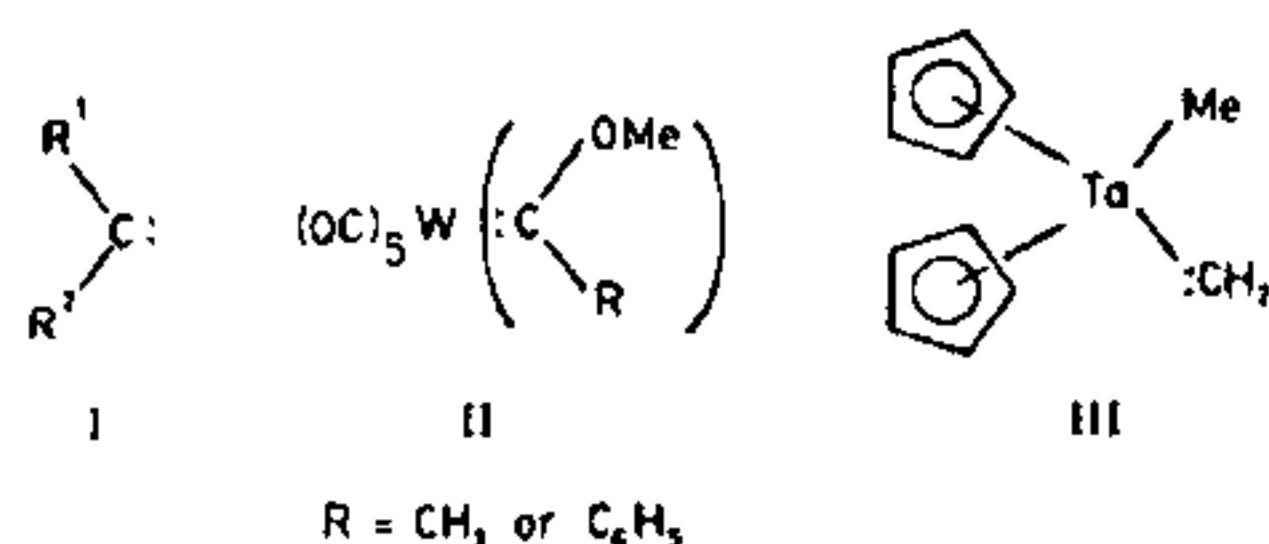


'Carbenes' in a bottle—From reactive intermediates to isolable species

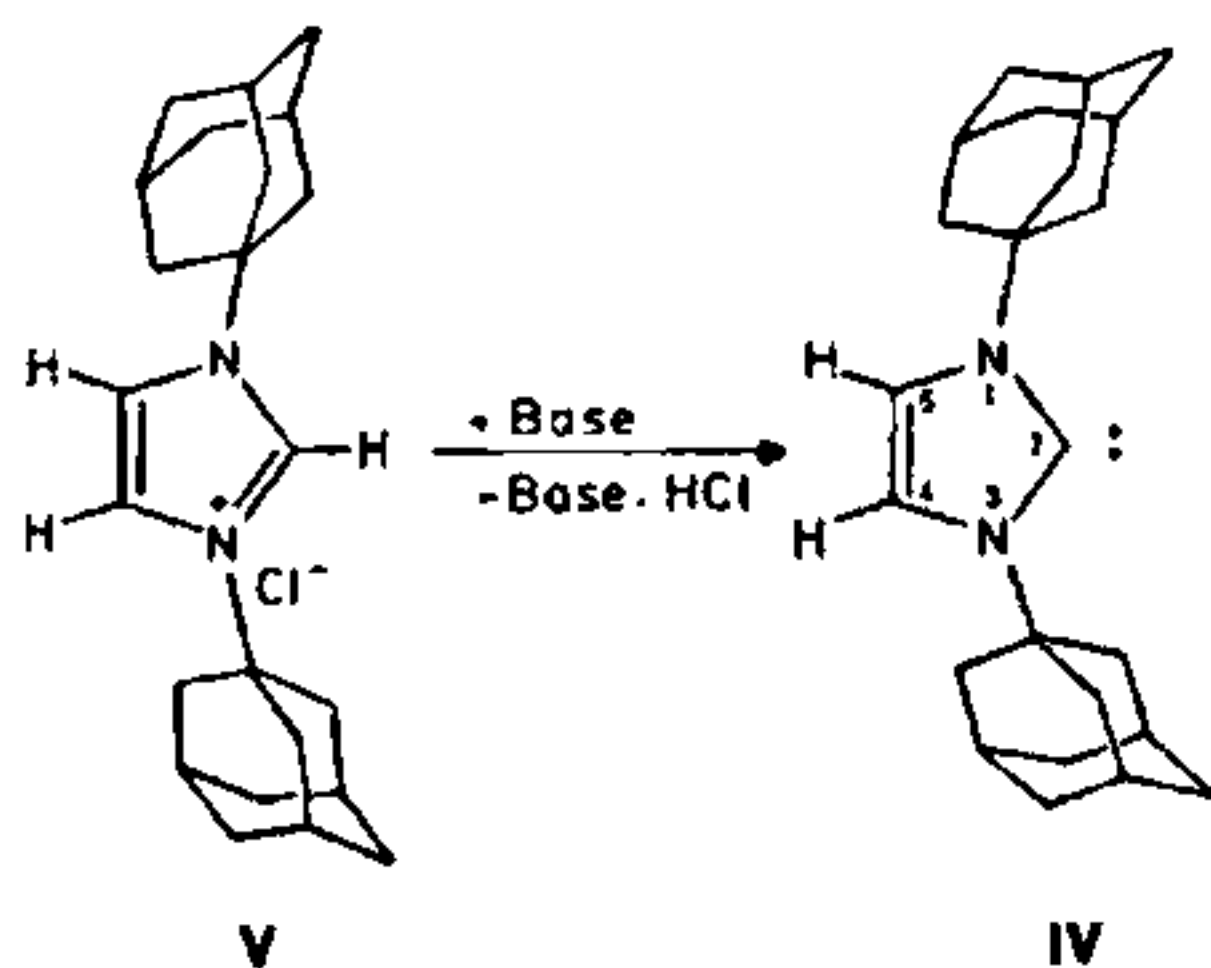
S. S. Krishnamurthy

Carbenes are divalent carbon species (I) long known to organic chemists as transient reactive intermediates. They can be stabilized by complexation with transition metals. The first stable transition-metal-carbene complexes were reported in 1964 by Fischer and co-workers¹ and were of the type II. More than a decade later, the isolation of a transition-metal complex (III) containing the parent methylene carbene (:CH₂)



was accomplished by Schrock² in Du Pont Laboratories, Wilmington, USA. From the same laboratories, Arduengo and coworkers³ now report the isolation of a stable crystalline carbene (IV)—a remarkable discovery, almost a dream come true.

