

biological journals with low sales and advertising revenues could probably benefit from the experience, the workshops and the vigour of their colleagues in the biomedical sciences.

Appendix: Memorandum submitted by Wyatt

Uniform requirements for manuscripts submitted to biomedical journals

The following changes would help the readers of journals:

1. References

(i) *Theses*. Theses are difficult to locate and consult. The citation should have the following information if possible: degree

(MS, MD, etc.), faculty, reference in *Dissertation Abstracts*.

(ii) *Books, conference proceedings and organization reports*. Publication details for these should contain greater detail for the more obscure organizations, e.g. post/zip code at the least, address in the case of obscure publishers or if privately printed (and ISSN code?).

2. Correspondence column

The contents page of each issue should contain the names of authors and the title of all letters in that issue. Many journals simply have a section 'Letters' with no contents list. Any reader trying to find a particular letter has to go through the

pages. Readers waste much time with unbound library copies and personal copies.

Reports on meetings etc. should also give the name of the meeting reviewed.

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RESEARCH NEWS

Bowls, boxes and ladders – New designs in hydrocarbon architecture

J. Chandrasekhar

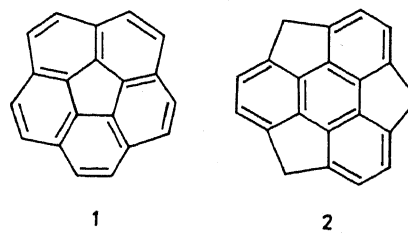
It is possible to construct a remarkably wide variety of organic frameworks even while strictly adhering to tetravalency of carbon and without seriously deviating from van't Hoff structural rules¹. Some of the more aesthetically pleasing arrangements have caught the imagination and challenged the professional skills of synthetic chemists. The successes involving cubane and related prismanes, tetrahedrane (albeit as a derivative), dodecahedrane, etc., represent some of the high watermarks. Pursuit of such goals, besides being intrinsically interesting, provides additional rewards along the way. The very effort is associated with the development of new methodologies, reagents, structures, and hence in new chemistry. The recent achievements of Goverdhan Mehta and coworkers (University of Hyderabad) in three different fronts exemplify the merits of reaching for the stars. The lessons learnt and strategies perfected from years of toil

with complex cage molecules have resulted in remarkable successes.

No cage structure has generated as much interest as buckminsterfullerene, C₆₀. But it is also a fact that many organic chemists have sulked amidst the general excitement. The main reason is that the molecule has somehow been made, but not 'synthesized'. Effective though the preparation of C₆₀ from graphite rods may be, it lacks the art and logic associated with conventional organic syntheses. There has been talk of constructing C₆₀ and other fullerenes using systematic methodology. While such approaches may not be optimal for making C₆₀, the studies are expected to lead to valuable insights on the chemistry of intermediate structures which link planar aromatics and three-dimensional fullerenes.

By deconstructing C₆₀, with its network of pentagons and hexagons, numerous beautiful subunits can be visualized. The molecule which gained prominence as a

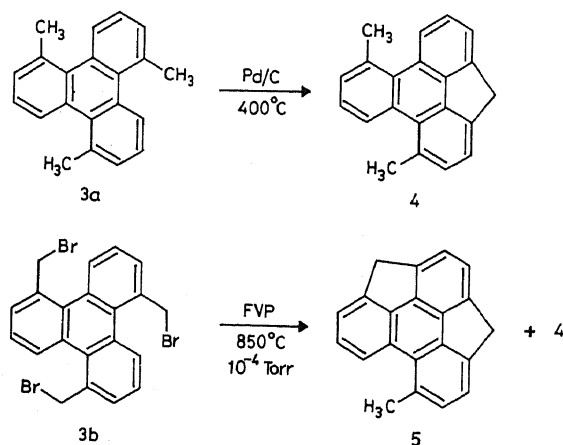
result of such an analysis is corannulene, C₂₀H₁₀, with a pentagon surrounded by five hexagons (1). The molecule has been



shown to have a bowl shape and inversion via the planar geometry has been studied using dynamic NMR². An alternative building block for C₆₀, consisting of a central hexagon surrounded by alternating pentagons and hexagons, has now been considered³. The presence of pentagons would ensure the curling up of the rings. Models reveal that the molecule is shaped like a flower with the rings forming the petals. With a typical organic

chemist's penchant for inventing colourful trivial names, Mehta has called the C_{21} hydrocarbon (2) 'sumanene', derived from suman (flower) in Hindi.

