

amino acid.² The Tyr residue does not rotate rapidly relative to the peptide backbone as indicated by the only slightly greater T_1 values of the aromatic carbons relative to those of the α -carbons of the cyclic moiety. The T_1 values of the Pro residue reflect the attachment of the Cys-6 residue to the imino nitrogen.¹¹ The relative T_1 values of the various CH_2 moieties of Pro provide insight into the rate and nature of interconversions between various ring-puckered forms. In TRH (Glu-His-Pro-NH_2) the relative mobilities are $\gamma > \beta > \delta$,³ whereas in Pro-Leu-Gly- NH_2 they are $\gamma > \beta \approx \delta$.² In oxytocin the β -carbon has roughly twice the mobility of the δ -carbon. We attribute the difference between the behavior of oxytocin and Pro-Leu-Gly- NH_2 to the influence of the Cys-Pro peptide bond in oxytocin on the time-averaged conformation of the Pro ring; in particular formation of this peptide bond inhibits the possibility of rapid endo-exo interconversion at the δ -carbon. A similar influence is obvious in the data for LVP (Figure 2, *vide infra*).

The α -carbons in the ring portion of LVP have T_1 values (Figure 2) very similar to those found in the ring portion of oxytocin. However, the relaxation times of the α -carbons in the linear tripeptide are all longer than those of the corresponding residues in oxytocin, indicating greater freedom for this moiety in LVP than in oxytocin. This correlates well with the conformational differences proposed by Walter for these two hormones.¹² The side chains of the Tyr and Phe residues in LVP have comparable mobilities, perhaps due to the proposed stacking of the two aromatic rings in aqueous medium.¹⁵ The T_1 values of corresponding carbon atoms are equal within experimental error (because of bad resolution no values are given for the para carbon of the aromatic ring of Phe). The NT_1 values for the ortho and meta carbons are essentially equal to those of the β -carbons. There is a difference of a factor of 2 in the NT_1 values of the α - and β -carbons of the aromatic residues. This leads us to conclude that the side chains are less restricted than the backbone but that rotation about the aryl- βCH_2 is not significantly faster than that about the α - β axis, in contrast to the behavior observed in substituted benzenes.¹⁶ The side chain of Lys provides an example of segmental motion with adjacent CH_2 carbons having *ca.* 1.7-fold T_1 differentials, as found recently in oligo- and poly-L-lysine.⁵ The Pro residue in LVP behaves qualitatively in the same manner as that in oxytocin, and we believe that the ring conformations of Pro are similar to that found in TRH,³ the γ -carbon being by far the most mobile in the Pro ring. The Asn side chain shows more mobility than the backbone of the ring, whereas the Gln γ -carbon has a considerably lower mobility than in oxytocin, suggesting the involvement of this side chain in some type of secondary structure.^{6h}

We calculate an effective overall correlation time (τ_c) for both compounds of 5×10^{-10} sec based on an average T_1 value of ≈ 95 msec for the α -carbons of the ring. This is in agreement with the value calculated for

(15) R. Deslauriers and I. C. P. Smith, *Biochem. Biophys. Res. Commun.*, **40**, 179 (1970).

(16) (a) G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists," Wiley-Interscience, Wiley, New York, N. Y., 1972; (b) D. Doddrell and A. Allerhand, *J. Amer. Chem. Soc.*, **93**, 1558 (1971); (c) G. C. Levy, *J. Magn. Resonance*, **8**, 122 (1972); (d) G. C. Levy, J. D. Cargioli, and F. A. L. Anet, *J. Amer. Chem. Soc.*, **95**, 1527 (1973).

a monomeric peptide in this molecular weight range¹⁴ and corresponds to an approximate diameter of 16 Å for neurohypophyseal hormones; from thin-film dialysis studies diameters of 14–15 and 16 Å were calculated for oxytocin and lysine vasopressin, respectively.¹⁷

These studies serve as a basis to relate conformational characteristics of neurohypophyseal hormones and synthetic analogs to their agonistic and antagonistic properties. Measurements on ¹³C-enriched neurohypophyseal peptides should allow monitoring of conformational changes and dynamic processes which occur on binding to their intracellular carrier proteins, the neurophysins.¹⁸

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(17) L. C. Craig, personal communication.

(18) Issued as N.R.C.C. Publication No. 33750.