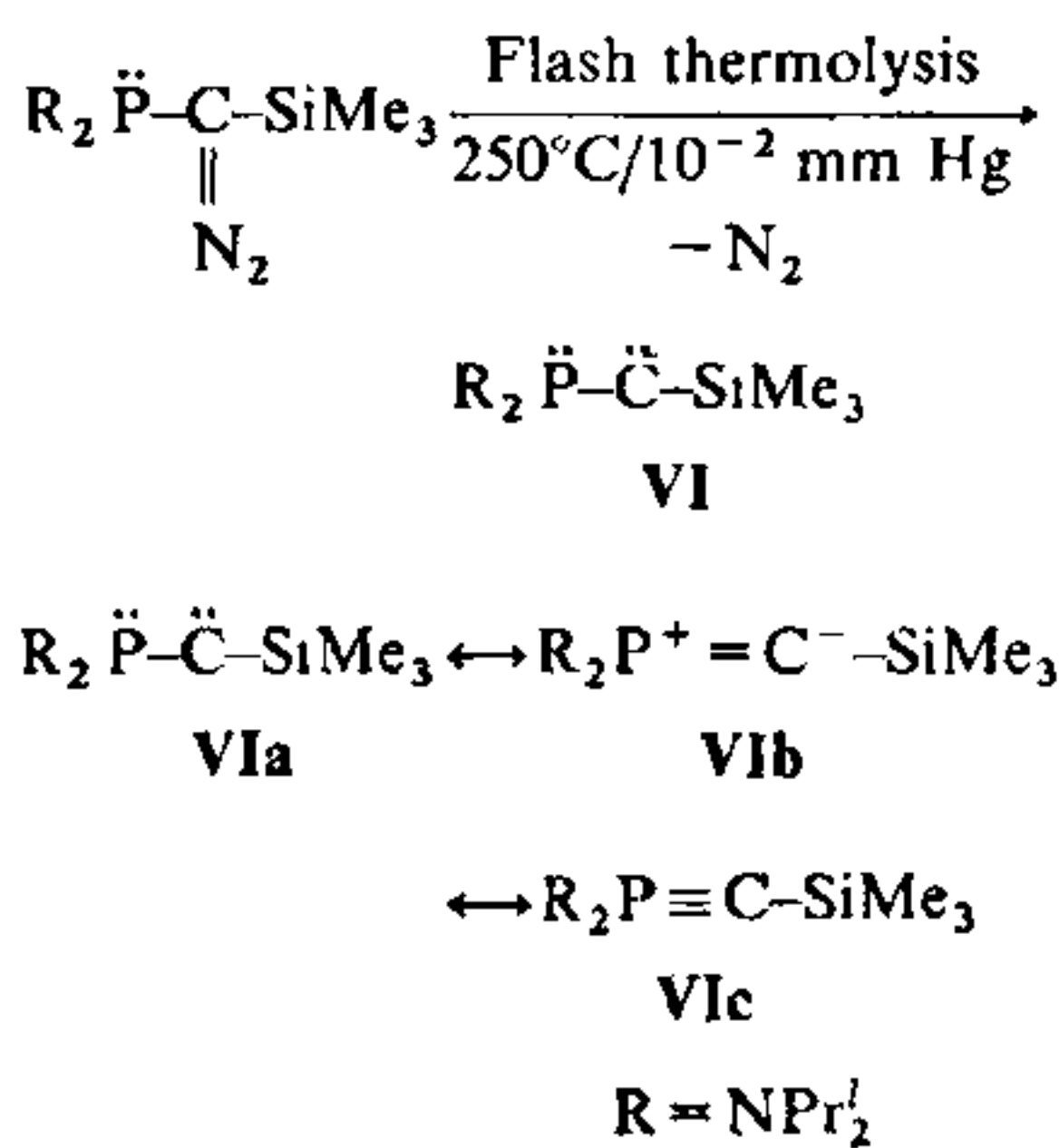
The Arduengo carbene IV was prepared by the deprotonation of 1,3-di-1-adamantylimidazolium chloride V in tetrahydrofuran with catalytic amounts of dimethyl anion (⁻CH₂S(O)CH₃) in the presence of sodium hydride or with potassium *tert*-butoxide:



Carbene IV is a solid with a melting point of 240–241°C. It crystallizes from toluene as colourless rectangular prisms. It is stable in the absence of oxygen and moisture. It has been fully characterized by elemental analyses, IR and NMR

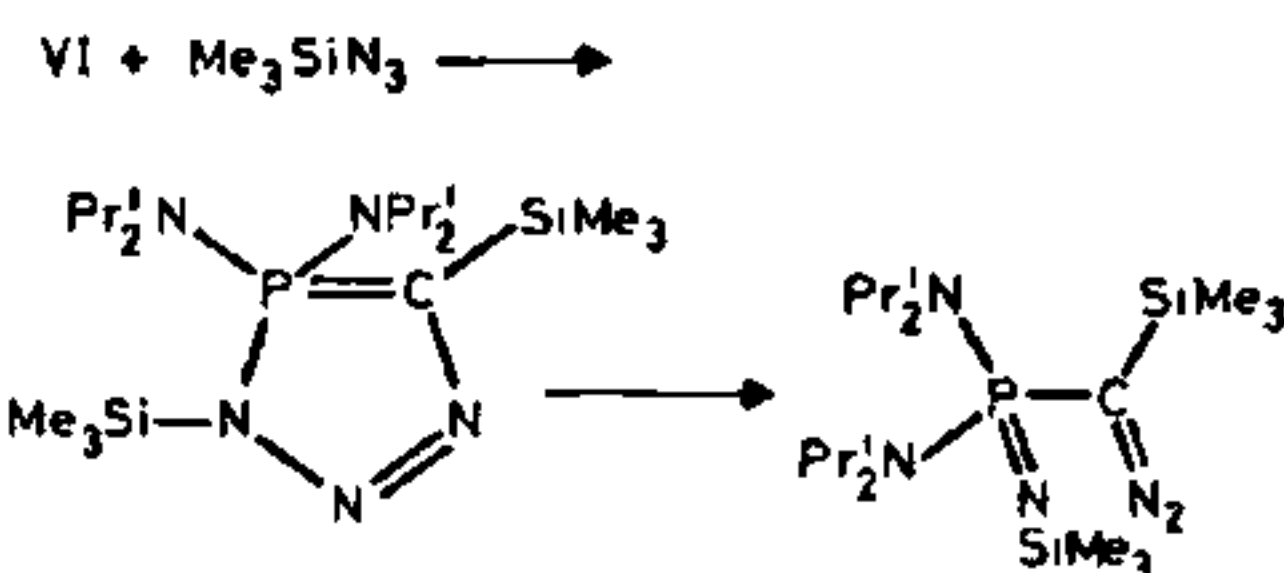
spectra, and by single-crystal X-ray diffraction. The bulky adamantyl substituents impart sufficient kinetic stability to the carbene to permit its isolation. Reinforcing this is an electronic stabilization that stems from π donation from the electron-rich π system (N=C=C-N) into the carbene out-of-plane p -orbital. This type of interaction as a stabilizing factor for nucleophilic carbenes was suggested by Wanzlick⁴ as long ago as 1962. In fact we can regard carbene IV as a Hückel 6- π system with 'aromatic' character, which is also in accord with its 'singlet' ground state⁵.

