CH_2D, CT_2H, etc.) depending on the reagent used ($LiAlH_4$, $LiAlD_4$, or $LiAlT_4$) in the two reduction steps. Thus, the (*pro-S*)-methyl group of (+)-**1** may be specifically identified. Furthermore, reduction of the ester of **10** to a methyl group could yield chrysanthemic acid labeled at that geometric site. Alternatively the "other" methyl groups in **7e** and **10** could be labeled by using the suitably labeled propionates for the reaction with **5**. In addition, the epimerization **11** → **12a** allows for the introduction of hydrogen isotopes at C-2 of (+)-**1**. Thus, multiple labels may be introduced into the chrysanthemate esters, the locations of which are known by "*transcription*" from the original sugar template.

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(2) For detailed discussion of these categories, see ref 1. Briefly, in "cyclic transfer" the chiral component of the target molecule is displayed in linear form so as to facilitate stereochemical correlations with Fischer projections of various sugars. The required segment is then fabricated from a suitable sugar template, excised if necessary therefrom, and incorporated into the target molecule. The majority of examples of the use of carbohydrates in asymmetric syntheses falls into this category although the synthetic targets vary widely as to their degree of modesty[3] and complexity.[4] In cyclic transfer, pyranoid or furanoid modules of the target molecule are prepared by attaching the required stereochemical and functional paraphernalia to an appropriate pyranose or furanose substrate, and than transferring the entire assembly as a discrete entity. Examples falling into this category are our syntheses of avenaciolide[5] and its congeners[6] and the various syntheses of thromboxane.[7]
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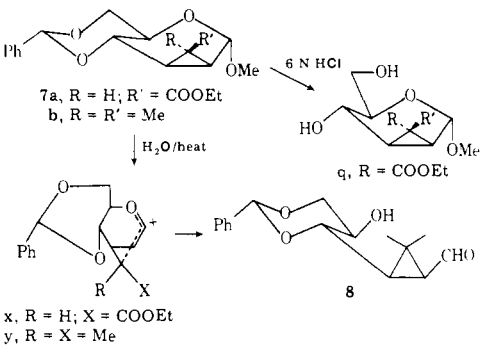
(15) These studies will be described in detail in the full paper.
(16) This compound gave satisfactory elemental and/or mass spectral analysis and spectroscopic (220-MHz, NMR, IR, UV) data.
(17) D. B. Denney, J. J. Vill, and M. J. Boskin, *J. Am. Chem. Soc.*, **84**, 3944 (1962).
(18) In a glass-lined monel pressure reactor, the phosphoropropionate **6** (5 equiv) was added dropwise to a suspension of sodium hydride (5 equiv) in dry dioxane and compound **5** (1 equiv) was then added. After 4 days at 160 °C the starting material was all consumed and the product was recovered by standard procedures.
(19) M. E. Evans, L. Long, and F. W. Parrish, *J. Org. Chem.*, **33**, 1074 (1968).
(20) The ease of hydrolysis of the glycosyl acetal in **7e** is readily rationalized by formation of the intermediate ion y which we had previously named "cyclopropylcarbinyl-oxocarbonium" to depict the two primary modes of stabilization operating therein.[21] In keeping with this rationalization, treatment of **7a** with 6 N HCl left the anomeric center completely untouched, removing instead the benzylidene acetal to give the diol q.[14a] Obviously,



the stabilization of the positive charge is not favored in the ion x because of the electron-withdrawing nature of the carboxylate group. On the other hand, the two methyl groups in y give added stabilization to the ion, thereby facilitating the formation of **8**.
(21) B. K. Radatus and B. Fraser-Reid, *J. Chem. Soc., Perkin Trans. 1*, 1872 (1975), and references cited therein.
(22) H. House, "Modern Synthetic Reactions", W. A. Benjamin, Menlo Park, Calif., 1972, p 701 ff.
(23) We are grateful to Professor Leslie Crombie for an authentic sample of (+)-**1**.
(24) Holder of a NRC (Canada) predoctoral studentship, 1978-1979.

