J. Am. Chem. Soc. **1982**, *104*, 5239-5240

cytochrome *P*-450[17] and of effecting DNA degradation via aerobic or anerobic activation. It seems reasonable to conclude that deglycobleomycin represents an attractive lead structure for synthetic modification, as well as a species that can help to define the range of metal-coordination geometries consistent with the expresion of bleomycin-like activity. The ability of deglycobleomycin to inhibit the growth of transformed mammalian cells via degradation of intracellular DNA is under active investigation.

Acknowledgment. We thank Professor Iwao Tabushi for a helpful discussion during the course of this work. This investigation was supported by PHS Research Grants CA27603 and CA-29235.

Registry No. 1a, 82691-97-2; deglycobleomycin A_2, 78193-35-8; **2a**, 82691-98-3; **2b**, 82691-99-4; **3**, 82692-00-0; **3**·NPS derivative, 82692-06-6; **3**·HCl, 82692-07-7; **4**, 82692-01-1; **4** di *N*-BOC, 82692-02-2; **4** BOC-pyrimidoblamic acid, 82692-05-5; N^{α},N^{im}-di-*tert*-butoxycarbonyl-L-erythro-β-hydroxyhistidine, 82692-03-3; benzyl (2*S*,3*S*,4*R*)-4-amino-3-hydroxy-2-methylvalerate, 82692-04-4; BOC-pyrimidoblamic acid, 75452-30-1; 2′-[2-(trifluoroacetamido)ethyl]-2,4′-bithiazole-4-carbonyl chloride, 76275-92-8; 3-(methylthio)propylamine, 4104-45-4; 2′-[2-(*tert*-butoxycarbonylamino)ethyl]-4-[3-(methylthio)propylaminocarbonyl]-2,4′-bithiazole, 78175-35-6; 2′-(2-aminoethyl)-4-[3-(methylthio)aminocarbonyl]-2,4′-bithiazole, 78175-36-7; 2,4-dinitrophenyl-*N*-(*o*-nitrophenylsulfenyl)threoninate, 82730-85-6; Fe(III), 20074-52-6; Cu(II), 15158-11-9; O_2, 7782-44-7.

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[1.1.1]Propellane[†]

Kenneth B. Wiberg* and Frederick H. Walker

Department of Chemistry, Yale University
New Haven, Connecticut 06511

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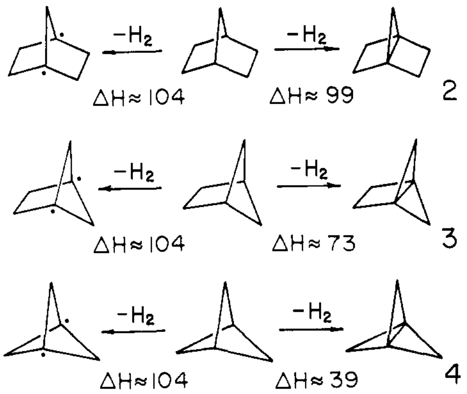
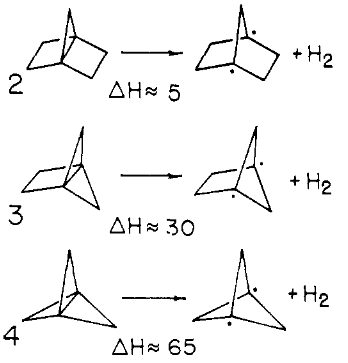
The propellanes having three small rings have been of considerable recent interest. Besides being the subject of a number of theoretical calculations,[1-3] both a [2.2.2]propellane (**1**) derivative[4] and the [2.2.1]propellane (**2**)[5] have been prepared. We have been interested in the possibility of preparing the [2.1.1]- (**3**) and [1.1.1]propellanes (**4**). In this connection, we have estimated the enthalpies of hydrogenolysis of **2**–**4** via extended basis set (6-31G*) ab initio calculations.[6] We may also estimate the energies of converting the bicycloalkanes to the corresponding bridgehead diradicals by using an approximate C–H bond dissociation energy of 104 kcal/mol.[7]



Scheme I



The strain energies of **2**–**4** were found to be approximately equal, whereas the strain energies of the corresponding bicycloalkanes change markedly.[8] This leads to the large difference in the enthalpies of hydrogenolysis. The formation of the propellanes from the corresponding bridgehead substituted bicycloalkanes[5] is essentially the reverse of this reaction, and the calculations suggest that this type of process should be considerably more facile for **4** than for either **2** or **3**.