The Arduengo carbene (IV) is *not*, however, the first 'bottleable' carbene as has been claimed by the Du Pont researchers³. That credit must go to Bertrand and coworkers⁶ of the National Centre for Scientific Research (CNRS) in Toulouse, France. Bertrand's group prepared the first 'bottleable' carbene (VI) by flash thermolysis of a phosphino diazo precursor, as shown below:

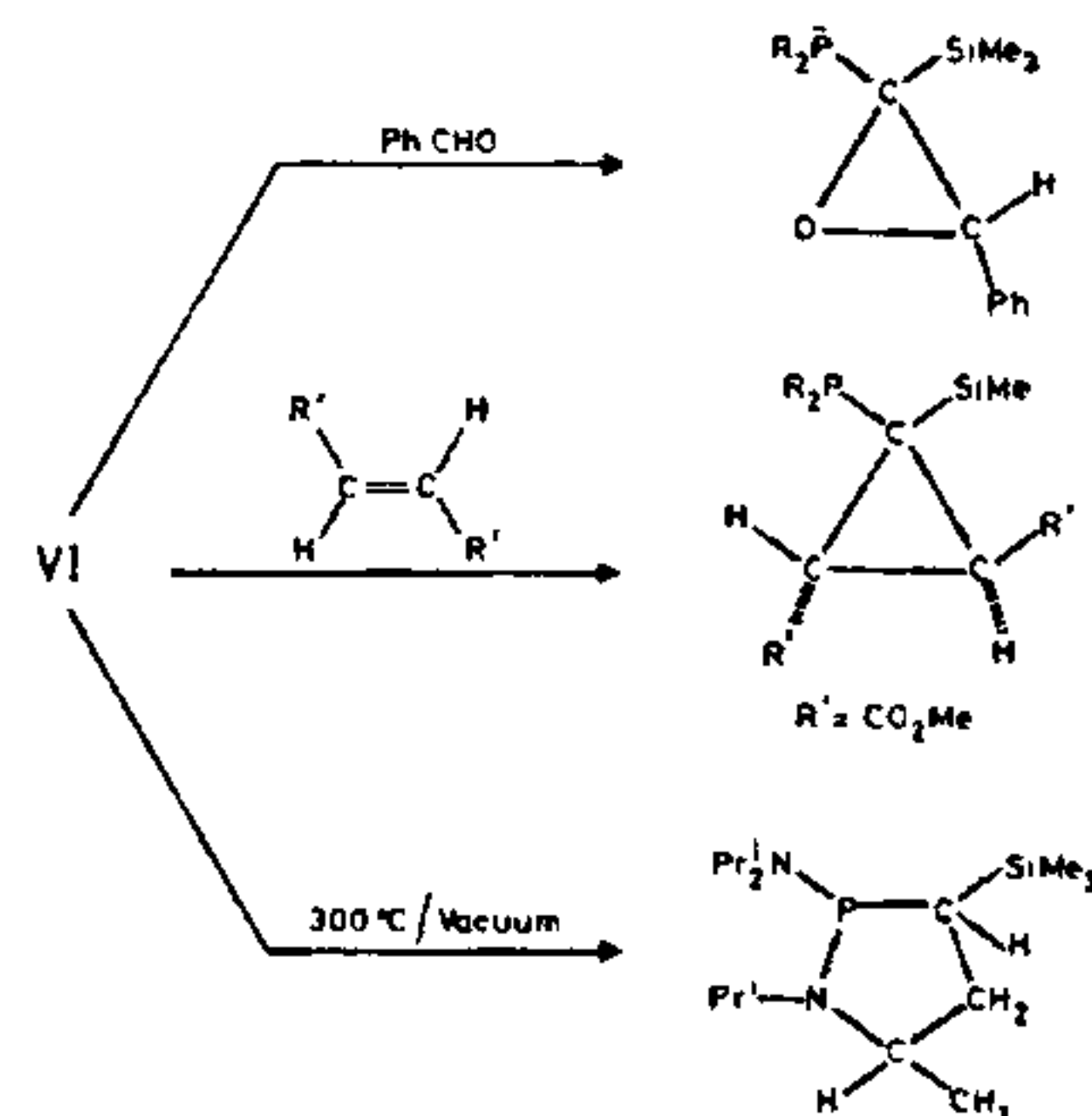


Compound VI has been isolated as a red, oily material (b.p. 75–80 C/10⁻² mm Hg) stable for several weeks at room temperature in benzene solution. Spectroscopically VI behaves as a phosphacetylene (VIa, VIc), while in terms of chemical reactivity it exhibits both carbenic (VIa) and a polarized phosphacetylenic (VIb, VIc) character. The multiple-bond character of VI is borne out by its reaction with Me₃SiN₃, which

is reminiscent of the reaction of azides with alkynes:



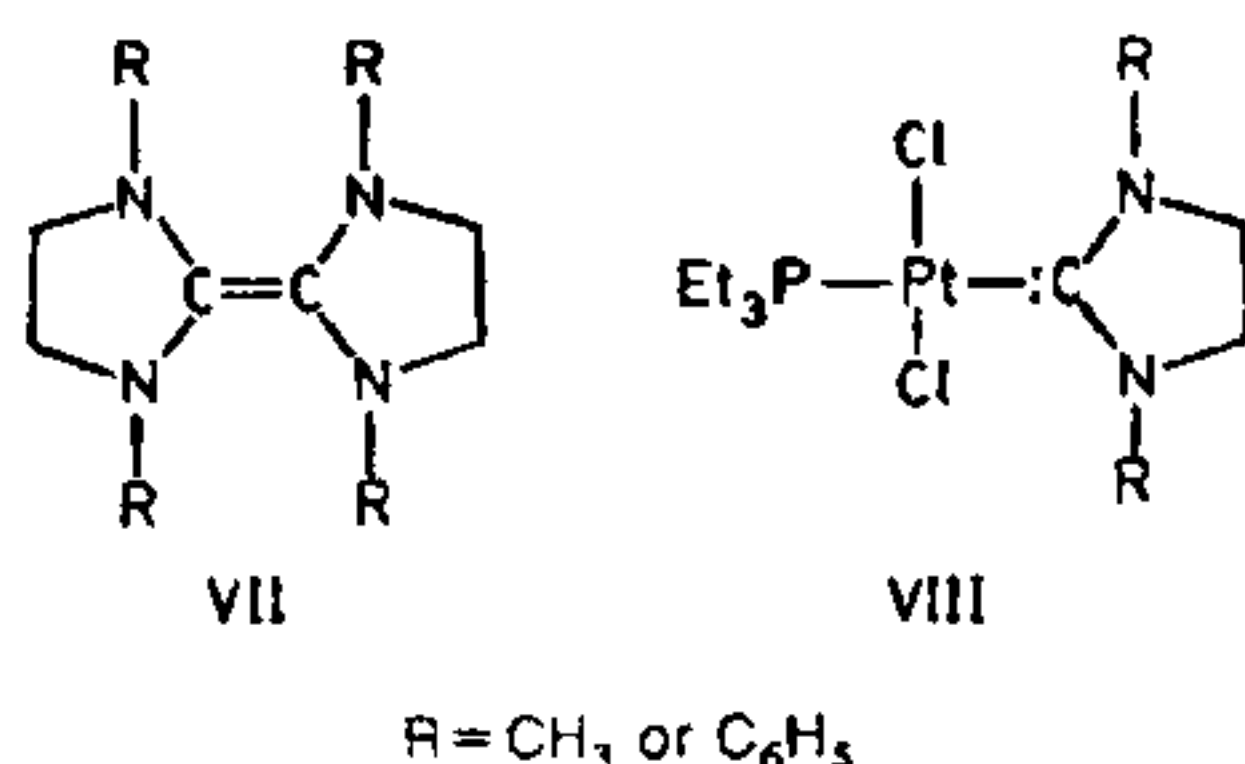
The carbenic character of VI is evident from its reactions with electron-poor olefins and benzaldehyde, which yield a cyclopropane and an oxirane respectively. Compound VI also undergoes an *intramolecular* C-H insertion reaction when heated under vacuum to give a five-membered ring compound (see below).



