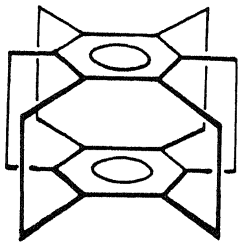
Molecules of the decade

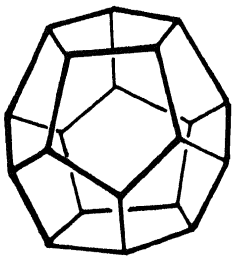
J. Chandrasekhar

Synthetic chemists frequently produce compounds that are, to borrow Roald Hoffmann's words, beautifully simple and simply beautiful. The eighties began with a detailed report on the synthesis of a truly spectacular molecule: $[2_6](1,2,3,4,5,6)$ cyclophane, **1** (ref. 1). It represents the culmination of a dream which began with the synthesis of paracyclophane, way back in 1951. With two benzene rings tied together in every possible chemical way, **1** is appropriately called (in keeping with the times) superphane. Boekelheide[1] succeeded in constructing this lovely structure and also in proving it with X-ray diffraction in 1981.



1

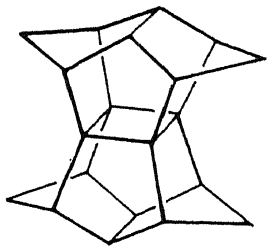
However, with due respect to superphane, the molecule organic chemists were waiting for more keenly was dodecahedrane, $C_{20}H_{20}$, **2**. This organic molecule, possessing the highest conceivable symmetry (120 symmetry operations), was expected to be quite stable But the molecular strain associated with potential precursors (e.g. secododecahedrane, with one C–C bond less), in addition to bad luck and entropy, proved to be the stumbling-block for even the best synthetic chemists in the business. After a long struggle, a dimethyl derivative was made[2], followed by the monomethyl compound[3], and finally the parent molecule itself[4]. It took (only) 23 steps to get to dodecahedrane from the cyclopentadienide ion. Paquette had proved yet again the essential requirements of successful research: patience, perseverance, and postdoctoral associates.



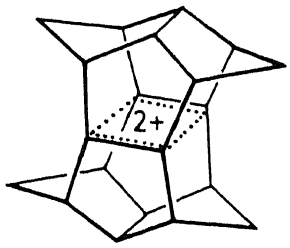
2

As was to be expected, other successful attempts on this Mount Everest of alicyclic chemistry followed, with Paquette himself coming up with a second procedure[5].

The quest for dodecahedrane also led to other interesting molecules. Pagodane, **3a**, is an example. Prinzbach and coworkers could make this molecule in substantial quantities, enabling Schleyer and his coworkers to convert it to dodecahedrane by catalytic isomerization in 8% yield[6]. In my prejudiced view, more interesting than pagodane is its monocation, with a half life of 2 days at German room temperature, and its dication, **3b**, which is both a diolefin dication and a cyclobutane dication[7].

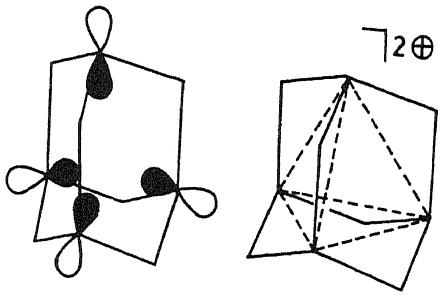


3a



3b

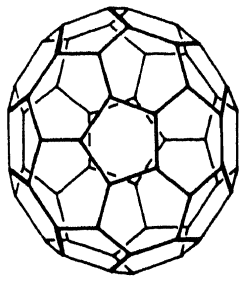
Having mentioned a dication, I have to mention the most remarkable of them all, the dehydroadamantyl system, **4** (ref. 8). The ion is unique in sporting a 4-centre, 2-electron bond in a perfectly tetrahedral arrangement. Note that there are no hydrogen atoms on any of the bridgehead carbons. The four hybrid orbitals at these carbons share two electrons and also most of the dipositive



4

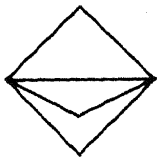
charge in an accommodative spirit characteristic of electron-deficient systems. Structural proof for the ion was provided essentially by ^{13}C-NMR spectroscopic parameters (in addition to molecular orbital calculations)[8].

With much less structural evidence, another molecule shot into the limelight in the mid-eighties. It is the curious case of a carbon compound that fascinated physical chemists more than it did organic chemists. Laser vaporization of graphite, followed by a mass-spectral analysis, indicated the formation of a series of C_n species (n=60–70). For C_{60} an icosahedral network structure, **5**, truncated at each pentagonal apex (nothing but the familiar soccer ball), was proposed[9]. Theoretical chemists thoroughly enjoyed playing with this molecule. The molecule has been named buckminsterfullerene, in honour of the creative American architect. Although there is as yet no concrete proof, the structure is generally considered plausible. A particularly unusual proof was a high-resolution electron micrograph of carbon, prepared by a sputtering method in which carbon was evaporated by arc discharge, which purported to show spherical C_{60} species[10].



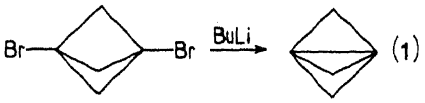
5

A more conventional synthetic approach was used[11] to generate a smaller carbon cluster, C_{18}. A systematic procedure for making such presumably monocyclic annulenes from appropriate precursors has also been suggested[12].



