn*- and all-*syn*-arrangement of the methylene bridges are of interest both from the molecular geometry and aromaticity viewpoint, since their C_{4n+2} carbon perimeter should become increasingly bent as the number of the CH_2-bridges is increased (Figure 2).

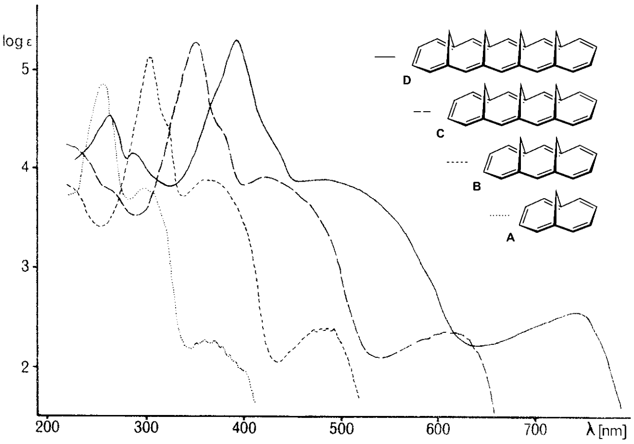
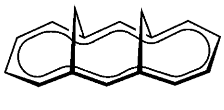


Figure 2. UV spectra of CH_2-bridged [4*n*+2] annulenes with 10, 14, 18, and 22π electrons (in cyclohexane).

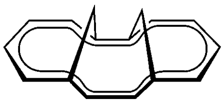
Applying preparative methods developed in our laboratory it was possible to synthesize the homologous series with 10, 14, 18, and 22π-electrons.[7] Although there is a clear increase in reactivity when going from **A** to **D** (Figure 2), according to the spectroscopic data, even the most strongly bent form **D** can still be regarded as aromatic: Again the experience is underlined that cyclically conjugated [4*n*+2]π-systems tolerate a significant deviation from planarity without loosing their aromatic character.

A practically total loss of aromaticity can, however, be induced if the carbon skeleton is deformed drastically.

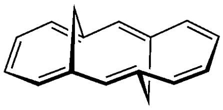
A demonstrative example of the geometry dependence of aromaticity is provided by the stereoisomeric pair of *syn*- (**78**) and *anti*-bismethano[14]annulene (**80**). Whereas **78** is a perfectly stable 14π-Hückel aromatic compound, the *anti*-isomer **80** is a polyolefinic hydrocarbon with fluctuating π-bonds. The bismethano[14]annulenes with a phenanthrene perimeter, **79** and **81**, are also known. However, the aromaticity of **79** is less pronounced that that of **78**. In contrast to **80**, the *anti*-isomer **81** no longer displays fluctuating π-bonds.



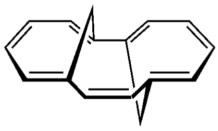
syn: aromatic
78



syn: aromatic
79

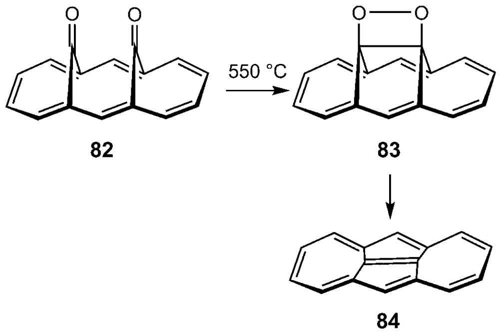


anti: olefin (fluctuating)
80



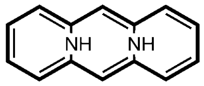
anti: olefin (non-fluctuating)
81

Besides the two pairs of bismethano[14]annulene stereoisomers, the thermally extraordinarily stable *syn*-carbonyl bridged [14]annulene **82**, with two parallel oriented carbonyl groups, deserves special comment. Contrary to expectations, this substrate shows only a very small tendency to fragment into anthracene and carbon monoxide on pyrolysis. It survives temperatures up to 550 °C (in the gas phase). Above this temperature, a till then unknown [2+2]-cycloaddition between the two carbonyl groups to furnish a 1,2-dioxetane (**83**) sets in. This reaction path is inferred from the observation that as the main product of the pyrolysis the new constitutional isomer of pyrene—herein called isopyrene (**84**)—is generated. The other assumed fragmentation product, singlet oxygen, has to date escaped detection.



9. Porphycene and Other Structural Variants of Porphyrin

Of the bridged [14]annulenes *syn*-1,6:8,13-bisimino[14]annulene (**85**) with an anthracene perimeter plays a key role, since it opens up a way to new horizons: the interdisciplinary field of the porphyrins. The study of **85** caused us to focus on the [18]annulene porphyrin model **86**, a tetrapyrrolic macrocycle which may be regarded as a doubly NH-bridged diaza[18]annulene. Provided that this formal analogy exists, a symbiotic relationship between annulene and porphyrin chemistry might be established.[8]



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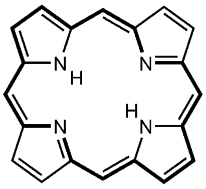

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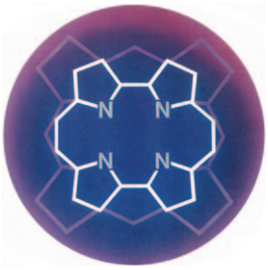
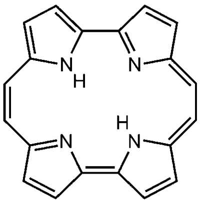
Pursuing this idea resulted in the design and preparation of porphycene (**87**), the most attractive of the six conceivable constitutional isomers of porphyrin with a N_4 core, molecules which nature appears to have forgotten.

