Table I. Reductive Deoxygenation of Phenazine Di-*N*-oxide 1

conditns[a]	ratio[b,c] phenazine di-*N*-oxide 1/ phenazine mono-*N*-oxide	phenazine di-*N*-oxide 1/ phenazine
aerobic	19.1	-[d]
anaerobic	7.5	9.5

[a] Carried out in 80 μL (total volume) of 2.5 mM sodium cacodylate, pH 7.5, containing 16.5 μg of sonicated calf thymus DNA, 50 μM 1, and 5 mM DTT. The reaction mixture was incubated at 25 °C for 22 h in the dark. DNA was removed by precipitation (2 volumes of ethanol, -80 °C), and the supernatant was analyzed by HPLC. [b] The product ratios were determined by reverse-phase HPLC on a Rainin Microsorb C_{18} column (4.6 mm × 10 cm, 3 μm) using a linear gradient of 20% → 60% CH_3OH in 0.1 M sodium phosphate, pH 6.2. [c] Elution volumes; phenazine di-*N*-oxide 1, 8.2 min; phenazine mono-*N*-oxide [2-[(3'-aminopropyl)amino]phenazine 5(10)-mono-*N*-oxide], 12.4 min; phenazine [2-[(3'-aminopropyl)amino]phenazine], 16.3 min. [d] Not detected.

A number of heterocyclic di-*N*-oxides have been reported to exhibit cytotoxicity toward mammalian and bacterial cells.[10] The mechanism of toxicity has been suggested to involve one-electron-reductive activation of the parent *N*-oxides, which could result in the production of $^{\bullet}OH$ and $O_2^{\bullet-}$ (Scheme I).[10c,d,11] While the locus of action of these agents has not been established, it seemed reasonable to anticipate that a heterocyclic di-*N*-oxide capable of binding to DNA and producing diffusible oxygen radicals would effect DNA strand scission.[12] Accordingly, 2-[(3'-aminopropyl)amino]phenazine 5,10-di-*N*-oxide (1) was prepared by treatment of 2-chlorophenazine 5,10-di-*N*-oxide[13] with 1,3-diaminopropane.[14]

Phenazine di-*N*-oxide 1 (10-500 μM concentrations) was incubated aerobically with *φX174* replicative form DNA in the presence of 100 μM dithiothreitol (DTT) (Figure 1). As shown, relaxation of supercoiled DNA was observed at all concentrations (and only where DTT was present) and increased in proportion to the concentration of 1 utilized. Essentially complete conversion of supercoiled (form I) DNA to relaxed (form II) DNA was achieved at 50 μM phenazine di-*N*-oxide, so this concentration was used to study the effects of O_2 and another reducing agent on the facility of DNA cleavage. As shown in Figure 2, compound 1 effected cleavage of the plasmid DNA anaerobically in the presence of both DTT and NADPH. The extent of DNA cleavage was greater with DTT than with NADPH, and also at the higher of the two concentrations employed for each reductant. Repetition of this experiment under aerobic conditions gave similar results.

In order to determine the fate of phenazine di-*N*-oxide 1 under the reductive conditions employed here, compound 1 was incubated with DTT and calf thymus DNA under both aerobic and anaerobic conditions. Reduction products were analyzed by HPLC in comparison with authentic synthetic standards;[14] the results are summarized in Table I. Under anaerobic conditions there was substantial conversion of phenazine di-*N*-oxide 1 to the respective phenazine mono-*N*-oxide(s) and to the parent phenazine derivative. In contrast, little reductive deoxygenation was observed under aerobic conditions. These results are consistent with Scheme I and suggest that reductive activation of phenazine 1 produces $O_2^{\bullet-}$ and $^{\bullet}OH$ under aerobic and anaerobic conditions, respectively. While $^{\bullet}OH$-mediated DNA cleavage might be thought to be substantially more facile, it may be noted that $O_2^{\bullet-}$ can, in principle, be produced catalytically under aerobic conditions.[15]

The present findings establish the utility of phenazine di-*N*-oxide to mediate DNA strand scission under conditions similar to those expected to obtain within an intact cell. The fact that this compound can be activated by the bioreductive agent NADPH argues for the potential therapeutic utility of this species, e.g., as part of an antisense oligonucleotide.[16]

Acknowledgment. This work was supported by Research Grant AI 27185, awarded by the National Institutes of Health, Department of Health and Human Services.

