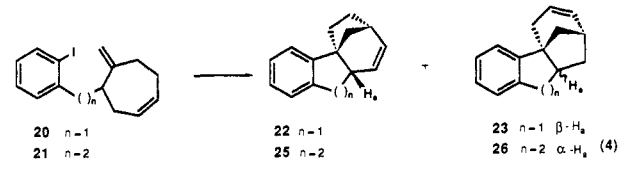
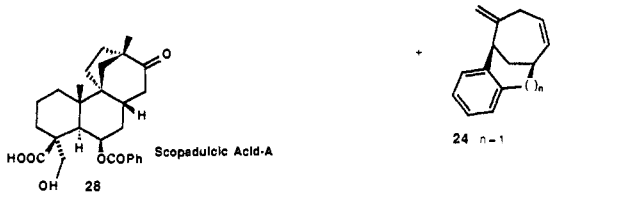
Initial insertion of the (aryl)palladium intermediate with the terminal vinyl group, which leads to monocyclization, was less important when this competing process would lead to the formation of a seven-membered ring. Thus, cyclization of **13** at 70 °C for 9 h proceeded to provide the angular tricycles **16**[9,15] and **18**[9,15] in a 1.3;1 ratio, respectively, and 67% yield (76% based on consumed **13**). It was key to the success of the bis-cyclization reaction that insertion of the proximal double bond provided a (σ-alkyl)palladium intermediate which could not decompose by simple β-hydrogen insertion. This limitation is clearly seen in the cyclization of **14** which afforded **19**[9] as the sole product.

The power of this chemistry for quickly assembling complex polycyclic systems is well-illustrated by cyclizations of the cyclic dienyl aryl iodides **20** and **21** (see eq 4). Cyclization[10] of **20**





provided a 1,2;1 mixture of tetracycle **22**[9] and tricycle **24**,[9] which were isolated after silica gel chromatography in yields of 43% and 25%, respectively. Ozonolysis of **22** provided a dialdehyde which showed a doublet for each aldehydic hydrogen, thus ruling out a tetracycle with the alternate bicyclo[3.2.1]octene partial skeleton (e.g., **23**).[16] That the bridgehead hydrogen H_a was β to the one-carbon bridge was established by NOE spectroscopy.[17] Initial insertion into the ring double bond was less prevalent in the cyclization of **21** (at 83 °C for 10 h) which proceeded in 90% yield to provide **25** and **26** in a ratio of 1,3:1, respectively.[18] Stereochemical assignments for **25** and **26** were based on relating, by NOE effects,[17] the angular hydrogen H_a with the cis related bridge of the bicyclooctene ring system. Tetracycles **25** and **26** contain carbon skeletons found in several diterpene natural products,[19,20] e.g., aphidicolin,[19a] stemodin,[19b] and the scopadulcic acids.[20] The conversion of **21** → **25** and **26** represents the first one-step construction of these ring systems from a bicyclic precursor.

In conclusion, the results described here provide the first demonstration that palladium-catalyzed alkene arylations can be accomplished in a tandem sense to form two rings. The high yields observed in many of these bis-cyclizations suggest that palladium-catalyzed polyene cyclizations that form more than two rings should be possible. We are actively exploring this possibility as well as the scope and total synthesis applications of the bis-cyclizations documented in this preliminary account.

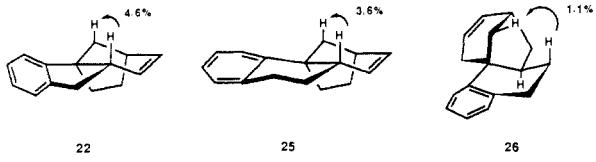
Acknowledgment. We particularly wish to thank Dr. Shoumo Chang for invaluable help with the 2D NMR studies. Financial support from the National Institutes of Health (GM-308950) and the NSF (Shared Instrumentation Grants) is gratefully acknowledged.

