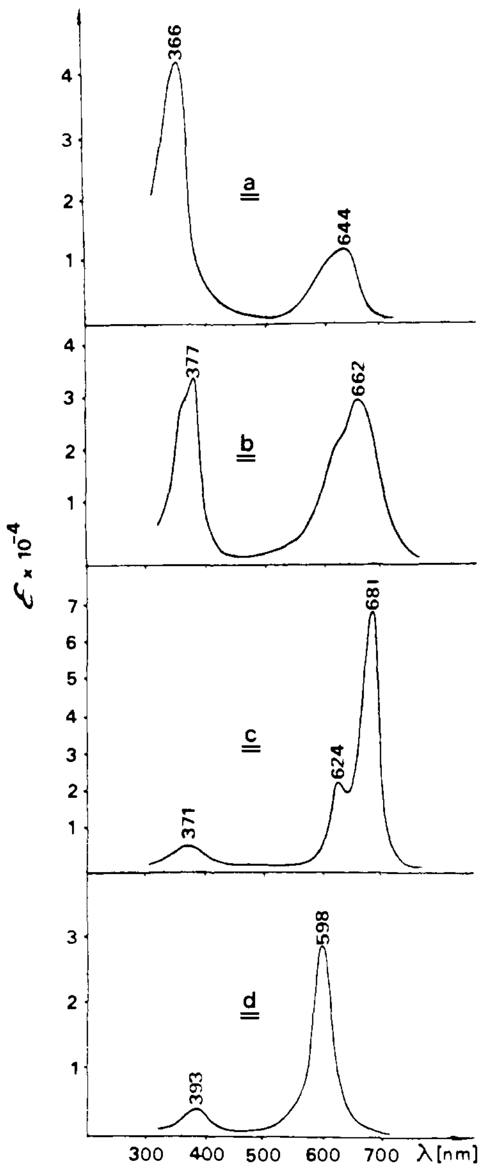


**Figure 1.** UV-vis spectra in $CH_2Cl_2$: (a) biliverdin **1**; (b) biliverdin **4**; (c) biliverdin **5**; (d) biliverdin **6**. The inflexions in the spectra of **4** and **5** are due to the presence of several conformers (see text).

the C3 side chain into the vicinity of N-22, but this requires a light-driven isomerization.

The $^1H$ NMR spectra of **4-6** revealed new features about extended biliverdins. The COSY and NOESY correlations (at 500 MHz) showed that the meso bridges which are not kept in the anti conformations by the rigid seven-membered rings retain their energetically favored *Z*-syn conformations (see Scheme I). While the $^1H$ NMR spectra of the helical-shaped biliverdins **1-3** are concentration independent, strong shifts were observed in the meso and vinyl signals of **4** when going from a concentrated ($10^{-2}$ M) to a dilute solution ($10^{-4}$ M).[12] This effect can be attributed to the presence in solution of associated (or stacked) forms, a fact which is well known in porphyrin chemistry.[17] A second feature of the $^1H$ NMR spectra of the extended biliverdins **4-6** is their temperature dependence, a property which is absent in the helical-shaped biliverdins **1-3**. In $CDCl_3$ at 21 °C, the $^1H$ NMR spectra of **4** showed broad signals, especially at the meso-H. At −80 °C a well-resolved $^1H$ NMR spectrum corresponding to a mixture of different conformers was obtained, where six meso-H and five methyl residues were detected.[18] The presence of different conformers in a rigidly held extended biliverdin was also recently reported.[9]