(10) (a) Suter, W.; Rosselet, A.; Knusel, F. *Antimicrob. Agents Chemother.* **1978**, *13*, 770. (b) Suter, W.; Rosselet, A.; Knusel, F. *Antimicrob. Agents Chemother.* **1981**, *20*, 336. (c) Crawford, D. L.; Scamehorn, R. G.; Hollstein, U.; Ryan, M. D.; Kovacic, P. *Chem.-Biol. Interact.* **1986**, *60*, 67. (d) Zeman, E. M.; Brown, J. M.; Lemmon, M. J.; Hirst, V. K.; Lee, W. W. *Int. J. Radiat. Oncol., Biol., Phys.* **1986**, *12*, 1239.

(11) Consistent with this scheme was the greater toxicity of these agents under hypoxic conditions,[10] and the recovery of the deoxygenated heterocycles when reductive activation occurred under conditions of hypoxia. See: Lauderoute, K. R.; Rauth, A. M. *Biochem. Pharmacol.* **1986**, *35*, 3417.

(12) We found that the cytotoxic agent 3-amino-1,2,4-benzotriazine 1,4-di-*N*-oxide,[10d,11] which would not be expected to bind to DNA, gave little relaxation of pBR322 plasmid DNA (approximately 17% conversion from supercoiled → relaxed circular DNA) even when employed anaerobically at 1.8 mM concentration (100 μM DTT, 25 °C, 30 min).

(13) (a) Vivian, D. L. *J. Am. Chem. Soc.* **1951**, *73*, 457. (b) Pachter, I. J.; Kloetzel, M. C. *J. Am. Chem. Soc.* **1952**, *74*, 971.

(14) A suspension of 2-chlorophenazine 5,10-di-*N*-oxide[13] (500 mg, 2.03 mmol) in 10 mL of DMF was treated with 1,3-diaminopropane (20 mL, 240 mmol) and K_2CO_3 (1.65 g, 11.9 mmol). The reaction mixture was heated at 60 °C for 22 h, then cooled, and filtered. The filtrate was concentrated, and the residue was purified by chromatography on silica gel; elution was with 1:1 CH_2Cl_2-CH_3OH containing 1% NH_4OH. 2-[(3'-Aminopropyl)amino]-phenazine 5,10-di-*N*-oxide was obtained as a dark purple powder: yield 450 mg (78%); mp 140-142 °C dec; silica gel TLC (50:50:1 CH_2Cl_2-CH_3OH-NH_4OH) R_f 0.17; ^1H NMR (CD_3OD) δ 1.93 (m, 2), 2.84 (t, 2), 3.38 (t, 2), 7.18 (d, 1, J = 2.9 Hz), 7.37 (dd, 1, J = 2.9, 12.9 Hz), 7.76 (m, 1), 7.90 (m, 1), 8.36 (d, 1, J = 12.9 Hz), 8.56 (d, 1, J = 7.5 Hz), and 8.59 (d, 1, J = 7.5 Hz); mass spectrum (chemical ionization, isobutane) m/z 285 $(M + H)^+$, 269, and 253. Also obtained as a byproduct was 2-[(3'-aminopropyl)amino]-phenazine 10-mono-*N*-oxide: yield 53 mg (10%); silica gel TLC (50:50:1 CH_2Cl_2-CH_3OH-NH_4OH) R_f 0.22; mass spectrum (chemical ionization, isobutane) m/z 269 $(M + H)^+$ and 253. Treatment of phenazine di-*N*-oxide 1 with 10% palladium on carbon in methanol afforded 2-[(3'-aminopropyl)-amino]phenazine in quantitative yield: mass spectrum (chemical ionization, methane) m/z 253 $(M + H)^+$.

(15) Although the species responsible for DNA strand scission have not been established definitively, it may be noted that $O_2^{\bullet-}$ can be converted to $^{\bullet}OH$ ($2H^+ + 2O_2^{\bullet-} \rightarrow O_2 + H_2O_2$, and $H_2O_2 + O_2^{\bullet-} \rightarrow {}^{\bullet}OH + {}^{-}OH + O_2$; see: Lesko, S. A.; Lorentzen, R. J.; Ts'o, P. O. P. *Biochemistry* **1980**, *19*, 3023) and that DNA strand scission mediated by 1 was substantially quenched in the presence of DMSO, a known scavenger of $^{\bullet}OH$ (Repine, J.; Pfenninger, O. W.; Talmage, D. W.; Berger, E. M.; Pettijohn, D. E. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 1001).