(14) The crude yield was 96%. Small amounts of deiodinated **12** (7%) and what is provisionally assigned as the trans isomer of **15** (8%) were also isolated by preparative GC.

(15) Stereochemistry was assigned in analogy with Orrell et al. (Orrell, K. G.; Packer, R. A.; Sik, V.; Whitehurst, J. S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 117).

(16) Tetracycle **22** was contaminated with ~10% of what is believed to be the alternative bicyclo[3.2.1]octene tetracyclic **23**. A triplet and doublet were observed for the CHO hydrogens of this minor product after ozonolytic cleavage.

(17) Key NOE's are shown below. ^{1}H NMR assignments were based on extensive 1- and 2-D NMR experiments.



(18) Also isolated by preparative GC was 8% of deiodinated **21**.

(19) For recent synthetic accomplishments and leading references, see: (a) Holton, R. A.; Kennedy, R. M.; Kim, H.-B.; Krafft, M. E. *J. Am. Chem. Soc.* **1987**, *109*, 1597. (b) White, J. D.; Somers, T. C. *Ibid.* **1987**, *109*, 4424.

(20) Hayashi, T.; Kishi, M.; Kawasaki, M.; Arisawa, M.; Shimizu, M.; Suzuki, S.; Yoshizaki, M.; Morita, N.; Tezuka, Y.; Kikuchi, T.; Berganza, L. H.; Ferro, E.; Basualdo, I. *Tetrahedron Lett.* **1987**, *28*, 3693.

Microwave Spectrum of Uracil

Ronald D. Brown,* Peter D. Godfrey, Donald McNaughton, and Anthony P. Pierlot

Department of Chemistry, Monash University Clayton, 3168 Australia

Received November 18, 1987

Biological systems are based on macromolecules stemming from a limited number of small molecules, notably 20 amino acids, five nitrogen heterocycles, and several pentoses and hexoses. Though small, these molecules are difficult to vaporize without extensive decomposition, and so detailed structural information about them has almost always been based on X-ray crystallographic studies rather than high-resolution vapor phase spectroscopic measurements. Hitherto the only species for which spectroscopic information has been obtained are urea[1] and glycine,[2] while gas-phase electron diffraction studies[3] and fluorescence spectra[4] have recently been reported for uracil. We now report the detection and analysis of the microwave spectrum of uracil, from which some limited structural information can be derived for comparison with results derived from crystallographic[5,6] and electron diffraction studies.[3]

Preliminary studies of the vaporization of uracil[7] had revealed that vaporization without decomposition was possible under carefully controlled conditions and provided a vapor pressure curve and heat of sublimation. An attempt to observe the microwave spectrum in a conventional Stark-modulated spectrometer incorporating a P-band cell in a thermal enclosure heated to 200 °C, a technique that had been successful for a microwave spectral study of urea,[1] produced marginal results,[7] inadequate for a definitive assignment of the spectrum. We have now developed a Stark-modulated spectrometer for microwave measurements on a seeded supersonic nozzle expanded beam of uracil in argon. The CW beam plume passes between parallel plates that produce the Stark field, the microwave beam, collimated with Teflon lenses, passing transversely between the plates to the detector. The microwave spectrum of the heterocycle has been observed at adequate S/N in the vicinity of 60 GHz, lines of S/N up to 10 or more being recorded with a time constant of 1 s. Table I gives the spectroscopic parameters derived from 65 assigned lines.

From the inertial defect it is apparent that uracil is essentially planar in the gas phase, in contrast to its structure in the crystal[6] (the electron diffraction study[3] could not detect small deviations from molecular planarity). Presumably lattice forces are responsible for the very small distortion observed in the latter.

(1) Brown, R. D.; Godfrey, P. D.; Storey, J. W. V. *J. Mol. Spectrosc.* **1975**, *58*, 445-450.