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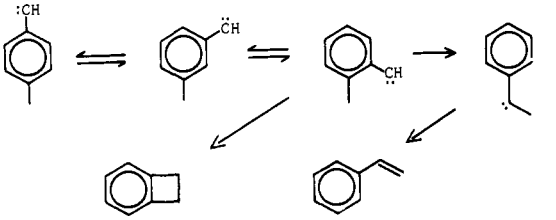
The Carboranylcarbene Rearrangement[1]

Sir:

The interconversion of substituted phenylcarbenes in the gas phase reveals itself through intramolecular trapping.[2] For instance, *p*-tolylcarbene gives benzocyclobutene and styrene through a series of intramolecular rearrangements passing over the meta and ortho isomers.



The analogy between benzene and the icosahedral carboranes (dicarba-*closo*-dodecaborane(12)s) has been often made.[3] It occurred to us that a question worth probing was the extent of stabilization conferred on a divalent carbon by an adjacent carborane polyhedron. To what extent would the reactions of phenylcarbene and diphenylcarbene be mimicked by those of carboranylcarbene and dicarboranylcarbene? How similar would the three-dimensional carborane cage compounds be to their more classically "two-dimensional" aromatic relatives?[4a] Although we are currently investigating intermolecular solution chemistry,[4b] we also conceived of examining the ability of the carborane cage to act as a conduit for the passage of divalent carbon from one position to another, much as does a benzene ring.[2,5] It is this reaction that we report here.

The required diazo compound **3c** was produced most conveniently from 1-vinyl-*o*-carborane (**1**)[6] by a sequence involving methylation to give 1-vinyl-2-methyl-*o*-carborane (**2**) and ozonolysis to give aldehyde **3a** which could be converted in unexceptional steps into the tosylhydrazone salt **3b**. Dry distillation at 60–100 °C (0.05 Torr) yielded diazo compound **3c** (diazo band, 2080; B-H, 2590 cm^{-1}).

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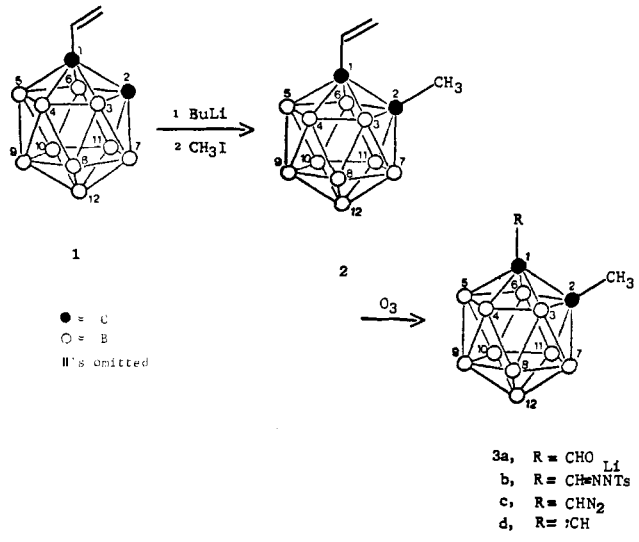
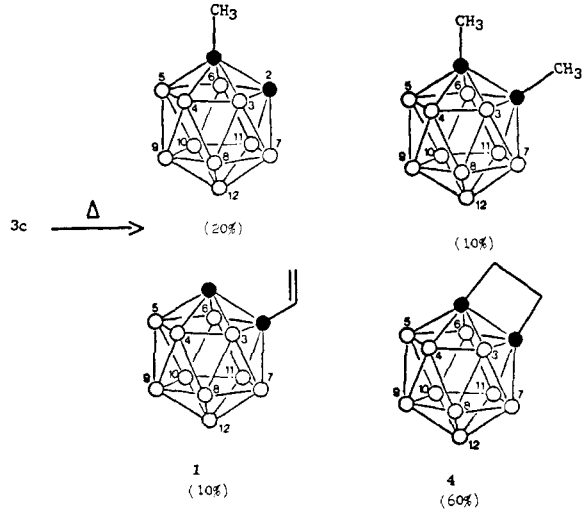
As direct flash vacuum pyrolysis of **3b** gave only small amounts of carboranes and large amounts of an unidentified