(16) Covalent attachment of 1 to an oligonucleotide via the aminopropyl group afforded an antisense oligonucleotide that gave cleavage of the complementary target at the expected site upon admixture of DTT (Nagai, K.; Hecht, S. M., unpublished results).

Preparation of Monomeric (η^6-Arene)OsNR Complexes and Their Exchange Reactions with Amines, Alcohols, and Thiols

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Most of the molecules that contain metal-imido groups are derived from the center of the transition series (i.e., group 5-8 metals).[1] Recent advances have extended this class of compounds to zirconium[2] and to iridium,[3] in an effort to generate more reactive M-N linkages. We report here the synthesis of reactive, monomeric, low-valent η^6-arene imido osmium complexes,[4-6] (η^6-

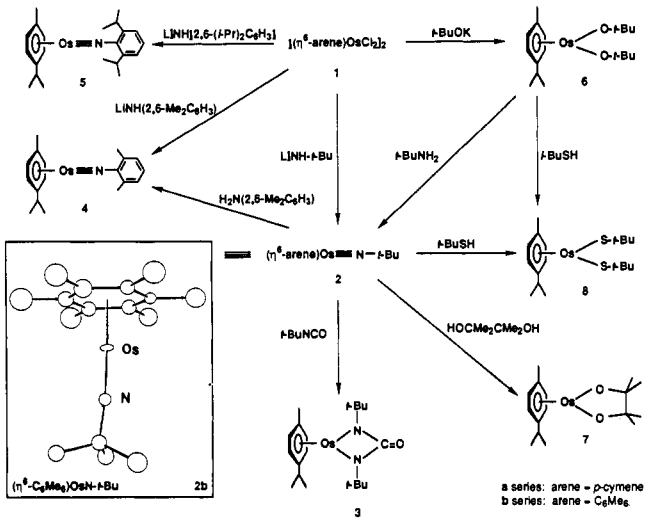
(1) For reviews of transition-metal imido chemistry, see: (a) Nugent, W. A.; Mayer, J M. *Metal Ligand Multiple Bonds*; John Wiley and Sons: New York, 1988. (b) Nugent, W. A.; Haymore, B. L. *Coord. Chem. Rev.* **1980**, *31*, 123. For a recent paper with a brief discussion of transition-metal imides, see: (c) Harlan, E. W.; Holm, R. H. *J. Am. Chem. Soc.* **1990**, *112*, 186.

(2) (a) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 8729. (b) Cummins, C. C.; Baxter, S. M.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1988**, *110*, 8731.

(3) Glueck, D. S.; Wu, J.-X.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1991**, *113*, 2041.

0002-7863/91/1513-5100$02.50/0

Scheme I



arene)OsNR, and show that they react with alcohols and thiols to give (arene)osmium bis(alkoxide) and bis(thiolate) complexes.

Scheme I summarizes the preparation and reactivity of the osmium imido compounds. Treatment of $[CymOsCl_2]_2$ (Cym = η^6-*p*-cymene) (**1a**) or $[(\eta^6\text{-}C_6Me_6)OsCl_2]_2$[6c] (**1b**) with 4 equiv of LiNH-*t*-Bu in tetrahydrofuran provided the imido compounds (η^6-arene)OsN-*t*-Bu (arene = Cym (**2a**) or C_6Me_6 (**2b**), respectively) as yellow crystals from pentane in 85–95% yield.[7] As was observed for the Cp*Ir compound,[3] the *tert*-butyl signals for **2a** and **2b** appear as a three-line pattern of intensity 1:1:1 (J = 1.5 Hz) in the ^{1}H NMR spectrum due to coupling to ^{14}N (I = 1).[8] Infrared stretching absorptions characteristic of monomeric imido ligands[1a] were observed at 1250 cm^{-1} for both **2a** and **2b**, which was confirmed by the 15-cm^{-1} shift of this absorption to 1235 cm^{-1} for CymOs^{15}N-*t*-Bu (**2a**-^{15}N), prepared from **1a** and Li^{15}NH-*t*-Bu.[9] The ^{1}H NMR spectrum of **2a**-^{15}N shows a doublet for the *tert*-butyl resonance (J = 2.4 Hz) due to coupling to ^{15}N (I = $^1/_2$). The ^{13}C{^{1}H} NMR spectrum of **2a**-^{15}N shows coupling into the *tert*-butyl group (both the primary and quaternary carbons, J = 0.6 Hz) as well as coupling into the arene ring carbons (J = 0.8 Hz).[10] Compound **2a**-^{15}N displays a singlet at −65.0 ppm (with respect to CH_3NO_2 in C_6D_6) in the ^{15}N NMR spectrum. The electron-impact mass spectra for **2a** and **2a**-^{15}N show [M]$^+$ at m/e 397 and 398, respectively.