Besides coining a name, Mehta, Shah and Ravikumar have also attempted to synthesize sumanene from trisubstituted triphenylene (Scheme 1)³. While cyclodehydrogenation of **3a** using Pd/C at 400°C led to the introduction of one pentagon (4), attempted dehydrohalogenation of **3b** enabled the construction of two of the pentagons (5). A crystal structure of the latter has been obtained. Formation of the final pentagon still remains elusive. If it is any consolation, molecular mechanics calculations also suggest that this last step would involve the largest build-up of strain. It would be of interest to devise chemical means of overcoming this unfavourable energetic factor to achieve sumanene. Nevertheless, from the point of view of systematic synthesis of C_{60} , 5 is also a useful precursor. The 'loose end' may even turn out to be handy for coupling a second C_{21} unit on way to the eventual construction of the C_{60} cage. After all, it is not essential to have all the rings in place in the building block. After getting the requisite number of carbon atoms approximately in the correct arrangement, the final sequence of bonds can perhaps be incorporated.



Scheme 1

Until C_{60} arrived on the scene, the carbon cage which held centre stage was dodecahedrane, $C_{20}H_{20}$. The first synthesis by Paquette starting from cyclopentadiene⁴ was considered the organic chemist's equivalent of the conquest of Mount Everest. A short cut based on

catalytic rearrangement of other C_{20} hydrocarbon precursors was also pursued in parallel. The effort eventually led to the second successful synthesis of dodecahedrane by Prinzbach, Schleyer and coworkers from a hydrocarbon named pagodane⁵. More recently, Gleiter and Karcher⁶ elegantly used insights concerning through-space and through-bond effects derived through photoelectron spectroscopy to make a propella-cubane, $C_{20}H_{24}$. Now another beautiful member to the C_{20} family of hydrocarbons has been added⁷.

Highly symmetric C_{20} hydrocarbons can be visualized by coupling four cyclopentadiene units in a cyclic arrangement. Head to head coupling results in the cyclic tetramer, 6. Alternative head to tail connectivity leads to the structure, 7. By [2+2] cycloaddition of the two pairs of double bonds in 7, a box-like saturated hydrocarbon (8) can be derived (see Figure 1 for a three-dimensional view). This $C_{20}H_{24}$ isomer with D_{2d} symmetry is built up of four-, five- and seven-membered rings. The structure may also be viewed as being constructed from a pair of orthogonally oriented tricyclic decanes (9), with a sequence of five-, four- and five-membered rings. Mehta and Reddy⁷ have recently successfully synthesized 8. With the prerogative of the

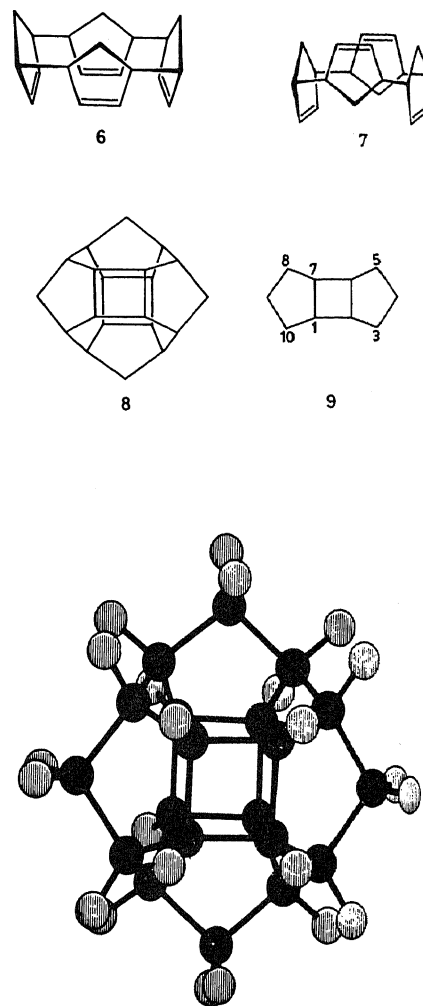
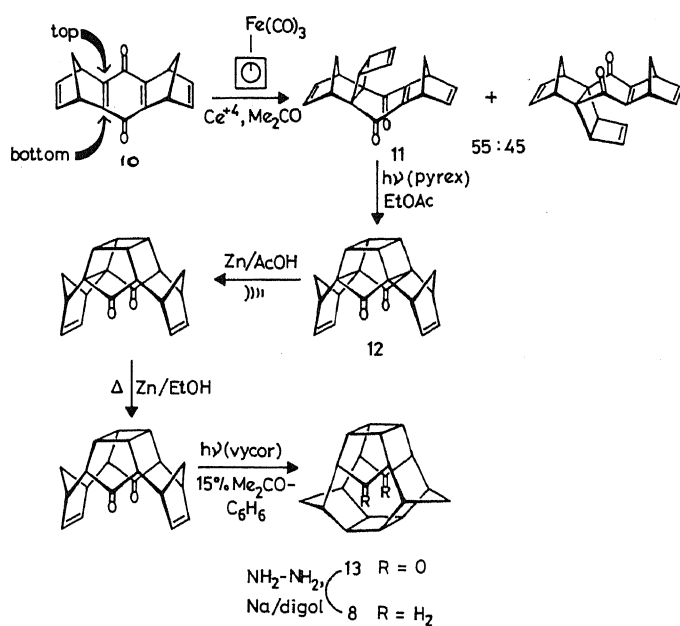