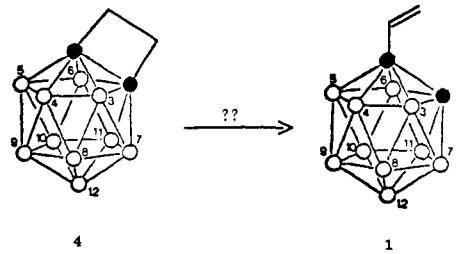
sulfone and other products, we turned to flow pyrolysis of diazo compound **3c** as the source of carbene **3d.** At 10^{-3} Torr with the hot tube maintained at 400–500 °C, only carboranes were produced from pyrolysis of **3c.** The method was not efficient, as much residue (largely azine) remained after evaporation through the hot tube, but it did cleanly produce products easily separable by simple gas chromatographic columns. The reaction yielded volatile products in ~50% yield based on pyrolyzed diazo compound.



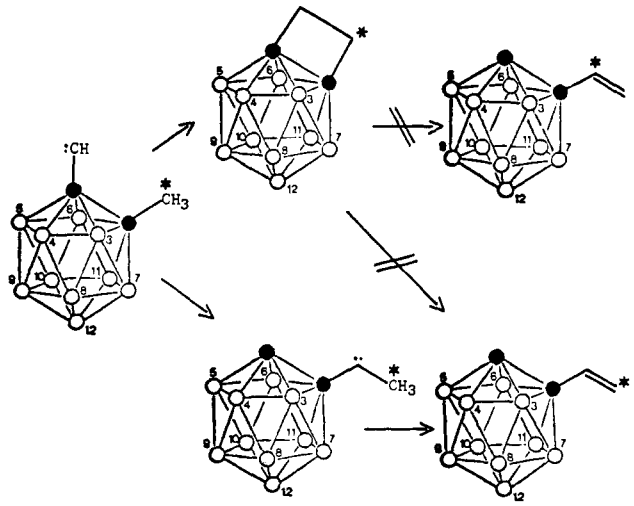
The products formed include 1-methyl-*o*-carborane, 1,2-dimethyl-*o*-carborane, and 1-vinyl-*o*-carborane (**1**), which were compared with authentic samples. A new compound, the carborane analogue of benzocyclobutene (**4**) also appears and is the major product. 1-Methyl-*o*-carborane is most likely formed by base-induced cleavage on tosylhydrazone salt formation, but the other compounds have no such trivial source. 1,2-Dimethyl-*o*-carborane is apparently a product of hydrogen abstraction by carbene **3d.** This is an uncommon but precedented reaction of carbenes[7] and this product appears here in unusually high yield. "Cyclobutene" **4** appears as a dividend in this reaction. Produced most likely by a simple carbon–hydrogen insertion of carbene **3d,** it represents the first example of a carborane fused to a four-membered ring. The related cyclopentene is known,[8] and several six-membered-ring compounds have been isolated,[3] but **4** now represents the current lower limit for carbocyclic rings fused to an *o*-carborane.[9] The structure of **4** (mp 261 °C, sealed tube) was secured by an examination of spectra. High-resolution mass spectroscopy established the composition as $B_{10}C_4H_{14}$. The ^1H NMR spectrum showed but a single peak at δ 2.9 ($CDCl_3$) for the carbon-bound hydrogens (compare benzocyclobutene at δ 3.0). Similarly, a single peak appears in the ^{13}C NMR spectrum (C_3D_6O) for the exo-polyhedral carbon at 36.39 ppm (benzocyclobutene, 29.4 ppm),[10a] along with a signal at 79.68 ppm for the cage carbons.[10b] As expected, the undecoupled signal for the methylene carbon appears as a triplet.

The most interesting product is 1-vinyl-*o*-carborane, analogous to the styrene produced from the rearrangement of tolylcarbene to methylphenylcarbene.[2] If this formal structural similarity carries over to the mechanistic details, then the divalent carbon has become incorporated into the polyhedral frame and an originally polyhedral carbon has been extruded to become the new divalent carbon. A determination of the mechanistic details awaits further labeling experiments. One further similarity to phenylcarbene chemistry appears on photolysis of **3c** in solution. Although **4** is formed, there is no 1-vinyl-*o*-carborane produced.