Although the values are approximate, the energies of dissociating the central bond of the propellanes are quite instructive (see Scheme I).[9] The [4.1.1]-,[10] [3.1.1]-,[11] and [2.2.1]propellanes[5] undergo rapid polymerization, presumably via a free-radical process. Our calculations suggest that [1.1.1]propellane will be relatively stable and unreactive. The activation energy for initiating a free-radical polymerization should be related to the energy of forming the diradical and will be relatively high for **4**. Similarly, the addition of a free radical to **4** will be much less exothermic than the corresponding reactions of **2** and **3**. The thermolysis of **4** also may have a relatively high activation energy since the energy of dissociating one of the side bonds also should be on the order of 60 kcal/mol.[12] Thus, **4** may be considerably less reactive than

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[†] Dedicated to Professor William v. E. Doering on his 65th birthday.

(1) Newton, M. D.; Schulman, J. M. *J. Am. Chem. Soc.* **1972**, *94*, 773.
(2) Stohrer, W.-D.; Hoffmann, R. *J. Am. Chem. Soc.* **1972**, *94*, 779.
(3) Newton, M. D.; Schulman, J. M. *J. Am. Chem. Soc.* **1972**, *94*, 4391.
(4) Eaton, P. E.; Temme, G. H., III *J. Am. Chem. Soc.* **1973**, *95*, 7508.
(5) Wiberg, K. B.; Walker, F. H.; Michl, J. *J. Am. Chem. Soc.* **1982**, *104*, 2056.

(6) Newton and Schulman[1] calculated the energies of bicyclo[1.1.1]pentane and [1.1.1]propellane with partial geometry optimization (the gradient method was not then available) using the 4-31G basis set. They found a central C–C bond length of 1.600 Å. With complete geometry optimization using the 6-31G* basis set, we obtain for bicyclopentane, $E = -193.90568$ hartrees, and for [1.1.1]propellane, $E = -192.69106$ hartrees, with a central bond length of 1.543 Å. Polarization functions were needed to properly describe the propellane. The reported enthalpy changes include corrections for zero-point energies and the change in enthalpy on going from 0 to 298 K. The details of these calculations will be reported separately.

(7) The bridgehead C–H bond dissociation energies are known to be larger than for normal tertiary bonds and larger even than for secondary C–H bonds. Thus, norbornane (Kooyman, E. C.; Vegter, G. C. *Tetrahedron* **1958**, *4*, 382) and bicyclo[2.1.1]hexane (Srinivasan, R.; Sonntag, F. I. *J. Am. Chem. Soc.* **1967**, *89*, 407) are halogenated exclusively at the methylene positions, and bicyclo[1.1.1]pentane (Wiberg, K. B.; Williams, V. Z. *J. Org. Chem.* **1970**, *35*, 369) has been found to be much less reactive than cyclohexane in halogenation. We have assumed that the bridgehead C–H bond dissociation energies are similar to that for methane (104 kcal/mol: Chupka, W. A. *J. Chem. Phys.* **1968**, *48*, 2337).

(8) Wiberg, K. B.; Wendoloski, J. *J. Am. Chem. Soc.* **1982**, *104*, 0000.

(9) Our conclusions concerning [1.1.1]propellane were in part anticipated by Newton and Schulman,[1] who calculated the energy of the triplet diradical derived from **4** to lie about 51 kcal/mol above the ground state. Similarly, they calculated the triplet formed by cleaving one of the side bonds to lie about 30 kcal/mol above the ground state. One would expect the singlet and triplet diradicals to have similar energies. Inclusion of polarization functions in the calculations will presumably increase the values by up to 20 kcal/mol (the extra stabilization of the [1.1.1]propellane by including these functions).

