assistance and useful discussions. We are also grateful to Professor M. F. Lappert and Professor M. Veith for supplying details of their work prior to publication.

Supplementary Material Available: A full table of crystallographic data and refinement, positional parameters for non-hydrogen atoms, bond distances and angles, anisotropic thermal parameters, and hydrogen coordinates for **1** (7 pages); table of observed and calculated structure factors for **1** (19 pages). Ordering information is given on any current masthead page.

Insertion of O_2 into the Mg–C Bonds of the Alkyl Derivatives $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR (R = CH_3, CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$): Formation of Alkylperoxo Derivatives and Oxygen Atom Transfer

Runyu Han and Gerard Parkin*

Department of Chemistry, Columbia University
New York, New York 10027

Received December 14, 1989

The selective oxidation of organic substrates by molecular oxygen plays a crucial role in a variety of industrial and biological processes.[1] Control of these oxidations is achieved by catalysts in which the active sites are metal centers, and as a consequence, the reactivity of metal complexes toward molecular oxygen is of fundamental importance. Furthermore, stoichiometric reactions of molecular oxygen with organometallic derivatives have also provided useful synthetic methods for the formation of alkyl hydroperoxides and alcohols.[2] In order to control such metal-based oxidation processes using molecular oxygen, it is essential to understand the factors that influence the reactivity of dioxygen with metal–alkyl derivatives. However, the reactions of organometallic derivatives with oxygen often produce complex mixtures, in part as a result of the indiscriminate reactivity of radical intermediates, and relatively few reactions result in the formation of single products. In this regard, the isolation of discrete products by the reaction of dioxygen with metal–alkyl derivatives, along with their subsequent reactivity, has provided a major challenge. Here we describe (i) the quantitative insertion of dioxygen into the Mg–C bond of the alkyl complexes $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR (3-Bu^{t}pz = 3-C_3N_2Bu^{t}H$_2$; R = CH_3, CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$), to give alkylperoxo derivatives $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgOOR, and (ii) the conversion of the alkylperoxo complexes to alkoxo derivatives, $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgOR, by oxygen atom transfer to either $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR or PPh_3.

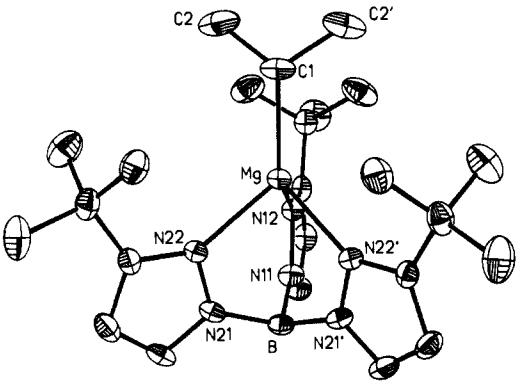

Figure 1. ORTEP diagram of $\{\eta^3$-HB(3-Bu^{t}pz)$_3$MgCH$(CH_3)_2$. For clarity, thermal ellipsoids are shown at 20% probability. Selected bond distances (Å) and angles (deg): Mg–C1, 2.182 (8); Mg–N12, 2.157 (6); Mg–N22, 2.170 (4); C1–C2, 1.515 (9); N11–N12, 1.377 (8); N21–N22, 1.375 (5); B–N11, 1.541 (11); B–N21, 1.537 (6); C1–Mg–N12, 124.8 (3); C1–Mg–N22, 124.0 (2); Mg–C1–C2, 119.1 (4); C2–C1–C2′, 106.6 (7); N12–Mg–N22, 93.1 (2); N22–Mg–N22′, 87.8 (2); N11–B–N21, 109.8 (4); N21–B–N21′, 110.8 (6).

We have recently reported the synthesis and reactivity of the primary alkyl derivatives $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR (R = CH_3, CH_2CH_3).[3] The secondary and tertiary alkyl derivatives $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR (R = $CH(CH_3)_2$, $C(CH_3)_3$)[4] may also be prepared by a similar procedure (eq 1), and the molecular structure of $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgCH$(CH_3)_2$ has been determined by single-crystal X-ray diffraction (Figure 1).[5]

$$R_2Mg \xrightarrow{Tl\{HB(3\text{-}Bu^tpz)_3\}} \{\eta^3\text{-}HB(3\text{-}Bu^tpz)_3\}MgR \qquad (1)$$