The isolation of **4** allows an important mechanistic possibility to be eliminated. It is known that at high temperature benzocyclobutene produces styrene.[11] One is obliged to ask if **4** could be the source of 1-vinyl-*o*-carborane. Prolonged heating of **4** at 350 °C in solution results in no change. However, this



control is faulty, as **4** is produced by carbon–hydrogen insertion in the gas phase where the excess energy of this exothermic reaction may not be easily dissipated. Simple heating in solution may not be adequate to reproduce "hot" enough **4.** Accordingly, we have decomposed **3c** labeled with ^{13}C in the methyl group. If a carbene rearrangement is responsible for the formation of 1-vinyl-*o*-carborane, then the label must reside exclusively in the terminal position. If **4** intrudes as an intermediate between **3d** and product, both olefinic carbons must be labeled. The ^{13}C spectrum of 1-vinyl-*o*-carborane is known[10b] and the two olefinic carbons appear at 122.4 and 132.7 ppm. No assignment is made in ref 10b, but styrene has related signals at 112.3 (terminal) and 135.8 (internal) ppm.[12] The labeled product formed in our reaction shows a single enhanced peak at 122.8 ppm. Further confirmation that



this represents the *terminal* vinyl carbon comes from the undecoupled spectrum in which this peak appears as a triplet. Thus **4** is not involved in the formation of the vinyl compound.

The detailed mechanism of rearrangement remains to be worked out as do the structures of any possible intermediates analogous to those postulated in the phenylcarbene rearrangement. Although even gross questions remain (can the carbene rearrangement traverse borons on its way to stability?), it is clear that one of our initial questions has been answered—the *o*-carborane polyhedral frame can act as a transport system for a carbene. To this extent the analogy between benzene and its three-dimensional cousin holds.

Acknowledgment. We thank Professor Paul v. R. Schleyer for stimulating our interest in carboranes and for convincing us that carboranes are tractable compounds.

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(4) (a) Preliminary results of S. Chari indicate that, at least for 1-carboranylcarbene in solution, they are. (b) Chari, S., preliminary results.
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(7) Generation of phenylcarbene in the gas phase gives small amounts of toluene for instance: Pacala, L. A.; Font, J.; Hollowood, F., unpublished results.
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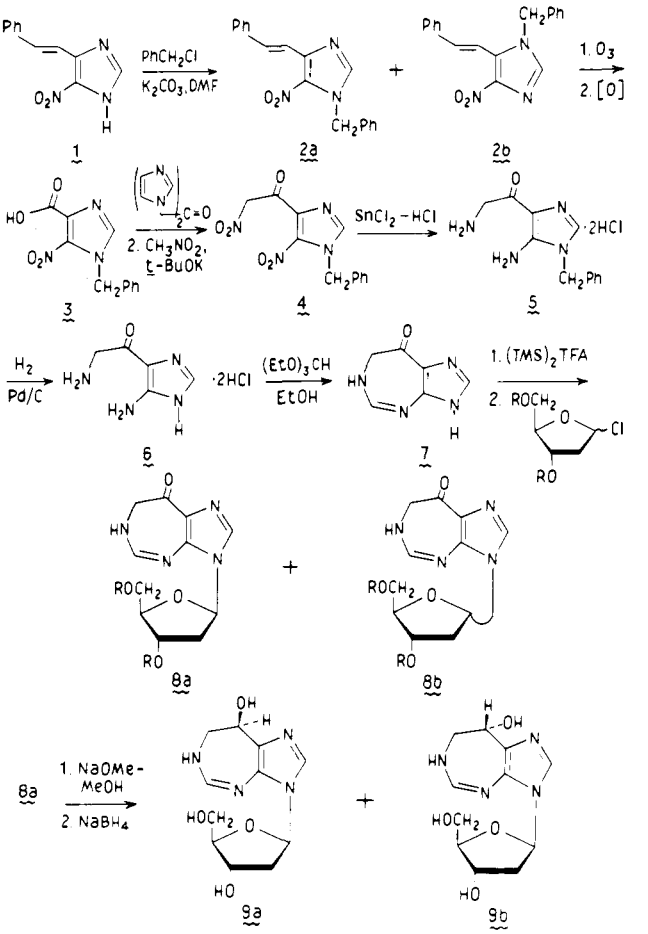
A Total Synthesis of Pentostatin,[1] the Potent Inhibitor of Adenosine Deaminase