(2) Brown, R. D.; Godfrey, P. D.; Storey, J. W. V.; Bassez, M. P. *J. Chem. Soc., Chem. Commun.* **1978**, 547-548. Suenram, R. D.; Lovas, F. J. *J. Mol. Spectrosc.* **1978**, *72*, 372-382. Suenram, R. D.; Lovas, F. J. *J. Am. Chem. Soc.* **1980**, *102*, 7180-7184.

(3) Ferenczy, G.; Harsanyi, L.; Rozsondai, B.; Hargittai, I. *J. Mol. Struct.* **1986**, *140*, 71-77.

(4) Fujii, M.; Tamura, T.; Mikami, N.; Ito, M. *Chem. Phys. Lett.* **1986**, *126*, 583-587.

(5) Parry, G. S. *Acta Crystallogr.* **1954**, *7*, 313-320.

(6) Stewart, R. F.; Jensen, L. H. *Acta Crystallogr.* **1967**, *23*, 1102-1105.

(7) Porter, A. P. Ph. D. Thesis, Monash University, 1979.

0002-7863/88/1510-2329$01.50/0 © 1988 American Chemical Society

Table I. Spectroscopic Parameters for Uracil[a]

A	3883878.25 (110)	D_K	0.4724 (43)
B	2023732.67 (101)	d_1	-0.02738 (28)
C	1330923.80 (60)	d_2	-0.006532 (94)
D_J	0.06029 (77)	Δ	-0.128 uÅ^2
D_{JK}	0.1047 (14)		

[a] In kHz except for Δ.

Furthermore, the rotational constants agree to within better than 1% with those expected for the diketo tautomer. We have not detected any strong lines that could be assigned to other tautomeric forms, implying that the diketo form is the most stable tautomer in the gas phase. This is in agreement with various theoretical studies of the relative stabilities of the tautomers,[8] the tautomer observed in the crystal[5,6] and that which is inferred as the major gas-phase tautomer from the fluorescence studies,[4] although in the latter a small fraction of a keto-enol tautomer was thought to exist.

We have been able to observe only relatively high-J lines for which precise Stark effect measurements are not feasible. However it has been possible to make limited observations of the Stark effect for the $18_{6,13}$-$17_{6,12}$ and $18_{4,14}$-$17_{5,13}$ lines from which we derive dipole moment components of μ_a = 1.61 D and μ_b = 3.52 D; hence, μ = 3.87 D (errors are estimated to be less than 10%). Our value for the total moment is close to the value (4.16 D) measured in dioxane solution.[9]

Further work is planned on other isotopic versions of uracil in order to derive more complete structural information.

Supplementary Material Available: A table of observed and calculated transition frequencies used to derive the data in Table I (4 pages). Ordering information is given on any current masthead page.

(8) Scanlan, M. J.; Hillier, I. H. *J. Am. Chem. Soc.* **1984**, *106*, 3737-3745. Les, A.; Ortega-Blake, I. *Int. J. Quantum Chem.* **1986**, *30*, 225-237.
(9) Kulakowski, I.; Geller, M.; Lesyng, B.; Weirzchowski, K. L. *Biochim. Biophys. Acta* **1974**, *361*, 119-130.

Structural Characterization by EXAFS Spectroscopy of the Binuclear Iron Center in Protein A of Methane Monooxygenase from *Methylococcus capsulatus* (Bath)

Agneta Ericson, Britt Hedman, and Keith O. Hodgson*

Stanford Synchrotron Radiation Laboratory and Department of Chemistry, Stanford University Stanford, California 94305

Jeffrey Green and Howard Dalton*

Department of Biological Sciences, University of Warwick, Coventry, CV4 7AL, United Kingdom

James G. Bentsen, Robert H. Beer, and Stephen J. Lippard*

Department of Chemistry Massachusetts Institute of Technology Cambridge, Massachusetts 02139