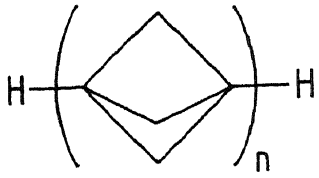
6

The surprise of the decade is the seemingly impossible [1.1.1]propellane, **6**. The molecule has two pyramidal tetracoordinate carbon atoms. Students of organic chemistry are expected to instinctively recognize the instability associated with such structures. However, Wiberg calculated a relatively (compared to other propellanes that had been made) small strain energy for this molecule. He believed in his computations sufficiently to make an attempt at synthesis of **6**. The shockingly simple procedure shown below worked[13]!



(1)

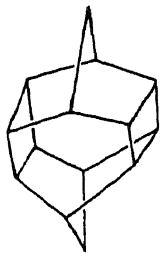
In a further interesting development, the propellane **6** was easily converted to a series of oligomers in a perfectly controlled fashion[14]. Many mind-boggling applications ('molecular-size civil engineering', 'nanotechnology') are being visualized[15] for this class of molecules, called the staffanes (**7**).



n = 2, ..6

7

I shall conclude with a molecule made in India: **8**, bishomohexaprismane,



8

the symmetrical, face-to-face dimer of norbornadiene. Mehta was successful[16] not only in synthesizing the molecule for the first time, but also in contributing a name with an Indian flavour, garudane, to the chemical literature.

1. Sekine, Y. and Boekelheide, V., *J. Am. Chem. Soc.*, 1981, **103**, 1777.
2. Paquette, L. A. and Balogh, D. W., *J. Am. Chem. Soc.*, 1982, **104**, 774.
3. Paquette, L. A., Ternansky, R. J., Balogh, D. W. and Taylor, W. J., *J. Am. Chem. Soc.*, 1983, **105**, 5441.
4. Paquette, L. A., Ternansky, R. J., Balogh, D. W. and Kentgen, G., *J. Am. Chem. Soc.*, 1983, **105**, 5446.
5. Paquette, L. A., Miyahari, Y. and Doecke, G. W., *J. Am. Chem. Soc.*, 1986, **108**, 1716.
6. Fessner, W.-D. *et al.*, *Angew. Chem. Intl. Ed. (Engl.)*, 1987, **26**, 452.
7. Prinzbach, H. *et al.*, *Angew. Chem. Intl. Ed. (Engl.)*, 1987, **26**, 457.
8. Bremer, M., Schleyer, P. V. R., Schotz, K., Kausch, M. and Schindler, M., *Angew. Chem. Intl. Ed. (Engl.)*, 1987, **26**, 761.
9. Kroto, H. W., Heath, J. R., O'Brien, C., Curl, R. F. and Smalley, R. E., *Nature (London)*, 1985, **318**, 162.
10. Iijima, S., *J. Phys. Chem.*, 1987, **91**, 3466.
11. Diederich, F. *et al.*, *Science*, 1989, **245**, 1088.
12. Rubin, Y. and Diederich, F., *J. Am. Chem. Soc.*, 1989, **111**, 6870.
13. Wiberg, K. B. and Walker, F. H., *J. Am. Chem. Soc.*, 1982, **104**, 5239.
14. Murthy, G. S., Hassenruck, K., Lynch, V. M. and Michl, J., *J. Am. Chem. Soc.*, 1989, **111**, 7262.
15. Hameroff, S. R., in *Ultimte Computing, Biomolecular Consciousness and Nano-Technology*, North Holland, Amsterdam, 1987, chapter 10.
16. Mehta, G. and Padma, S., *J. Am. Chem. Soc.*, 1987, **109**, 7230.

J. Chandrasekhar is in the Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012

Does fatty acyl CoA have a role in cellular transport possibly through protein modification?

Amitabha Chaudhuri

THOUGH most proteins are synthesized in the cytoplasmic milieu, internal structural signals dictate functional sequestration and compartmentalization in the cell. The transport machinery that recognizes these signals sorts distinct proteins to the cell surface and to the organelles present in the eukaryotic cell. These signals arise from distinct post-translational modifications that occur in the cell. Besides targeting proteins to respective locations, post-translational modifications like phosphorylation and dephosphorylation, ADP-ribosylation, etc., modulate the function of many proteins. Attachment of lipid molecules to proteins is one such modification, the importance of which has been realized lately. Proteins whose functions are modulated by attachment of lipid molecules have been defined as amphitropic proteins[1].

The nature of the modification of proteins by lipids is, without exception, covalent. Three kinds of modifications are reported. Myristylation involves the attachment of myristic acid to the *N*-terminal glycine through an amide linkage. Palmitic acid is linked through thio-ester and oxy-ester linkages and lastly complex phospholipid tail may be attached to many proteins[2]. The signal for palmitoylation has been apparently identified as a consensus Cys-A-A-X box present at the carboxy terminus of many palmitoylated proteins, in which A represents any aliphatic amino acid[3]. The donor of the lipid moiety in palmitoylation is the CoA derivative of the fatty acid[4].

The true functional significance of this modification is still debatable, barring few exceptions. An obvious consequence of acylation of soluble proteins is its membrane attachment. However, all membrane-bound proteins are not always acylated. In a few instances, membrane attachment has been correlated to distinct functional significance as in the *ras* protein. *Ras* protein is the functional product of *ras* gene, associated with neoplastic development. This protein from various sources has been shown to bind guanine