The monomeric nature of **2b** was confirmed by an X-ray diffraction study performed on a single crystal.[11] An ORTEP diagram is provided in Scheme I. Compound **2b** adopts the same "pogo-stick" geometry observed for Cp*IrN-*t*-Bu. The nearly linear Os–N–C angle of 174.1 (7)° and the short Os–N bond distance of 1.737 (7) Å are consistent with Os–N multiple bonding.[1a] This is the first structurally characterized osmium(II) imide; the high oxidation state derivatives show similar Os–N distances (1.65–1.74 Å) and Os–N–C angles (164–179°).[4a–d] The crystal structure of the dimeric ruthenium(II) compound $[(\eta^6\text{-}C_6H_6)Ru(\mu\text{-}N\text{-}2,6\text{-}(Me_2CH)_2C_6H_3)]_2$ has appeared recently.[12]

Compound **2a** undergoes a reaction with the heterocumulene *t*-BuNCO when heated at 45 °C for 36 h in benzene to provide blue-green metallacycle **3** in >98% yield.[13,14] Complex **3** readily sublimes at 60 °C/80 mTorr and exhibits [M]$^+$ at m/e 496 in the electron-impact mass spectrum. An IR absorption due to the CO stretch is observed at 1656 cm^{-1}, and the carbonyl carbon appears in the ^{13}C{^{1}H} NMR spectrum at 174.4 ppm. Although possibly involved in the metal-catalyzed synthesis of urea derivatives, addition reactions of the type described are rare for metal–imido compounds.[2a,3,13a]

Imide **2a** reacts with a variety of X–H bonds (X = N, O, S). Addition of 3.4 equiv of $H_2N(2,6\text{-}Me_2C_6H_3)$ to a benzene solution of **2a** resulted in amine/imido exchange, leading to formation of the purple aryl imide $CymOsN(2,6\text{-}Me_2C_6H_3)$ (**4**) after 2 h at room temperature in 77% yield by ^{1}H NMR integration against an internal standard.[15] Analysis of the volatile materials by ^{1}H NMR spectrometry showed free *t*-$BuNH_2$. Complex **4** was synthesized independently in 96% yield by addition of 4.2 equiv of $LiNH(2,6\text{-}Me_2C_6H_3)$ to **1a** in THF. A related proton-transfer reaction with the more hindered amine, $H_2N[2,6\text{-}(i\text{-}Pr)_2C_6H_3]$, gave no exchange product as shown by ^{1}H NMR spectrometry. However, the expected $CymOsN[2,6\text{-}(i\text{-}Pr)_2C_6H_3]$ (**5**) was prepared from **1a** and 4 equiv of $LiNH[2,6\text{-}(i\text{-}Pr)_2C_6H_3]$ in THF

(4) For structurally characterized Os imides, see: (a) Nugent, W. A.; Harlow, R. L.; McKinney, R. J. *J. Am. Chem. Soc.* **1979**, *101*, 7625. (b) Griffith, W. P.; McManus, N. T.; Skapski, A. C.; White, A. D. *Inorg. Chim. Acta* **1985**, *105*, L11. (c) Shapley, P. A. B.; Own, Z.-Y.; Huffman, J. C. *Organometallics* **1986**, *5*, 1269. (d) Anhaus, J. T.; Kee, T. P.; Schofield, M. H.; Schrock, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 1643. For a reference to an unpublished structure, see: (e) Williams, D. S.; Schofield, M. H.; Anhaus, J. T.; Schrock, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 6728 and ref 10 therein. For other isolated high oxidation state Os imides, see: (f) Chatt, J.; Dilworth, J. R. *J. Chem. Soc., Chem. Commun.* **1972**, 549. (g) Patrick, D. W.; Truesdale, L. K.; Biller, S. A.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2628. (h) Che, C.-M.; Lam, M. H.-W.; Mak, T. C. *J. Chem. Soc., Chem. Comm.* **1989**, 1529. (i) Danopoulos, A. A.; Wilkinson, G.; Hussain-Bates, B.; Hursthouse, M. D. *J. Chem. Soc., Dalton Trans.* **1991**, 269. A low oxidation state Os imide [Os(II)] is known, but its reactivity and structure are not reported: (j) McGlinchey, M. J.; Stone, F. G. A. *J. Chem. Soc. Chem. Commun.* **1970**, 1265. An Os imide is believed to be an intermediate: (k) Barner, C. J.; Collins, T. J.; Mapes, B. E.; Santarsiero, B. D. *Inorg. Chem.* **1986**, *25*, 4323.