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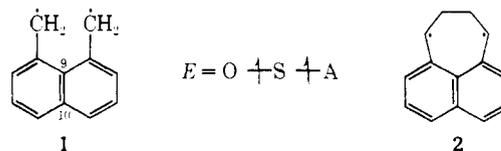
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Synthesis and Characterization of a 1,8-Naphthoquinodimethane

Sir:

Although Hückel MO theory is naive by the standards of today's sophisticated calculations, it has been eminently successful at predicting the aromaticity of cyclic systems containing an array of $(4n + 2)\pi$ electrons. One of its other outstanding achievements, although less well known and appreciated, is its success in predicting triplet ground states for organic molecules such as the cyclopentadienyl cation,¹ trimethylenemethane,² tetramethyleneethane,³ and *m*-xylylene.⁴

Hückel theory also predicts that 1,8-naphthoquinodimethane (**1**) should possess a triplet ground state.



In addition to the five bonding molecular orbitals (MO's), which contain a total of ten π electrons, this species has a pair of degenerate nonbonding MO's at $E = 0$, one of which is symmetric (S) to the plane bisecting the molecule and going through the C-9–C-10 bond and the other which is antisymmetric (A) to this

(1) M. Saunders, *et al.*, *J. Amer. Chem. Soc.*, **95**, 3017 (1973), and references cited therein.

(2) (a) P. Dowd, *J. Amer. Chem. Soc.*, **88**, 2587 (1966); P. Dowd and K. Sachdev, *ibid.*, **89**, 715 (1967); P. Dowd, A. Gold, and K. Sachdev, *ibid.*, **90**, 2715 (1968).

(3) (a) P. Dowd, *J. Amer. Chem. Soc.*, **92**, 1066 (1970); (b) W. Roth and G. Erker, *Angew. Chem., Int. Ed. Engl.*, **12**, 503 (1973).

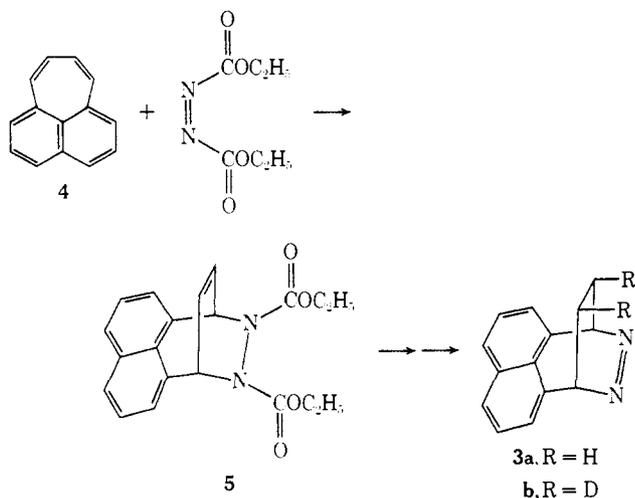
(4) (a) G. Kothe, K. H. Deukel, and W. Suemmermann, *Angew. Chem., Int. Ed. Engl.*, **9**, 906 (1967); (b) G. R. Luckhurst, G. F. Pedulli, and Tiecco, *J. Chem. Soc. B*, 329 (1971).

plane.⁵ According to Hund's rule, one of the remaining two π electrons of this species will go into the S MO and the other will go into the A MO, with their spins unpaired, thus the prediction of a triplet ground state.

There are numerous reactions in the literature where a 1,8-naphthoquinodimethane could be an intermediate,⁶ but in none of them has the existence of such a species been demonstrated, let alone characterized. We wish to report the synthesis and characterization of just such a species, the 1,8-naphthoquinodimethane (**2**).

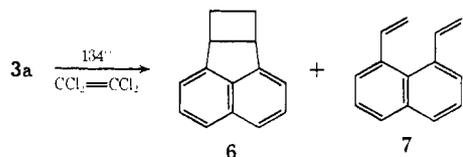
As an ideal, one would clearly want to prepare a totally planar 1,8-naphthoquinodimethane, but molecular models suggest that this is not attainable for **1** and **2**. Because more stereochemical information might be available from reactions of **2**, it was chosen for study.

The synthesis of the azo compound **3a**,⁷ the source of



2, was straightforward. The Diels-Alder adduct **5** was prepared by treating pleiadene (**4**)⁸ with ethyl azodicarboxylate in refluxing CCl_4 . Hydrogenation of **5** and removal of the ester linkages by standard procedures afforded **3a**, a relatively stable compound.