Treatment of the alkyl complexes $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR (R = CH_3, CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$) with excess O_2 at room temperature results in the formation of the alkylperoxo derivatives $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgOOR (eq 2). The reactions of the deriv-

$$\{\eta^3\text{-}HB(3\text{-}Bu^tpz)_3\}MgR + O_2 \rightarrow \{\eta^3\text{-}HB(3\text{-}Bu^tpz)_3\}MgOOR \qquad (2)$$

atives $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR (R = CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$) with O_2 are both instantaneous (<5 min) and quantitative, as judged by ^{1}H NMR spectroscopy. In contrast, the reaction of O_2 with $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgCH$_3$ is significantly slower ($t_{1/2}$ ~ 9h at room temperature) than for the other alkyl derivatives.[6]

The products obtained from the reactions of $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgR with $^{17}O_2$ (41%) have been investigated by ^{17}O NMR spectroscopy. Specifically, each complex shows two ^{17}O NMR resonances in the ranges δ 102–183 and 323–427 for the peroxo (MgOOR) unit, which thus suggests that ^{17}O NMR spectroscopy may be a powerful method for the characterization of alkylperoxo complexes. The MgOOR group is further characterized by IR absorption bands in the ranges 889–935 cm^{-1} (ν_{O-O}) and 608–660 cm^{-1} (ν_{Mg-O}) that are assigned on the basis of the shifts observed for the isotopomers $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$-Mg^{18}O^{18}OR.[7] Other supporting evidence that the products are

(1) (a) Mimoun, H. *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: Oxford, 1987; Vol. 6, pp 317–410. (b) Sheldon, R. A.; Kochi, J. K. *Metal Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, 1981. (c) Grasselli, R. K.; Burrington, J. D. *Adv. Catal.* **1981**, *30*, 133–163. (d) Grasselli, R. K.; Burrington, J. D.; Brazdil, J. F. *Faraday Discuss. Chem. Soc.* **1981**, *72*, 203–223. (e) Sheldon, R. A. *J. Mol. Catal.* **1983**, *20*, 1–26. (f) Martell, A. E. *Pure Appl. Chem.* **1983**, *55*, 125–135. (g) Malmstrom, B. G. *Annu. Rev. Biochem.* **1982**, *51*, 21–59. (h) Perutz, M. F. *Annu. Rev. Biochem.* **1979**, *48*, 327–386. (i) Jones, R. D.; Summerville, D. A.; Basolo, F. *Chem. Rev.* **1979**, *79*, 139–179. (j) White, R. E. *Annu. Rev. Biochem.* **1980**, *49*, 315–356. (k) Guengerich, F. P.; Macdonald, T. L. *Acc. Chem. Res.* **1984**, *17*, 9–16. (l) Collman, J. P. *Acc. Chem. Res.* **1977**, *10*, 265–272.

(2) (a) Brilkina, T. G.; Shushunov, V. A. *Reactions of Organometallic Compounds with Oxygen and Peroxides*; Illiffe Books Ltd.: London, 1969. (b) Kharasch, M. S.; Reinmuth, O. *Grignard Reactions of Nonmetallic Substances*; Prentice-Hall: New York, 1954. (c) Davies, A. G. *Organic peroxides*; Swern, D., Ed.; Wiley-Interscience: New York, 1972; Vol. 2, Chapter 4, pp 337–354. (d) Walling, C.; Buckler, S. A. *J. Am. Chem. Soc.* **1955**, *77*, 6032–6038. (e) Blackburn, T. F.; Labinger, J. A.; Schwartz, J. *Tetrahedron Lett.* **1975**, 3041–3044. (f) Panek, E. J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1972**, *94*, 8768–8775. (g) Hock, H.; Kropf, H.; Ernst, F. *Angew. Chem.* **1959**, *71*, 541–545. (h) Sosnovsky, G.; Brown, J. H. *Chem. Rev.* **1966**, *66*, 529–566. (i) Porter, C. W.; Steele, C. *J. Am. Chem. Soc.* **1920**, *42*, 2650–2654. (j) Hock, H.; Ernst, F. *Chem. Ber.* **1959**, *92*, 2716–2723. (k) Hock, H.; Ernst, F. *Chem. Ber.* **1959**, *92*, 2723–2732. (l) Hock, H.; Ernst, F. *Chem. Ber.* **1959**, *92*, 2732–2740.

(3) Han, R.; Looney, A.; Parkin, G. *J. Am. Chem. Soc.* **1989**, *111*, 7276–7278.