Received September 14, 1987

Soluble methane monooxygenase (MMO) from *Methylococcus capsulatus* (Bath)[1-3] activates dioxygen for incorporation into a remarkable variety of substrates[2] including methane, which is required for bacterial growth (eq 1). MMO is a three-component

$$CH_4 + NADH + H^+ + O_2 \xrightarrow{MMO} CH_3OH + NAD^+ + H_2O \quad (1)$$

enzyme. Protein A (M_r 210 000), believed to be the oxygenase component, contains two iron atoms per molecule of protein.[4] Protein B (M_r 15 700) serves a regulatory function and lacks prosthetic groups,[5] while protein C, the reductase component of the enzyme, is an iron-sulfur flavoprotein (M_r 42 000) responsible for electron transfer from NADH to protein A.[6] Recently, a binuclear iron center was postulated[7] to occur in protein A based on the finding that one-electron reduction gives rise to electron spin resonance (ESR) signals (g 1.95, 1.88, 1.78) very similar to those observed for the binuclear mixed-valence Fe_2(III,II) centers in semimet hemerythrin (Hr)[8] and purple acid phosphatase (PAP).[9] In conjunction with model studies, extended X-ray absorption fine structure (EXAFS) spectroscopy has proved to be a powerful method for identifying bridged binuclear iron centers in Hr,[10,11a] ribonucleotide reductase (RR),[11] and PAP.[12] Here we report iron K-edge EXAFS results on semireduced protein A of MMO which support the occurrence of a binuclear iron center (Fe-Fe distance, 3.41 Å), with no short μ-oxo bridge.

Purified protein A of *M. capsulatus* (Bath) MMO[4] was dissolved in 25 mM pH 7.0 Pipes buffer, concentrated, diluted with glycerol to a final concentration of 10% glycerol, frozen in liquid nitrogen, and stored at -80 °C. The final protein concentration was ~385 mg/mL, and the iron content was determined by flameless atomic absorption spectroscopy to be 2.1 ± 0.1 mol Fe (3.8 mM Fe) per mol protein. X-ray absorption data were collected at the Stanford Synchrotron Radiation Laboratory on the focused beam line II-2 under dedicated conditions (3.0 GeV, 50-65 mA) by using a Si(111) double-crystal monochromator. All protein data were measured at 10 K as Mn filtered fluorescence excitation spectra monitored by an argon-filled ionization chamber.[13] Data reduction and analysis were performed as previously reported.[14,15] Curve-fitting techniques were applied by using empirical phase and amplitude parameters for various Fe-X scattering pairs obtained from the following models: Fe-O and Fe-C, [Fe(acetylacetonate)$_3$];[16] Fe-N, [Fe(1,10-phenanthroline)$_3$](ClO$_4$)$_2$;[17] Fe-Fe, [Fe$_2$(OH)(OAc)$_2$(HBpz$_3$)$_2$](ClO$_4$) (**1**).[18] Data were also collected for [Fe$_2$O-