The UV-vis spectrum of **1** (Figure 1a) shows the expected strong UV absorption of a helical-shaped biliverdin ($\epsilon$(vis)/$\epsilon$(UV) = 0.27). The partially extended chromophore **4** (Figure 1b) shows the expected[3] increase in vis absorption ($\epsilon$(vis)/$\epsilon$(UV) = 0.90). In the more rigid biliverdin **5** (5*Z*-anti, 10*Z*-syn, 15*Z*-anti) the Soret band almost disappeared ($\epsilon$(vis)/$\epsilon$(UV) = 11.0, Figure 1c). In biliverdin **6** (5*Z*-syn, 10*E*-anti, 15*Z*-syn) only a very weak UV absorption remained ($\epsilon$(vis)/$\epsilon$(UV) = 8.0, Figure 1d). The "extention effect" is therefore more pronounced when a conformation change takes place at the C10 meso bridge than at the C5 or C15 bridges. When the (*ZZZ*)-ethiobiliverdin IV-$\gamma$ ($\epsilon$(vis)/$\epsilon$(UV) = 0.27) was photoisomerized to the diasteroisomeric forms *EZZ* and *EZE*,[7a] their $\epsilon$(vis)/$\epsilon$(UV) ratios were found to increase to approximately 0.43 and 0.33. These ratios are much lower than those obtained for **5** and **6** (see above). It is therefore evident that a conformational change at the meso bridges has a more pronounced effect on the vis spectra of the biliverdins than a configurational change, a fact which allows us to further probe into the optical properties of the biliproteins.

**Acknowledgment.** This work was made possible by a grant (GM-11973) from NIH (PHS). Support from CONICET (Argentina) is also gratefully acknowledged. J.B.I. is grateful to CONICET for a fellowship. We thank Professor Kevin M. Smith (Davis, California) for calling our attention to this problem.

---

(16) This also explains why base treatment of a 2,17-bis(2-chloroethyl)-biliverdin gave the expected biliverdin IX-$\alpha$ (ref 11) and not a neopterobilin analogue.

(17) Scheer, H.; Katz, J. J. In *Porphyrins and Metalloporphyrins*; Smith, K. M. Ed.; Elsevier: Amsterdam, 1975; p 399 and references therein. It is conceivable that, as is the case for hemoproteins, the binding of extended biliverdins to proteins is a mechanism used by nature to prevent their aggregation.

(18) $^1H$ NMR (500 MHz) **4** ($CDCl_3$ at 193 K, $10^{-2}$ M) $\delta$ 6.90, 6.55 (H-10), 6.70, 6.09 (H-5), 6.26, 5.90 (H-15), 2.22, 2.16, 2.09, 2.08, 1.87 ($CH_3$). Compare with spectrum of **4** at 294 K (ref 12).

---

## Structure of the 2-Norbornyl Cation

Wolfram Koch† and Bowen Liu*

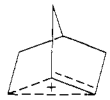
*IBM Almaden Research Center*
*San Jose, California 95120-6099*

Douglas J. DeFrees

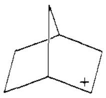
*Molecular Research Institute*
*Palo Alto, California 94304*

*Received June 23, 1988*

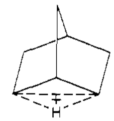
The structure of the 2-norbornyl cation is possibly the most widely debated issue in physical and organic chemistry. A review of the extensive experimental and theoretical work on this subject can be found in the December 1983 issue of *Acc. Chem. Res.*[1-4] Our ab initio force constant calculations using a range of basis sets show that the nonclassical structure of 2-norbornyl cation (**1**) corresponds to a minimum in the potential energy surface. This finding, combined with previous theoretical results, necessitates the conclusion that the gas-phase structure of the 2-norbornyl cation is nonclassical.



(1)



(2)



(3)

Self-consistent field (SCF) calculations were performed by using a vectorized IBM version of the GAUSSIAN 86 program.[5] The basis

---

† Present address: IBM Wissenschaftliches Zentrum, Tiergartenstrasse 15, D-6900 Heidelberg, FRG.