(10) Hamon, D. P. G.; Trenerry, V. C. *J. Am. Chem. Soc.* **1981**, *103*, 4962. Szeimies-Seebach, U.; Harnish, J.; Szeimies, G.; Meerssche, M. V.; Germain, G.; Declerq, J. P. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 848. Szeimies-Seebach, U.; Szeimies, G. *J. Am. Chem. Soc.* **1978**, *100*, 3966.

(11) Gassman, P. G.; Proehl, G. S. *J. Am. Chem. Soc.* **1980**, *102*, 6862. Mlinaric-Majerski, K.; Majerski, Z. *Ibid.* **1980**, *102*, 1418.

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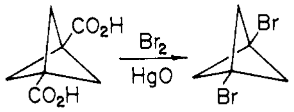
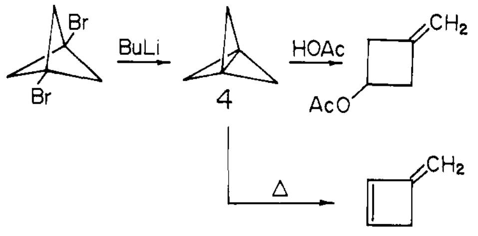
[2.2.2]propellane (**1**), which has a half-life of only an hour at 20 °C.[4]

We are now able to present a striking confirmation of these conclusions. 1,3-Dibromobicyclo[1.1.1]pentane (eq 1) was prepared from bicyclo[1.1.1]pentane-1,3-dicarboxylic acid, described by Applequist and Wheeler,[13] via a Hunsdiecker reaction (mp 119.5–120.5 °C; NMR ($CDCl_3$) δ 2.57 (s); Anal. C, H, Br). The product of the reaction of the dibromide with *tert*-butyllithium in pentane–ether was examined by GC (15 ft, 20% Apiezon L, 50 °C, 50 mL/min). Besides the peaks due to solvent and *tert*-butyl bromide, there appeared only one component, having a retention time of 3.6 min.



The ^1H NMR spectrum of this material had only a singlet at δ 2.06 ($CDCl_3$ solution). The ^{13}C NMR spectrum had bands at 1.0 ppm (quaternary carbon) and 74.2 ppm (methylene carbon, $J_{^{13}C-H}$ = 165 Hz). The mass spectrum had a peak at m/e = 66, suggesting that it is C_5H_6. It reacted with acetic acid to form 3-methylenecyclobutyl acetate.[14] In the gas phase, it rearranged with an approximate half-life of 5 min at 114 °C to give 3-methylenecyclobutene[15] (eq 2).



These data show that the compound is [1.1.1]propellane (**4**). Addition of a proton may give either the bicyclo[1.1.1]pentyl cation or the bicyclo[1.1.0]butyl-1-carbinyl cation. We have previously shown that both ions will give the 3-methylenecyclobutyl cation.[16,17] The thermolysis product may be derived by cleavage to 3-methylenecyclobutylidene (the reverse of adding a carbene to an alkene) followed by a hydrogen migration to give 3-methylenecyclobutene.[18]

The downfield shift of the methylene protons may appear surprising since they are formally part of a cyclopropane ring. However, one of the methylene protons of bicyclobutane appears at relatively low field (δ 1.5),[17] and this trend may easily be accentuated in **4**. The ^{13}C NMR spectrum is in accord with the observation that the bridgehead carbon of bicyclo[1.1.0]butane is shifted upfield and the methylene carbon is shifted downfield in comparison to other cycloalkanes.[19] The infrared spectrum (CS_2 solution) had strong bands at 3069, 3006 (CH stretch), 1093 (CCH bend), and 603 cm^{-1} (antisym CC stretch), which may be compared with the corresponding bands of [2.2.1]propellane (3056, 2997, 1044, 530 cm^{-1}),[5] [2.1.1]propellane (3050, 2995, 1101, 574 cm^{-1}),[20] and bicyclo[1.1.0]butane (3055, 2954, 1113, 735 cm^{-1}).[21] A very intense band occurring between 500–600 cm^{-1} appears to be characteristic of the small ring propellanes.[5]