(5) For a discussion of late metal terminal oxo compounds, see: Mayer, J. M. *Comments Inorg. Chem.* **1988**, *8*, 125.

(6) (a) Cabeza, J. A.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1985**, 573. For a review of (η^6-arene)Ru and (η^6-arene)Os chemistry, see: (b) Le Bozec, H.; Touchard, D.; Dixneuf, P. H. *Adv. Organomet. Chem.* **1989**, *29*, 163. For more recent (arene)osmium compounds, also see: (c) Kiel, W. A.; Ball, R. G.; Graham, W. A. G. *J. Organomet. Chem.* **1990**, *383*, 481. (d) Stahl, S.; Werner, H. *Organometallics* **1990**, *9*, 1876. (e) Werner, H.; Roder, K. *J. Organomet. Chem.* **1989**, *367*, 339. (f) Roder, K.; Werner, H. *J. Organomet. Chem.* **1989**, *367*, 321. (g) Schultz, M.; Stahl, S.; Werner, H. *J. Organomet. Chem.* **1990**, *394*, 469. (h) Bennett, M. A.; Weerasuria, A. M. M. *J. Organomet. Chem.* **1990**, *394*, 481.

(7) All compounds were characterized by ^{1}H and ^{13}C{^{1}H} NMR and IR spectroscopy, and elemental analysis was obtained where possible (**2a,b**, **3**, **4**, **7**, **8**). Electron-impact mass spectral results are reported by the most abundant isotopes (except for **2a**-^{15}N): ^{12}C, ^{1}H, ^{14}N, ^{16}O, ^{192}Os, ^{32}S. Details are provided as supplementary information.

(8) Compounds with axially symmetric electron density at the nitrogen nucleus (i.e., other imides and alkyl isocyanides) frequently show similar coupling. Observation of this phenomenon suggests a linear X–N–C linkage: see ref 1b, p 143, and references therein.

(9) Gilchrist, J.; Collum, D., personal communication. For a full experimental description of the preparation of $H_2{}^{15}N(t\text{-}Bu)$, see ref 3.

(10) The observed coupling constants are consistent with the formula $J(^{14}N\text{–}X) = -0.713[J(^{15}N\text{–}X)]$ derived from the magnetogyric ratio of the N isotopes ($\gamma^{14}/\gamma^{15} = -0.713$). The doublets in the ^{13}C{^{1}H} NMR spectrum were seen only by zerofilling on the FID. These values are consistent with other $J(^{15}N\text{–}^{13}C)$: Levy, G. C.; Lichter, R. L. *Nitrogen-15 Nuclear Magnetic Resonance Spectroscopy*; John Wiley and Sons: New York, 1979. This coupling is not observed for **2a** due to small coupling constants, as predicted by the formula above.

(11) The X-ray diffraction study was carried out by Dr. Frederick J. Hollander, director of the University of California, Berkeley, X-ray diffraction facility (CHEXRAY). Crystal data: $C2/c$, V = 3173.4 (14) Å^3, Mo Kα (λ = 0.71073 Å) μ = 80.3 cm^{-1}; d_{calcd} = 1.77 g/cm^{-3}, a = 13.6502 (26) Å, b = 13.2523 (27) Å, c = 18.0151 (56) Å, α = 90.0°, β = 103.15 (20)°, γ = 90.0°, T = −105 °C, Z = 8; the final residuals for 78 variables refined against the 1737 data for which $F^2 > 3\sigma(F^2)$ were R = 5.6%, wR = 6.9%, and GOF = 3.11. The R value for all 2076 data was 6.7%. Only the osmium atom was refined anisotropically; all other atoms were refined isotropically. Details of the structure determination are provided as supplementary material.

(12) Kee, T. P.; Park, L. Y.; Robbins, J.; Schrock, R. R. *J. Chem. Soc., Chem. Commun.* **1991**, 121.

(13) For reviews of transition-metal isocyanate chemistry, see: (a) Braunstein, P.; Nobel, D. *Chem. Rev.* **1989**, *89*, 1927. (b) Cenini, S.; LaMonica, G. *Inorg. Chim. Acta* **1976**, *18*, 279.