(4) In view of the sterically demanding nature of the tris(3-*tert*-butylpyrazolyl)hydroborato ligand, it is possible that the ground state of the *tert*-butyl derivative is η^2-coordinated, $\{\eta^2$-HB(3-Bu^{t}pyz)$_3\}$MgC$(CH_3)_3$, although this structure cannot be observed down to −90 °C in the ^{1}H NMR spectrum.

(5) Crystal data for $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgCH$(CH_3)_2$: orthorhombic, *Pnma*, a = 17.171 (2) Å, b = 15.893 (7) Å, c = 10.034 (3) Å, V = 2738 Å^3, Z = 4, ρ(calcd) = 1.09g cm^{-3}, μ(calcd) = 0.9 cm^{-1}, λ(Mo Kα) = 0.71073 Å (graphite monochromator); 4115 unique reflections with $3° < 2\theta < 60°$ were collected, of which 1024 reflections with $F > 5\sigma(F)$ were used in refinement; R = 6.44%, R_w = 6.06%, goodness of fit = 1.4.

(6) The reaction of O_2 with $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgCH$_3$ is also accompanied by ca. 30% decomposition, so that the product $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgOOCH$_3$ has only been characterized spectroscopically.

0002-7863/90/1512-3662$02.50/0

alkylperoxo complexes include (i) the independent synthesis of the *tert*-butylperoxo derivative, $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOOC(CH}_3)_3$, by the reaction of $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgCH}_3$ with $(CH_3)_3COOH$ (eq 3), and (ii) the formation of the alkoxo derivative $\{\eta^3$-HB-(3-Bu^{t}pz)$_3\}$MgOR[8] and Ph_3PO upon treatment of $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgOOR with PPh_3 (eq 4).

$$\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgCH}_3 + (CH_3)_3COOH \rightarrow \{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOOC(CH}_3)_3 + CH_4 \quad (3)$$

$$\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOOR} + PPh_3 \rightarrow \{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOR} + Ph_3PO \quad (4)$$

Although a number of well-characterized examples of reactions of dioxygen with metal-alkyl complexes have been reported, isolated products are commonly alkoxo derivatives, $[L_nMOR]$,[9] with relatively few examples involving isolation of alkylperoxo complexes, $[L_nMOOR]$.[10] The selective formation of alkylperoxo complexes in the reactions of $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}$MgR with O_2 is presumably a consequence of the sterically demanding ligand environment that hinders bimolecular oxygen atom abstraction from the alkylperoxo complex by the alkyl derivative, which is the commonly suggested pathway for the formation of alkoxo derivatives (eq 5). In accord with this suggestion, $\{\eta^3$-HB(3-

$$L_nMOOR + L_nMR \rightarrow 2L_nMOR \quad (5)$$

Bu^{t}pz)$_3\}$MgOOCH(CH$_3$)$_2$ and $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgCH(CH}_3)_2$ do not react rapidly at room temperature to give the alkoxo derivative $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOCH(CH}_3)_2$, but rather require heating to 80 °C to effect this transformation (eq 6).

$$\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOOPr}^i + \{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgPr}^i \xrightarrow{80\ ^\circ C} 2\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOPr}^i \quad (6)$$

The direct insertion of ground-state triplet oxygen into metal-carbon bonds has been considered to be unlikely since the products would be formed in a high-energy triplet state. Indeed, the rearrangement and racemization of alkyl groups, and inhibition of oxygenation by radical traps, have provided strong evidence for mechanisms involving radical intermediates (eq 7-9) in the reactions of metal-alkyls with O_2.[11] Although the insertion of

$$L_nMR + O_2 \rightarrow L_nMOO^\bullet + R^\bullet \text{ (initiation)} \quad (7)$$

$$R^\bullet + O_2 \rightarrow ROO^\bullet \quad (8)$$

$$L_nMR + ROO^\bullet \rightarrow L_nMOOR + R^\bullet \quad (9)$$

O_2 into the Mg-C bonds of the derivatives $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgR}$ (R = CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$) is too rapid to be studied, small quantities (<2%) of galvinoxyl, a radical trap, inhibit the reaction $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgCH}_3$ with O_2, thus supporting the above radical-chain sequence for formation of the alkylperoxo derivatives $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}$MgOOR.