Thus, despite the pessimism previously expressed concerning the preparation and stability of **4**,[22] it is the most easily prepared and the most stable of compounds **1**–**4**. The properties and reactions of **4** continue to be investigated. The nature of the central bond is of special interest with regard to theories of chemical bonding. Localized orbital calculations suggest that it has a bond order close to zero.[1] How can this be reconciled with an apparent bond dissociation energy close to that of the π bond in ethylene? This question is being explored. In addition, the energy changes on going from the propellanes to their singlet diradicals are being calculated by using the GVB[23] formalism which permits correct dissociation.

Acknowledgment. This investigation was supported by National Science Foundation Grant No. CHE-81-21421. We also acknowledge the support of the NSF Northeast Regional NMR facility at Yale University, which is funded by Grant No. CHE-79-16210 from the Chemistry Division of NSF. We especially appreciate the invaluable assistance of S. Kass in obtaining the NMR spectra.

Registry No. 4, 35634-10-7; bicyclo[1.1.1]pentane-1,3-dicarboxylic acid, 56842-95-6; 1,3-dibromobicyclo[1.1.1]pentane, 82783-71-9; 3-methylenecyclobutyl acetate, 18218-27-4; 3-methylenecyclobutene, 27538-13-2.

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[12] For bicyclo[1.1.0]butane, ΔH_f = 51.9 kcal/mol (Wiberg, K. B.; Fenoglio, R. A. *J. Am. Chem. Soc.* **1968**, *90*, 3395) and with a normal methylene equivalent of −4.9 kcal/mol, $\Delta H_f \sim$ 47 kcal/mol for 1-methylbicyclobutane. A C–H bond dissociation energy of ~104 kcal/mol at the bridgehead and ~96 kcal/mol at the methyl group was used.

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[14] Authentic 3-methylenecyclobutyl acetate was prepared from 3-methylenecyclobutanol; NMR (270 MHz, $CDCl_3$) δ 2.06 (s, 3 H), 2.75–2.86 (m, 2 H), 3.00–3.11 (m, 2 H), 4.89 (quint, 2 H, J = 2 Hz), 5.02 (quint, 1 H, J = 7 Hz). Cf.: Applequist, D. E.; Fanta, G. F. *J. Am. Chem. Soc.* **1960**, *82*, 6393. Nishimura, A.; Kato, H.; Ohta, M. *Ibid.* **1967**, *89*, 5083.

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[18] Methylenecyclobutane has ΔH_f = 29.1 kcal/mol (Good, W. D.; Moore, R. T.; Osborn, A. G.; Douslin, D. R. *J. Chem. Thermodyn.* **1974**, *6*, 303), and this places the 3-methylenecyclobutylidene at $\Delta H_f \sim$ 120 kcal/mol. For the [1.1.1]propellane, $\Delta H_f \sim$ 89 kcal/mol, and with an activation energy of about 30 kcal/mol, the activated complex for the thermolysis has an energy close to that of the carbene. It may be possible to obtain some [1.1.1]propellane from the carbene in competition with hydrogen migration. This will be examined.

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Three-Coordinate Binuclear Copper(I) Complex: Model Compound for the Copper Sites in Deoxyhemocyanin and Deoxytyrosinase

Kenneth D. Karlin,* Yilma Gultneh, John P. Hutchinson, and Jon Zubieta

Department of Chemistry and
Center for Biological Macromolecules
State University of New York at Albany
Albany, New York 12222

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Tyrosinase and hemocyanin are metalloproteins that contain electronically coupled binuclear copper active sites.[1-4] These are often classified together with the binuclear sites in laccase, ascorbate oxidase, and ceruloplasmin as type 3 copper.[5] Both proteins are known to interact with dioxygen as part of their physiological function: hemocyanins[1,6] function as O_2 carriers in

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