Figure 1. Computer generated drawing of golcondane.

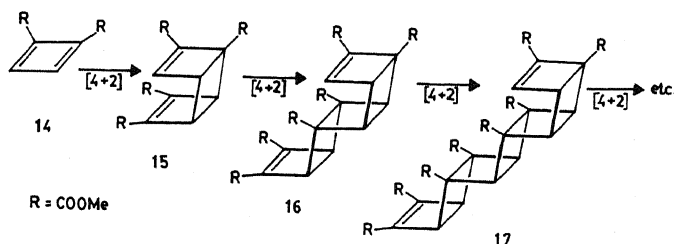
norborno-1,4-benzoquinone (10) with cyclobutadiene, generated *in situ* from its tricarbonyl iron complex by treatment with cerium ammonium nitrate. The cycloaddition occurs with marginal face selectivity. The major top face adduct (11) is then converted to a bishomocubanedione (12) by a [2+2]-photocycloaddition. Two of the C-C bonds adjacent to the carbonyl units are reduced in successive steps. As a result, the remaining C=C bonds are brought closer. A second photocycloaddition leads to the nonacyclic dione (13). All that is needed after that is a simple deoxygenation to get golcondane (8), which however seems to have caused considerable anxiety. Eventually a modified Wolff-Kirschner reduction did the trick⁷.

original discoverers, the authors have proposed a name for the hydrocarbon. They have called it Golcondane, to coincide with the quadricentennial celebration of the founding of Hyderabad.

The synthesis is fairly short (Scheme 2). It starts with the cycloaddition of *syn*-bis-



Scheme 2



Scheme 3

Structural proof comes from ¹³C NMR spectrum of golcondane (3 signals, $\delta = 45.63, 41.04, 39.21$). The crystal structure of the dione has also been obtained. For the record, the calculated strain energy of golcondane is 132 kcal/mol, exactly double that of dodecahedrane (MM2 data).

Can we expect new chemistry from the golcondane framework? Going by the remarkable transformations being carried out by Paquette, Prinzbach and Gleiter on dodecahedrane, pagodane and propellacubane, respectively, the answer has to be a resounding yes. Rearrangement of the golcondane skeleton to dodecahedrane is in itself an attractive possibility. The presence of four-membered rings in golcondane should provide the same driving force as in pagodane. Further, the cycloreversion isomers 6 and 7 remain attractive goals. These structures serve as ideal platforms for evaluating through-space and through-bond interactions.

Cyclobutadiene generated *in situ* in the first step of Scheme 2 has also been exploited in a different context, viz., to build multifused cyclobutanoid systems. Just as squares are useful building blocks for a variety of shapes, the chemical equivalent, cyclobutane, can also be concatenated to derive interesting structures. In fact, chemists have let their imagination run riot, visualizing stars and crosses made of cyclobutanes, (israelane and helvetane)⁸. Less fanciful is the concept of linear-fused cyclobutanes, built like a staircase. A family of [*n*]-ladderanes can be thought of, but characterized examples are limited to *n* = 1–3. Controlled oligomerization of substituted cyclobutadiene generated from its iron tricarbonyl complex has now been used to construct higher ladderanes⁹.