**Table I.** Vibrational Frequency of the Normal Mode Converting **1** → **2**

| method/basis | $\nu^a$ (cm$^{-1}$) | $E_{tot}$ (hartree) |
|---|---|---|
| RHF/3-21G | 137i | −269.702 33 |
| RHF/4-31G | 136i | −270.801 10 |
| RHF/6-31G | 154i | −271.084 21 |
| RHF/6-311G | 182i | −271.128 54 |
| RHF/4-31G* | 70 | −270.932 31 |
| RHF/6-31G* | 53 | −271.200 61 |
| RHF/6-311G* | 116 | −271.245 66 |
| RHF/6-31G** | 69 | −271.218 71 |
| MP2/6-31G* | 291 | −272.134 07 |

[a] This is the lowest vibrational frequency in Hartree–Fock but the second lowest in MP2.

sets used are 3-21G, 4-31G, 6-31G, 6-311G, 4-31G*, 6-31G*, 6-311G*, and 6-31G**.[6] For each basis, the nonclassical structure was determined by automatic energy minimization in $C_s$ symmetry. This was followed by analytic force constant calculations at the optimized geometry. The lowest vibrational frequency and the total energy of the optimized geometry obtained with each basis set are listed in Table I. All frequencies listed correspond to the same symmetry-breaking vibrational mode which moves the system toward a classical structure. For unpolarized basis sets, the nonclassical structure has one imaginary frequency and therefore corresponds to a saddle point, not a minimum. With the addition of one set of d functions to the carbon basis the nonclassical structure becomes a minimum with no imaginary vibrational frequencies. The lowest frequency corresponds to the same symmetry-breaking vibrational mode which has the imaginary frequency in the unpolarized basis set calculations. Improvements of the basis set beyond the 6-31G* level, expansion of the sp basis, and addition of p functions to the H basis make the lowest frequency larger, i.e., the potential well steeper. Further expansion of the basis set will not qualitatively change this result. Therefore, the nonclassical structure is a minimum in the Hartree–Fock potential energy surface of the 2-norbornyl cation.

Second-order Moller–Plesset perturbation theory (MP2)[6] vibrational frequencies were calculated by numerical differentiation of analytical gradients with the 6-31G* basis at the MP2/6-31G* optimized structure of the nonclassical 2-norbornyl cation. The lowest vibrational mode, with a frequency of 255 cm$^{-1}$, corresponds to the second lowest SCF vibrational mode. The vibrational mode that moves the system toward a classical structure is the second lowest mode at 291 cm$^{-1}$. Thus electron correlation makes the nonclassical well considerably steeper, increasing the vibrational frequency by 238 cm$^{-1}$.

Our previous calculations[7] showed (1) there is no potential minimum in the 6-31G* SCF potential energy surface corresponding to a classical structure of the 2-norbornyl cation (**2**) (the classical structure found in 4-21G and 4-31G SCF calculations is an artifact of inadequate basis set); (2) the edge-protonated structure (**3**) corresponds to a saddle point; and (3) electronic correlation favors a nonclassical structure over classical structures determined by small basis set calculations. The last result is supported by an independent calculation.[8] These results, taken together with our current result, force the conclusion that the 2-norbornyl cation is nonclassical in the gas phase.

In a recent paper, Dewar, Healy, and Ruiz[9] criticized previous theoretical work on the 2-norbornyl cation for not having calculated force constants with the basis sets used in optimizing the geometry. They concluded that there is "no reason to believe that the symmetrical structure is not in fact the transition state for interconversion of two unsymmetrical $\pi$ complexes." Their conclusion ignores the first two of our previous findings listed above. Since neither the classical structure nor the edge-protonated structure correspond to potential minima, it is difficult to imagine what the symmetric structure could be a transition state for. Nevertheless, our present result directly answers their criticism. Force constant calculations using extended basis sets show unequivocally that the symmetric structure is a minimum.

The data in Table I suggest that the 6-31G* basis can give reliable structures for carbocations. This is supported by our calculations in progress on $C_3H_7^+$ and $C_4H_7^+$.