The decomposition of **3a** in degassed tetrachloroethylene at 134° followed first-order kinetics⁹ ($E_a = 28.7$ kcal/mol and $\Delta S^\ddagger (134.0^\circ) = -6.7$ eu) and gave two products in 7 to 1 ratio. They were separated on a 5% silver nitrate-silica gel column and the major product identified as 1,8-naphthocyclobutane (**6**)¹⁰ and the



(5) C. A. Coulson and A. Streitwieser, Jr., "Dictionary of π -Electron Calculations," W. H. Freeman, San Francisco, Calif., p 112.

(6) For some examples, see (a) L. A. Carpino, *J. Amer. Chem. Soc.*, **85**, 2144 (1963); (b) P. M. Weintraub, *Chem. Ind. (London)*, 1296 (1970); (c) A. G. Schultz, *et al.*, *J. Amer. Chem. Soc.*, **92**, 6086 (1970); (d) J. Meinwald and J. W. Young, *ibid.*, **93**, 725 (1971); (e) J. Meinwald and J. A. Kapecki, *ibid.*, **94**, 6235 (1972); (f) S. Nelsen and J. P. Gillespie, *ibid.*, **94**, 6238 (1972).

(7) All new compounds gave satisfactory spectral and analytical data. These will be reported in our full paper.

(8) (a) R. M. Pagni and C. R. Watson, Jr., *Tetrahedron Lett.*, 59 (1973); (b) I. Murata and K. Nakasuji, *ibid.*, 47 (1973).

(9) The kinetics were monitored by following the disappearance of the n, π^* transition ($\lambda_{\text{max}} 4110 \text{ \AA}$ ($\epsilon 1065$)) of **3a**. Rate constants of 1.88×10^{-3} , 2.96×10^{-4} , and $7.41 \times 10^{-4} \text{ sec}^{-1}$ were obtained at 128.8, 134.0, and 145.0° , respectively.

(10) Naphthocyclobutane (**6**) was prepared by hydrogenation of the naphthocyclobutene.

minor product as 1,8-divinylnaphthalene (**7**).¹¹ No other products, such as dimeric materials, were detected in this reaction. Control experiments showed that **6** and **7** were initial products of the reaction and that they did not interconvert or yield new compounds under the reaction conditions.

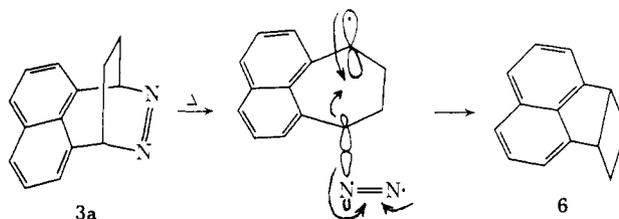
Subsequent runs in degassed methanol, benzene, cyclohexane, and carbon tetrachloride gave similar results. In none of these reactions were dimers, products derived by hydrogen or chlorine abstraction, or solvent addition compounds found.¹²⁻¹⁴

Decomposition of **3a** in degassed iodobenzene and hexafluorobenzene and in 1-chloronaphthalene run in air also afforded only **6** and **7** in a ratio between 5 and 7 to 1. It might have been anticipated in these latter reactions that an excited-state singlet, **2**, to ground-state triplet, **2**, interconversion would have been facilitated. Had this occurred, one would have expected the formation of dimers because of the presumed long-lived nature of the ground-state triplet.¹² Yet there is no indication of this.

CIDNP^{3b,14} and $\text{esr}^{1-3,14}$ have also been used to detect the presence of triplet biradicals. Several attempts to detect a CIDNP in the thermal decomposition of **3a** have all failed and the results are at best inclusive.^{15,16}

All the above results strongly suggest that quinodimethane **2** is short lived, and that the products, **6** and **7**, derive from either a singlet ground state or an unquenchable triplet excited state of **2**.¹⁷

The conclusions reached above presuppose that **2**, either singlet or triplet, is an intermediate in the decomposition. One can imagine, however, that **6** and **7** are formed without the intervention of **2**. If this occurred, one would anticipate that **6** be formed with inversion of configuration,¹³ *i.e.*



Although this reaction is hypothetical, one would expect

(11) R. H. Mitchell and F. Sondheimer, *Tetrahedron*, **24**, 1397 (1968).

(12) The formation of dimers^{3b,13,14} and "trapped" adducts has been used as circumstantial evidence for the existence of long-lived triplet intermediates.