Oligomerization of cyclobutadiene generally stops at the dimer stage. Frontier orbital analysis by Jemmis and Sastry (University of Hyderabad) revealed

the difficulty associated with further cycloaddition⁹. The dimer is a poor dienophile to react with another molecule of cyclobutadiene due to unfavourably large frontier orbital energy gaps. If a couple of electron-withdrawing groups, COOH or COOMe, are present the problem may be overcome. The corresponding 1,2-substituted cyclobutadiene remains a fairly active diene, while its dienophilic character is significantly enhanced. The latter effect is particularly important in maintaining the reactivity of the dimer. Of the two C=C bonds in the dimer, the one with two ester substituents should be reactive towards another cyclobutadiene molecule. The continued presence of a disubstituted activated C=C bond in the adduct must keep the oligomerization going.

The above suggestions based on simpler frontier orbital arguments were brought to life (Scheme 3) by Viswanath and Mehta, with crucial contributions from Kunwar (IICT, Hyderabad) as also from Reddy (ARDEC, New Jersey). Treatment of tricarbonyl iron complex of dimethyl 1,2-cyclobutadiene-dicarboxylate with cerium ammonium nitrate in dry acetone followed by usual work up and separation revealed the presence of crystalline dimer, trimer and tetramer in approximately 3:2:1 ratio. The regio- and stereochemistry of additions have been characterized through ¹H and ¹³C NMR in conjunction with NOE experiments and NOESY spectra. Thus the largest structure obtained in this work corresponds to [7]-ladderane. Additional work has shown the formation of higher ladderanes. Mehta and coworkers have now apparently managed up to [13]-ladderane¹⁰.

A remarkable feature of the ladderanes synthesized above is the presence of the highly polar ester groups essentially on one face of the ladder. This disposition may be expected to confer interesting properties to these molecules. The presence of strained ring systems in a sequence should allow for interesting long range through-bond effects. Further, the rigidity associated with the cyclobutane units should make ladderanes reliable spacers. The end-to-end distance in [13]-ladderane has been estimated to be 1.7 nm, bringing it into consideration for nano-scale applications.

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SCIENTIFIC CORRESPONDENCE

Sulphur-35 labelling

³⁵S-labelled amino acids and nucleotides are increasingly used in protein translation studies and making probes for genetic materials. The need for exercising utmost caution when using these products has been emphasized¹. The impediment in the synthesis and application of ³⁵S-labelled compounds lies in their radiotoxicity to the biological system. While unleashing the energy of 48.8 keV (average), ³⁵S decay is expected to inflict cellular damage but this fact seems to have received scant attention. During the production of ³⁵S amino acids in our laboratory, we have observed growth inhibition and cell killing in micro-organisms exposed to ³⁵S milieu. We noticed that similar constraints have been experienced by others also. Therefore, we felt the need to understand the effects of ³⁵S β-particles at the cellular level. Here we discuss about the contribution of β-irradiation to ³⁵S cytotoxicity.

The cellular damage caused by β-particles in the absence of transmutational effect was assessed by subjecting the diploid yeast *Saccharomyces cerevisiae* strain D₇ to ³⁵S milieu under non-growth conditions (0–4°C). The strain reverts to tryptophan independence by intragenic recombination upon exposure to genotoxic agents². Convertants are scored by plating the treated samples on omission medium not containing tryptophan. The detailed methodology is described elsewhere³.

Induction of gene conversion is a reliable indicator of DNA damage². ³⁵S

negatrons (β-rays) were efficient in inflicting genotoxicity as judged by the induction of tryptophan prototrophy through gene conversion. Sublethal doses up to 100 Gy enhanced the gene conversion frequency in a dose-dependent manner. The survival response study reveals a mean lethal dose of 140 Gy. The relative biological effectiveness values of ³⁵S β-particles relative to ⁶⁰Co γ-rays for lethality and gene conversion were 1.6 and 1.7, respectively. When lethally irradiated cells were subjected to liquid-holding recovery (LHR), the survival increased significantly, indicating their ability to recover from potentially lethal damage. Such recovery depends on the nature of damage and the availability of inherent repairing process⁴.

Another important aspect of ³⁵S decay, involving transmutation, has not been investigated by us. However, it has been shown that the transmutational effect is unlikely to contribute significantly to the lethality of ³⁵S-incorporated organism⁵. At the same time, the ability of ³⁵S to cause DNA lesions *in situ* and cell inactivation even under unincorporated state (without imposing transmutational insult) highlights the significance of negatrons. The radiosensitivity may be higher by many orders in the case of mammalian cell lines. Prolonged incubation and excessive addition of ³⁵S tracers in such sensitive systems may lead to misinterpretation of results. The potential of tracer doses to invalidate the results has also been reported for other radioisotope(s)⁶. Hence, the need arises

for optimizing the level of ³⁵S to be used in various tracer applications such that the tracer itself does not interfere with the test system.

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