Calculations presented above were done on IBM 3090 Model 200 computers at the IBM Data Systems Division's Kingston Numerically Intensive Computing Center and the IBM Dallas National Engineering and Scientific Support Center. The force constant calculation with the 6-31G* basis required only 5 h of processor time and 9 h of elapsed time. These calculations demonstrate the capabilities of ab initio computational chemistry, the new GAUSSIAN 86 program, and modern supercomputers.

**Acknowledgment.** We thank Y. Singh, Director of the IBM Kingston NIC Center, for providing the computing resource and P. Sonnenberg of the same organization for facilitating our calculations. Thanks also go to D. Gerson of the IBM Dallas National Engineering and Scientific Support Center for making available computing resource and facilitating our calculations.

**Registry No.** 2-Norbornyl cation, 24321-81-1.

---

(1) Grob, C. A. *Acc. Chem. Res.* **1983**, *16*, 426.

(2) Brown, H. C. *Acc. Chem. Res.* **1983**, *16*, 432.

(3) Olah, G. A.; Prakash, G. K. S.; Saunders, M. *Acc. Chem. Res.* **1983**, *16*, 440.

(4) Walling, C. *Acc. Chem. Res.* **1983**, *16*, 448.

(5) Frisch, M.; Binkley, J.; Schlegel, H.; Raghavachari, K.; Melius, C.; Martin, R.; Stewart, J.; Bobrowicz, F.; Rohlfing, C.; Kahn, L.; DeFrees, D.; Seeger, R.; Whiteside, R.; Fox, D.; Fluder, E.; Pople, J. GAUSSIAN 86, Carnegie-Mellon Quantum Chemistry Publishing Unit: Pittsburgh, PA, 1984.

(6) See Hehre et al. (Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley Interscience: New York, NY, 1986; Chapter 4) for a description of the various basis sets and MP2 perturbation theory.

(7) Yoshimine, M.; McLean, A. D.; Liu, B.; DeFrees, D. J.; Binkley, J. S. *J. Am. Chem. Soc.* **1983**, *105*, 6185.

(8) Raghavachari, K.; Haddon, R. C.; Schleyer, P. v. R.; Schaefer, H. F., III. *J. Am. Chem. Soc.* **1983**, *105*, 5915.

(9) Dewar, M. J. S.; Healy, E. F.; Ruiz, J. M. *J. Chem. Soc., Chem. Commun.* **1987**, 943.

---

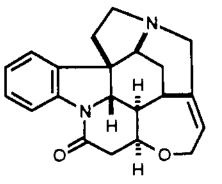
# Total Synthesis of (±)-Vallesamidine

Dan A. Dickman and Clayton H. Heathcock*

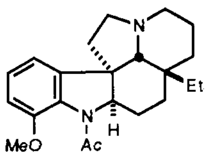
*Department of Chemistry, University of California*
*Berkeley, California 94720*

*Received October 21, 1988*

A great amount of research has been devoted to the synthesis of 2,3,3-trialkylindoline alkaloids.[1] Most synthetic approaches to these alkaloids have utilized one of two strategies. The first common strategy, exemplified in Woodward's landmark synthesis of strychnine (**1**),[2] uses a 2,3-disubstituted indole, which is further alkylated at C-3. The second general approach to the 2,3,3-trialkylindoline skeleton employs the Fischer indole synthesis[3] for



**1**



**2**

---

(1) (a) Cordell, G. A.; Saxton, J. E. *Alkaloids* (*N.Y.*) **1981**, *20*, 1–295. (b) Cordell, G. A. *Alkaloids* (*N.Y.*) **1979**, *17*, 199–384. (c) Smith, G. F. *Alkaloids* (*N.Y.*) **1960**, *8*, 591–671.

(2) Woodward, R. B.; Cava, M. P.; Ollis, W. D.; Hunger, A.; Daniker, H. V.; Schenker, K. J. *J. Am. Chem. Soc.* **1954**, *76*, 4749–4751.

(3) Robinson, G. M. *The Fischer Indole Synthesis*; Wiley: New York, 1983.

0002-7863/89/1511-1528$01.50/0