It is perhaps this *chameleonic* character of VI that led Arduengo *et al.*³ to make no reference to the earlier work of Bertrand and coworkers. This has raised the interesting controversy⁷ of how this omission went unnoticed by the referees and the editor of the *Journal of the American Chemical Society*. It may be noted that the phosphinocarbene VI has a hetero atom (P) with a lone pair adjacent to the carbenic centre, whereas in the Arduengo carbene IV the carbenic centre is flanked by two nitrogen atoms each of which bears a lone pair of electrons. Hence there is more resemblance between the two

carbenes than meets the eye at first glance.

The year 1981 may be regarded as a watershed in the development of the chemistry of multiple-bonded heavier main-group elements. In that year, stable compounds containing a silicon-carbon, silicon-silicon and phosphorus-phosphorus double bonds were isolated and their structures established by single-crystal X-ray diffraction⁸. The isolation of such compounds was made possible by the incorporation of sterically bulky substituents such as adamantyl or 2,4,6-tris(*tert*-butyl) phenyl groups. It is indeed surprising that it took nearly another decade for the isolation of a carbene such as IV, considering the fact that nucleophilic carbene complexes of the type VIII were investigated extensively by Lappert and coworkers⁹ in the University of Sussex, UK in the early seventies. The carbene complexes of type VIII were prepared from the electron-rich olefin precursor VII, which contains an imidazolidine skeleton. Such are the vagaries and vicissitudes of scientific discoveries: often a small step leading to significant pro-



gress may take several years for no apparent reasons.

The isolation of stable, 'bottleable' carbenes such as IV and VI has opened up a vast area of study of the electronic structures and chemical reactivity of this exciting class of compounds.

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First 3D structure of a DNA virus

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The three-dimensional structure of the single-stranded-DNA (ss-DNA) canine parvovirus reported¹ by Rossmann's group at Purdue University, USA, is the first report of a DNA-virus structure determined at near-atomic resolution by X-ray crystallographic procedures.

Parvoviruses cause a number of diseases in animals, including man. Young or unborn animals are specially susceptible to autonomous parvoviruses. Canine parvovirus is a remarkable example of the emergence of a new pathogen. It spread widely within a few months of its first discovery in 1978 and is now endemic in all populations of canids.

Canine parvovirus particles are spherical in shape, approximately 255 Å in diameter, and have a relative mass of 5.5 to 6.2 million daltons. The viral

protein coat encapsulates an ss-DNA genome of about 5000 nucleotides. The number and type of distinct structural proteins in different parvovirus capsids are variable. Canine parvovirus protein coat consists of 60 copies of a combination of three proteins, VP2, VP3 and VP1. In contrast, empty virus particles—devoid of their DNA—contain predominantly VP2. The viral protein subunits are organized in icosahedral symmetry. Despite the complexity of organization of the protein subunits and nucleic acid, the virus is found to form exceptionally well-ordered crystals under favourable conditions. The three-dimensional structure of this virus has now been determined by X-ray diffraction techniques. Rossmann and coworkers have been able to determine this large structure essentially by exploiting the

phase information hidden in the molecular symmetry of the virus particle. Rossmann himself has been responsible for the development of much of the theoretical background required for structure determination or refinement of biological macromolecules by this method.

The final electron-density map computed at 3.25-Å resolution allowed confident tracing of the 584 residues of VP2, except for the amino-terminal 38 residues. The viral coat protein folds into a structure, a part of which resembles the now familiar eight-stranded β-barrel motif found in several ss-RNA plant and animal viruses (Figure 1). The barrel structure not only conforms to the standard topology, but also includes some of the helical intrusions between β-strands found in the structure