(13) P. S. Skell and R. G. Doerr, *J. Amer. Chem. Soc.*, **89**, 4684, 4688 (1967).

(14) J. A. Berson, *et al.*, *J. Amer. Chem. Soc.*, **93**, 1544 (1971), and earlier work.

(15) (a) Traces of dimeric products, undetected by other spectroscopic means, might have been detected by the extraordinarily sensitive CIDNP. See G. L. Closs, *J. Amer. Chem. Soc.*, **93**, 1546 (1971). (b) It is not clear whether the monomeric products **6** and **7** should exhibit CIDNP even if they are formed from triplet intermediates. See L. Salem and C. Rowland, *Angew. Chem., Int. Ed. Engl.*, **11**, 92 (1972).

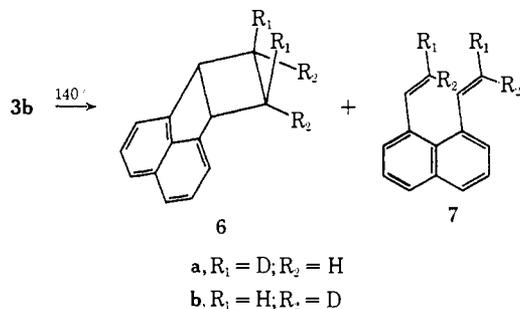
(16) Low temperature irradiation of **3a** did afford a triplet state of **2**. The photochemistry of **3a** and esr studies of **2** will be discussed in a subsequent paper: R. M. Pagni, C. R. Watson, Jr., J. E. Bloor, and J. R. Dodd, *J. Amer. Chem. Soc.*, submitted for publication.

(17) It is important to emphasize again that this presumes that a ground-state triplet would be long-lived and have a different chemical behavior.

(18) For examples of azo decomposition where the reaction, in part, may bypass a biradical intermediate, see (a) W. R. Roth and M. Martin, *Justus Liebig's Ann. Chem.*, **702**, 1 (1967); (b) E. L. Allred and R. L. Smith, *J. Amer. Chem. Soc.*, **91**, 6766 (1969); (c) P. B. Condit and R. G. Bergman, *Chem. Commun.*, 4 (1971).

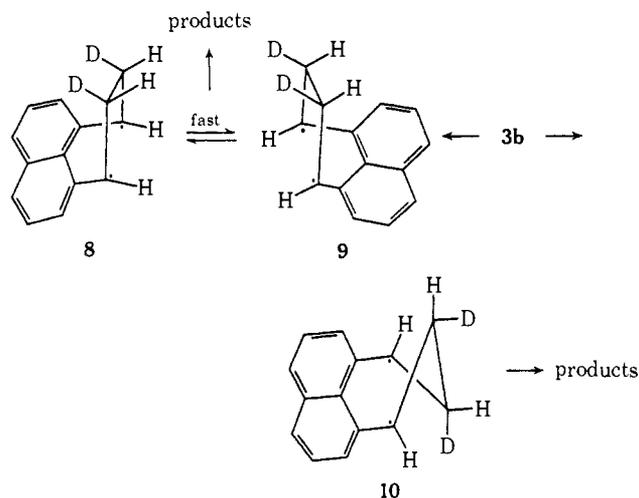
the two pathways, with or without the presence of **2**, to yield differing stereochemical results. To delve into this question, the deuterated molecule **3b** was prepared.¹⁹

When **3b** was decomposed in 1-chloronaphthalene at 140°, only deuterated **6** and **7** in a 6 to 1 ratio were



formed. Nmr analysis of the deuterated **6** showed the formation of 50% **6a** and 50% **6b**. Similar analysis of the deuterated 1,8-divinylnaphthalene revealed the formation of 50% **7a** and 50% **7b**.²⁰ The ratios, **6a/6b** and **7a/7b**, were shown to be constant by following the reaction as a function of time. Control experiments demonstrated that authentic **6a** did not equilibrate its label under the reaction conditions. Furthermore, Nelsen has shown^{6f} that **7a** undergoes *cis,trans* isomerization to the extent of only 10% at 350°, a temperature far higher than those used here. It seems clear that the product ratios and deuterium distributions reported above are indeed the initial ones.