(1) Colby, J.; Dalton, H. *Biochem. J.* **1976**, *157*, 495-497.
(2) Colby, J.; Stirling, D. I.; Dalton, H. *Biochem. J.* **1977**, *165*, 395-402.
(3) Colby, J.; Dalton, H. *Biochem. J.* **1978**, *171*, 461-468.
(4) (a) Woodland, M. P.; Dalton, H. *J. Biol. Chem.* **1984**, *259*, 53-59. (b) Woodland, M. P.; Dalton, H. *Anal. Biochem.* **1984**, *139*, 459-462.
(5) Green, J.; Dalton, H. *J. Biol. Chem.* **1985**, *260*, 15795-15801.
(6) Lund, J.; Woodland, M. P.; Dalton, H. *Eur. J. Biochem.* **1985**, *147*, 297-305.
(7) Woodland, M. P.; Patil, D. S.; Cammack, R.; Dalton, H. *Biochim. Biophys. Acta* **1986**, *873*, 237-242.
(8) (a) Wilkins, R. G.; Harrington, P. C. *Adv. Inorg. Biochem.* **1983**, *5*, 51-85. (b) Harrington, P. C.; Wilkins, R. G. *Coord. Chem. Rev.* **1987**, *7*, 195-214.
(9) Antanaitis, B. C.; Aisen, P. *Adv. Inorg. Biochem.* **1983**, *5*, 111-136.
(10) (a) Hendrickson, W. A.; Co, M. S.; Smith, J. L.; Hodgson, K. O.; Klippenstein, G. L. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 6255-6259. (b) Elam, W. T.; Stern, E. A.; McCallum, J. D.; Sanders-Loehr, J. *J. Am. Chem. Soc.* **1983**, *105*, 1919-1923. (c) Hedman, B.; Co, M. S.; Armstrong, W. H.; Hodgson, K. O.; Lippard, S. J. *Inorg. Chem.* **1986**, *25*, 3708-3711.
(11) (a) Scarrow, R. C.; Maroney, M. J.; Palmer, S. M.; Que, L., Jr.; Roe, A. L.; Salowe, S. P.; Stubbe, J. *J. Am. Chem. Soc.* **1987**, *109*, 7857-7864. (b) Scarrow, R. C.; Maroney, M. J.; Palmer, S. M.; Que, L., Jr.; Salowe, S. P.; Stubbe, J. *J. Am. Chem. Soc.* **1986**, *108*, 6832-6834. (c) Bunker, G.; Peterson, L.; Sjöberg, B.-M.; Sahlin, M.; Chance, M.; Chance, B.; Ehrenberg, A. *Biochemistry* **1987**, *26*, 4708-4716.
(12) Kauzlarich, S. M.; Teo, B. K.; Zirino, T.; Burman, S.; Davis, J. C.; Averill, B. A. *Inorg. Chem.* **1986**, *25*, 2781-2785.
(13) (a) Lytle, F. W.; Greegor, R. B.; Sandstrom, D. R.; Marques, E. C.; Wong, J.; Spiro, C. L.; Huffman, G. P.; Huggins, F. E. *Nucl. Instr. Meth.* **1984**, *226*, 542-548. (b) Stern, E. A.; Heald, S. M. *Rev. Sci. Instr.* **1979**, *50*, 1579-1582.
(14) Energy calibration was performed by using the internal standard method (Scott, R. A.; Hahn, J. E.; Doniach, S.; Freeman, H. C.; Hodgson, K. O. *J. Am. Chem. Soc.* **1982**, *104*, 5364-5369), assigning the first inflection point of the Fe K absorption edge for Fe foil as 7111.2 eV. The normalized background-subtracted data were converted to k-space by assuming a threshold energy (E_0) of 7130 eV. The photoelectron wave vector k is defined by $k = (2m_e(E - E_0)/\hbar^2)^{1/2}$, where m_e is the electron mass.
(15) (a) Eccles, T. K. Ph.D. Dissertation, Stanford University, 1977. (b) Cramer, S. P.; Hodgson, K. O. *Prog. Inorg. Chem.* **1979**, *15*, 1-39. (c) Scott, R. A. *Meth. Enzymol.* **1985**, *117*, 414-459.
(16) (a) Roof, R. B. *Acta Crystallogr.* **1956**, *9*, 781-786. (b) Iball, J.; Morgan, C. H. *Acta Crystallogr.* **1967**, *23*, 239-244.
(17) Synthesized according to Johansson (Johansson, L. *Chem. Scr.* **1976**, *9*, 30-35). The crystal structure of the perchlorate salt has not been determined, but the [Fe(phenanthroline)$_3$]$^{2+}$ complex structure can be assumed to be identical with that of the corresponding iodide salt. The synthesis of the latter was reported in the same paper, and the crystal structure determination by Johansson et al. (Johansson, L.; Molund, M.; Oskarsson, Å. *Inorg. Chim. Acta* **1978**, *31*, 117-123).

0002-7863/88/1510-2330$01.50/0 © 1988 American Chemical Society