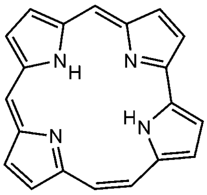
Porphycene (**87**) was prepared by M. Köcher in our laboratories by reduction of α,α′-dipyrroldialdehyde with a zinc/copper couple; it turned out to be a strongly fluorescent, indigo-blue pigment, which according to studies together with J. Michl, G. Hohlneicher, and K. Schaffner displays in its physical and chemical properties a strong resemblance to porphyrin. In particular—and just like porphyrin—it forms numerous metal complexes.

In addition to porphycene (**87**) the constitutional isomers hemiporphycene (**88**), corrphycene (**89**), and isoporphycene

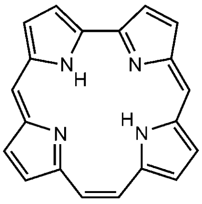




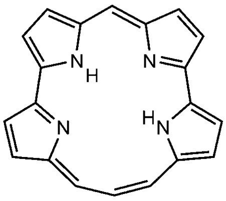
Porphycene
87



Hemiporphycene
88



Corrphycene
89



Isoporphycene
90

(**90**) have in the meantime resulted from our preparative efforts,[9] the relative energies of which have been calculated by K. Houk employing the PM3 method. According to these studies **87** and **86** have comparable stabilities, whereas the other isomers have considerably higher relative energies.

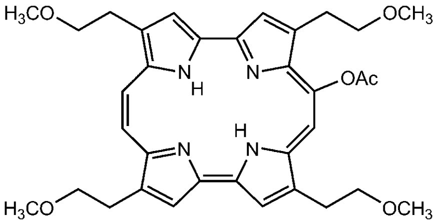
If the porphyrins are viewed from the standpoint of an annulene chemist[10]—as outlined above—a wide spectrum of variants, far beyond the porphyrin constitutional isomers, is conceivable, among them the oxygen, sulfur, and selenium analogues, which all should exist as 18π-cations, as well as "figure eight" cyclooctapyrroles.

10. Summary

The research of our group, spanning a period of more than half a century, is considered by many colleagues as an integral whole. This assessment is valid irrespective of the structural diversity of the molecules investigated, since all these organic compounds are related to each other in an evolutionary way, thus forming a kind of network. Apart from the Cologne team quite a number of organic chemists got interested in the exploration of cyclooctatetraene when Reppe generously provided his precious chemical (in liter-flask quantities!) to university professors (in particular to S. Winstein, R. Criegee, R. Huisgen, G. Schröder, and R. Pettit) for research purposes. From the outset (1953), our scientific efforts profited from the fact that several important small carbocyclic compounds had hitherto defied synthesis (benzene oxide, cyclopropabenzene, octalene) or did not exist in the minds of chemists at all (1,6-methano-[10]annulene, porhycene). It was through the discovery of the Hückel aromatic hydrocarbon 1,6-methano[10]annulene that the concept of aromaticity became a recurrent theme through our research.

In retrospect it sounds rather strange that my initial report on small carbon rings (lecture at a Berlin GDCh-meeting) on which I had pinned high hopes, did not elicit great enthusiasm. Actually a senior colleague commented on my work as follows: "*Herr Vogel, your chemistry is quite nice but the subject of your research is too exotic to earn you a professorship*". There were some indications, however, that small carbon rings would attract more interest in the United States than on my home ground. Indeed, hardly had I recovered from the sobering remarks of my colleague when I received an invitation from Donald Cram (a future Nobel Laureate) at the University of California at Los Angeles to give a lecture series on my research. It was through the West Coast lectures, the Winstein Memorial lecture, and other events that I was able to develop and maintain rewarding professional and personal contacts for decades with the UCLA until my retirement. Fittingly, a colleague from UCLA, Professor Ken Houk, was a co-author of our last publication from Cologne in the porphyrin field. In parallel, we initiated over the years numerous collaborations with experts to convey a further interdisciplinary touch on our work.

Towards the end, a most visible aspect of our research, the phenomenon of color entered the picture.[11] If, in addition to the indigo blue porphycene, the yellow to red bridged annulenes are taken into account, then our compounds cover a substantial part of the electronic spectrum. Obviously, our multifaceted research that started under the heading of valence isomerization of small carbocyclic rings is perceived by us not only as a scientific but also an aesthetic pleasure. With Dr. A. Cross, the former vice-president of Syntex, a firm, Cytopharm, Inc. (Menlo Park, California) was founded, in which the highly promising substituted porphycene derivative **91** was developed and which has been successful in clinical trials.



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