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Registry No. $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgCH}_3$, 122519-72-6; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgCH}_2\text{CH}_3$, 122519-82-8; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgCH(CH}_3)_2$, 125950-40-5; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgC(CH}_3)_3$, 125950-41-6; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOOCH}_3$, 125950-42-7; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOOCH}_2\text{CH}_3$, 125950-43-8; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOOCH(CH}_3)_2$, 125950-44-9; $\{\eta^3$-HB(3-Bu^{t}pz)$_3\}$MgOOC(CH$_3$)$_3$, 125950-45-0; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}$-MgOCH$_3$, 125950-46-1; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOCH}_2\text{CH}_3$, 125950-47-2; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgOCH(CH}_3)_2$, 125950-48-3; $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}$-MgOC(CH$_3$)$_3$, 122519-77-1.

Supplementary Material Available: Tables of spectroscopic data for all new compounds and tables of crystal and intensity collection data, atomic coordinates, bond distances and angles, and anisotropic displacement parameters and an ORTEP drawing for $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgCH(CH}_3)_2$ (15 pages); listing of observed and calculated structure factors for $\{\eta^3\text{-HB(3-Bu}^t\text{pz)}_3\}\text{MgCH(CH}_3)_2$ (6 pages). Ordering information is given on any current masthead page.

(7) ν_{O-O} for alkylperoxy derivatives are typically in the range 850-950 cm^{-1}. (a) Booth, B. L.; Haszeldine, R. N.; Neuss, G. R. H. *J. Chem. Soc., Dalton Trans.* **1982**, 37-41. (b) Saussine, L.; Brazi, E.; Robine, A.; Mimoun, H.; Fischer, J.; Weiss, R. *J. Am. Chem. Soc.* **1985**, *107*, 3534-3540. (c) Strukul, G.; Ros, R.; Michelin, R. A. *Inorg. Chem.* **1982**, *21*, 495-500. (d) Mimoun, H.; Charpentier, R.; Mitschler, A.; Fischer, J.; Weiss, R. *J. Am. Chem. Soc.* **1980**, *102*, 1047-1054. (e) Strukul, G.; Michelin, R. A.; Orbell, J. D.; Randaccio, L. *Inorg. Chem.* **1983**, *22*, 3706-3713. (f) Momoun, H.; Mignard, M.; Brechot, P.; Saussine, L. *J. Am. Chem. Soc.* **1986**, *108*, 3711-3718. (g) Nishinaga, A.; Tomita, H.; Ohara, H. *Chem. Lett.* **1983**, 1751-1754. (h) Ferguson, G.; Monaghan, P. K.; Parvez, M.; Puddephatt, R. J. *Organometallics* **1985**, *4*, 1669-1674. (i) Giannotti, C.; Fontaine, C.; Chiaroni, A.; Riche, C. *J. Organomet. Chem.* **1976**, *113*, 57-65. (j) Tatsuno, Y.; Otsuka, S. *J. Amer. Chem. Soc.* **1981**, *103*, 5832-5839. (k) van Asselt, A.; Santarsiero, B. D.; Bercaw, J. E. *J. Am. Chem. Soc.* **1986**, *108*, 8291-8293. (l) Mimoun, H.; Chaumette, P.; Mignard, M.; Saussine, L. *Nouv. J. Chim.* **1983**, *7*, 467-475. (m) Espenson, J. H.; Melton, J. D. *Inorg. Chem.* **1983**, *22*, 2779-2781. (n) Giannotti, C.; Fontaine, C.; Septe, B. *J. Organomet. Chem.* **1974**, *71*, 107-124. (o) Nishinaga, A.; Tomita, H.; Nishizawa, K.; Matsuura, T.; Ooi, S.; Hirotsu, K. *J. Chem. Soc., Dalton Trans.* **1981**, 1504-1514.

(8) The alkoxo derivatives $\{\eta^3\text{-HB(3-Bu}^t\text{pyz)}_3\}\text{MgOR}$ (R = $CH(CH_3)_2$, $C(CH_3)_3$) have also been synthesized independently by the reaction of $\{\eta^3$-HB(3-Bu^{t}pyz)$_3\}$MgCH$_3$ with ROH. Also see ref 3.