Sir:

Pentostatin[1-3] (**9a**) has been shown to be the most potent inhibitor known[4] for adenosine deaminase (adenosine aminohydrolase, E.C. 3.5.4.4), the enzyme responsible for the N^6-deamination of adenine nucleosides. This compound has generated considerable interest as a potentially useful drug for use in combination with certain adenine nucleosides, especially ara-A,[5] whose antiviral and antitumor properties[6-9] are greatly enhanced, both in vitro and in vivo, in the presence of miniscule amounts of pentostatin. Moreover, pentostatin has alone demonstrated a most unique activity as an immunosuppressant,[10,11] acting to prevent the maturation of lymphocytes to limit their role in the immune response.

Herein is described a total, practical synthesis of pentostatin from an available imidazole precursor. In attacking the problem of a total synthesis, it was early recognized that the problem was essentially twofold: (1) developing a synthesis of the unique, chiral, five- and seven-membered fused-ring heterocyclic aglycone, and (2) devising a scheme whereby the fragile 2-deoxy sugar could be efficiently incorporated in the synthetic sequence.[12]



Toward developing a synthesis of the heterocyclic moiety, a diamine **6** was envisioned as a reasonable precursor for the 1,3-diazepinone **7**, the latter being formed via insertion of a one-carbon fragment into **6**. To this end, the chemistry evolved in the following manner. 5-Nitro-4-styrylimidazole (**1**), prepared by an improvement in the published procedure[13] from the condensation of 4-methyl-5-nitroimidazole and benzaldehyde in base (>80%), afforded, upon benzylation with benzyl chloride in *N,N*-dimethylformamide–potassium carbonate, an ~75:25 mixture (>95%) of the benzyl isomers **2a** and **2b**, respectively.[14] Ozonolysis of the mixture of **2a** and **2b**, followed by oxidation of the ozonide with performic acid, gave the crystalline carboxylic acid **3**, isolated directly from the reaction mixture: 75%; mp 155–156 °C dec; λ_{max}^{MeOH} 290 nm (ϵ 4350); ν(C=O) 1736 cm^{-1}; NMR δ 5.50 (s, 2, $-CH_2Ph$), 7.37 (m, 5, aryl), 8.17 (s, 1, 2H).[15] Elaboration of the $-CH_2N<$ portion of the molecule, usually a most difficult process, was achieved in a straightforward manner by C-acylation of potassium methanenitronate, using the imidazoyl derivative of the acid **3**, a new process[16] found to be exceedingly useful for a general synthesis of α-nitro ketones. Data for **4**: 75% yield; mp 107–108.5 °C; λ_{max}^{MeOH} 298 nm (ϵ 4900); ν(C=O) 1642 (NO_2), 1561 cm^{-1}; NMR δ 5.61 (s, 2, $-CH_2Ph$), 6.27[17a] (s, 2, $-CH_2NO_2$), 7.22–7.46 (m, 5, aryl), 8.42 (s, 1, 2*H*). Reduction of the nitro groups on **4** was cleanly effected using 6 equiv of tin(II) chloride in concentrated hydrochloric acid to give the *N*-benzyl diamine dihydrochloride **5** (74%; mp 155 °C dec; $\lambda_{max}^{H_2O}$ 303 nm (ϵ 13 200); ν(C=O) 1620 cm^{-1}; NMR δ 4.14 (d, 2, J = 6.0 Hz, $-CH_2NH_2$), 5.33 (s, 2, $-CH_2Ph$), 7.36

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