The lack of inversion in **6** as well as the lack of preference for *cis*- or *trans*-**7** conclusively prove that **2** is an intermediate in these reactions and it reacts as if it were planar. Molecular models suggest, however, that planar **2** would be highly strained; on the other hand, a bent (**8**) and a twisted (**10**) form of **2** seem plausible intermediates. Both of these intermediates can give the observed stereochemistry by mechanisms shown below.²¹



(19) The deuterium was incorporated into the system by treating **5** with deuteriodiimide. Full details and assignments will be given in our full paper.

(20) This is actually not correct. One cannot say, in this case, the actual isomers of **7** which are present. One only knows that half the label is *cis* and half is *trans*.

(21) Twisted **2** and the nonplanar forms, **8** and **9**, may be related. Twisted **2** may be the species by which **8** and **9** interconvert.

In conclusion, this study has demonstrated the existence of 1,8-naphthoquinodimethane (**2**), a species which previously had not been characterized. Further work will attempt to determine which multiplicity of **2** and which conformation of **2** is responsible for the formation of the products **6** and **7**.

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Localized Orbitals in Large Boron Hydrides. $\text{B}_{16}\text{H}_{20}$ and Related Molecules

Sir:

The geometrical structures of the six large boranes ($\text{B}_{16}\text{H}_{20}$,¹ $\text{B}_{18}\text{H}_{22}$,² *i*- $\text{B}_{18}\text{H}_{22}$,³ $\text{B}_{20}\text{H}_{18}^{2-}$,⁴ photo- $\text{B}_{20}\text{H}_{18}^{2-}$,⁵ and $\text{B}_{20}\text{H}_{16}$ ⁶) established by X-ray diffraction methods are closely related to structures of smaller boranes. We have now established the corresponding relationships of the valence structures, exemplified here by a comparison of $\text{B}_{16}\text{H}_{20}$ with $\text{B}_{10}\text{H}_{14}$ and B_8H_{12} .⁷ Localized orbitals, objectively obtained, greatly simplify the earlier valence descriptions of these complex molecules.

In the method, widely applicable to complex molecules,⁸ we derive localized molecular orbitals (LMO's) by Boys' procedure^{8,9} from a high quality molecular orbital approximation (PRDDO¹⁰) to self-consistent field theory. The Boys procedure gives localized orbitals by maximizing the separation of the centroids of the molecular orbitals. Only dipole moment integrals over occupied molecular orbitals, $\langle \phi_i | \mathbf{r} | \phi_j \rangle$, are needed for the Boys method. (The Edmiston-Ruedenberg¹¹ (ER) method requires all two-electron integrals over occupied molecular orbitals.) The Boys procedure has been coupled here with the PRDDO technique yielding an efficient method for obtaining localized orbitals. The only significant difference, between these results and those obtained by the ER procedure, is found for 1,2- $\text{C}_2\text{B}_4\text{H}_6$ where the Boys procedure makes all three-center bonds central while ER yields two combinations each

(1) L. B. Friedman, R. E. Cook, and M. D. Glick, *Inorg. Chem.*, **9**, 1452 (1970).

(2) P. G. Simpson and W. N. Lipscomb, *J. Chem. Phys.*, **39**, 26 (1963).

(3) P. G. Simpson, K. Folting, R. D. Dobrott, and W. N. Lipscomb, *J. Chem. Phys.*, **39**, 2339 (1963).

(4) C. H. Schwalbe and W. N. Lipscomb, *Inorg. Chem.*, **10**, 151 (1971).

(5) B. G. DeBoer, A. Zalkin, and D. H. Templeton, *Inorg. Chem.*, **7**, 1085 (1968).

(6) R. D. Dobrott, L. B. Friedman, and W. N. Lipscomb, *J. Chem. Phys.*, **40**, 866 (1964).

(7) (a) J. H. Hall, D. S. Marynick, and W. N. Lipscomb, *J. Amer. Chem. Soc.*, **96**, 770 (1974); (b) J. H. Hall, D. A. Dixon, T. A. Halgren, D. A. Kleier, and W. N. Lipscomb, to be submitted for publication.

(8) J. H. Hall, D. A. Kleier, T. A. Halgren, and W. N. Lipscomb, to be submitted for publication.

(9) S. F. Boys, "Quantum Theory of Atoms, Molecules and the Solid State," P. O. Löwdin, Ed., Academic Press, New York, N. Y., 1966, p 253.

(10) T. A. Halgren and W. N. Lipscomb, *J. Chem. Phys.*, **58**, 1569 (1973).

(11) C. Edmiston and K. Ruedenberg, *Rev. Mod. Phys.*, **35**, 467 (1963).