(9) (a) Lubben, T. V.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1987**, *109*, 424-435. (b) Brindley, P. B.; Scotton, M. J. *J. Chem. Soc., Dalton Trans.* **1981**, 419-423. (c) Parkin, G.; Schaefer, W. P.; Marsh, R. E.; Bercaw, J. E. *Inorg. Chem.* **1988**, *27*, 3262-3264. (d) Parkin, G.; Bercaw, J. E. *Polyhedron* **1988**, *7*, 2053-2082. (e) Bottomley, F.; Magill, C. P.; White, P. S. *J. Am. Chem. Soc.* **1989**, *111*, 3071-3073. (f) Saussine, L.; Brazi, E.; Robine, A.; Minoun. H.; Fischer, J.; Weiss, R. *J. Am. Chem. Soc.* **1985**, *107*, 3534-3540. (g) Nishinaga, A.; Tomita, H.; Ohara, H. *Chem. Lett.* **1983**, 1751-1754. Also see ref. 2e.

(10) (a) Fontaine, C.; Duong, K. N. V.; Merienne, C.; Gaudemer, A.; Giannotti, C. *J. Organomet. Chem.* **1972**, *38*, 167-178. (b) Chiaroni, A.; Pascard-Billy, C. *Bull. Soc. Chim. Fr.* **1973**, 781-787. (c) Jensen, F. R.; Kiskis, R. C. *J. Organomet. Chem.* **1973**, *49*, C46-C48. (d) Cleaver, W. M.; Barron, A. R. *J. Am. Chem. Soc.* **1989**, *111*, 8966-8967. Also see ref 7n.

(11) (a) Davies, A. G.; Roberts, B. P. *Acc. Chem. Res.* **1972**, *5*, 387-392. (b) Davies, A. G.; Roberts, B. P. *J. Chem. Soc., Dalton Trans.* **1968**, 1074-1078. (c) Lamb, R. C.; Ayers, P. W.; Toney, M. K.; Garst, J. F. *J. Am. Chem. Soc.* **1966**, *88*, 4261-4262. (d) Walling, C.; Cioffari, A. *J. Am. Chem. Soc.* **1970**, *92*, 6609-6611. (e) Howden, M. E. H.; Maercker, A.; Burdon, J.; Roberts, J. D. *J. Am. Chem. Soc.* **1966**, *88*, 1732-1742. (f) Panek, E. J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1972**, *94*, 8768-8775. (g) Jensen, F. R.; Kiskis, *J. Organomet. Chem.* **1973**, *49*, C46-C48. (h) Davies, A. G.; Roberts, B. P. *J. Am. Chem. Soc. B* **1968**, 1074-1078. Als see refs 2e and 9b.

New Nuclear Magnetic Resonance Experiment for Measurements of the Vicinal Coupling Constants $^3J_{HN\alpha}$ in Proteins

Dario Neri, Gottfried Otting, and Kurt Wüthrich*

Institut für Molekularbiologie und Biophysik
Eidgenössische Technische Hochschule—Hönggerberg
CH-8093 Zürich, Switzerland

Received October 12, 1989

The NMR[1] method of protein three-dimensional structure determination[2,3] makes use primarily of distance constraints measured with ^{1}H-^{1}H nuclear Overhauser enhancement (NOE) experiments.[4] High-quality structure determinations further

(1) Abbreviations: NMR, nuclear magnetic resonance; 2D, 3D, two-dimensional, three-dimensional; COSY, 2D correlated spectroscopy; BPTI, bovine pancreatic trypsin inhibitor; 434 repressor(1-69), N-terminal DNA-binding domain of the 434 repressor comprising 69 residues; $^3J_{HN\alpha}$, homonuclear vicinal amide proton-C$^\alpha$ proton coupling constant. In the product operator formalism used, H^N denotes an amide proton, H$^\alpha$ a C$^\alpha$ proton, and N a nitrogen-15 spin.

(2) Wüthrich, K.; Wider, G.; Wagner, G.; Braun, W. *J. Mol. Biol.* **1982**, *155*, 311-319.

(3) Wüthrich, K. *NMR of Proteins and Nucleic Acids*; Wiley: New York, 1986.

(4) (a) Wemmer, D. E.; Reid, B. R. *Annu. Rev. Phys. Chem.* **1985**, *36*, 105-137. (b) Kaptein, R.; Boelens, R.; Scheek, R. M.; Van Gunsteren, W. F. *Biochemistry* **1988**, *27*, 5389-5395. (c) Clore, G. M.; Gronenborn, A. M. *Protein Eng.* **1987**, *1*, 275-288. (d) Würthrich, K. *Science* **1989**, *243*, 45-50. (e) Wüthrich, K. *Acc. Chem. Res.* **1989**, *22*, 36-44.

0002-7863/90/1512-3663$02.50/0