(14) A dimeric nitrogen-bridged structure for **3** is unlikely since such a structure would exhibit diastereotopic isopropyl methyl and inequivalent aromatic proton signals in the ^{1}H and ^{13}C{^{1}H} NMR spectra. One would also expect to observe two different types of *tert*-butyl resonances. An X-ray diffraction study of the dimer $[(p\text{-cymene})Ru[(N\text{-tol})_2CO]]_2$ displays these characteristics: (a) Michelman, R. I.; Andersen, R. A.; Bergman, R. G., unpublished results. This property of the *p*-cymene ligand is commonly observed. For examples, see: (b) Bennett, M. A.; Ennett, J. P. *Organometallics* **1984**, *3*, 1365.

(15) Crystal structures of yellow $Cp^*IrN(2,6\text{-}R_2C_6H_3)$ (R = Me, *i*-Pr) show that these compounds are monomers: see ref 3. Strong IR bands observed for compounds **4** and **5** at 1220 cm^{-1} and 1189 cm^{-1}, respectively, are likely due to vibrations involving the imido ligands.

and isolated by crystallization from CH_3CN in 36% yield.[15] The tertiary proton and carbon resonances for the *i*-Pr groups on the aryl imide ligand are broadened at room temperature in purple **5**, presumably due to hindered rotation about the $(i\text{-Pr})\text{-}C_6H_3$ bonds. The ^1H NMR signal sharpens into a septet at 40 °C while no other line-shape changes are observed.

Reactions of **2a** with alcohols depend on the nature of the substituent. Complex **2a** did not react with *t*-BuOH at room temperature, but the deep red $CymOs(O\text{-}t\text{-}Bu)_2$ (**6**) could be prepared by treatment of **1a** with 2 equiv of *t*-BuOK in THF.[16] Complex **6** was characterized spectroscopically, but repeated attempts to isolate it in analytically pure form have not succeeded. The bis(*tert*-butoxide) **6** was converted to the monomeric imido complex **2a** upon addition of $t\text{-}BuNH_2$, demonstrating that $\Delta G° > 0$ for the **2a** + *t*-BuOH reaction. In contrast to these observations with *t*-BuOH, addition of pinacol $(HOC(CH_3)_2C(CH_3)_2OH)$ to **2a** in pentane led to >98% yield (by ^1H NMR integration against an internal standard) of the red pinacolate $CymOs[OC(CH_3)_2C(CH_3)_2O]$ (**7**).[17] The compound was isolated in 34% yield on a preparative-scale reaction after purification by crystallization from diethyl ether. Electron-impact mass spectroscopy of complex **7** shows the monomeric molecular ion at *m/e* 442.

Although **2a** does not react with *t*-BuOH, addition of *t*-BuSH to **2a** in toluene gave the violet $CymOs(S\text{-}t\text{-}Bu)_2$ (**8**) in 95% yield.[18] The bis(*tert*-butoxide) **6** was also converted to **8** upon addition of 2 equiv of *t*-BuSH. In each case, $t\text{-}BuNH_2$ or *t*-BuOH was observed by ^1H NMR spectrometry as a byproduct of the transformation. Variable-temperature ^1H and $^{13}C\{^1H\}$ NMR studies show no line-shape changes from 25 to −80 °C.[19] The thiolate **8** is monomeric in the mass spectrum, showing $[M]^+$ at *m/e* 504, but no peak at higher mass. Attempts to prepare $CymOs(NH\text{-}t\text{-}Bu)_2$ for direct comparison with **6**, **7**, and **8** by addition of limited amounts (2 equiv) of LiNH-*t*-Bu to **1a** led only to a mixture of **1a** and **2a**.

Monomeric compounds **2a** and **2b** provide additional evidence for the enhanced reactivity of late transition metal imides. These complexes have opened up an opportunity to study Os–X bonds (X = N, O, S) in low-valent osmium compounds and to prepare unusual late transition metal heteroatom bonded complexes. Experiments aimed at exploring these possibilities are under way.

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Supplementary Material Available: Spectroscopic (**2–8**) and analytical data (**2a,b**, **3**, **4**, **7**, and **8**) and details of the structure determination for complex **2b**, including experimental description and ORTEP drawing showing full atomic numbering, tables of crystal and data collection parameters, positional parameters and their estimated standard deviations, and intermolecular distances and angles (11 pages); tables of observed and calculated structure factors for **2b** (13 pages). This material is included with the archival edition of the journal, available in many libraries. Alternatively, ordering information is given on any current masthead page.

(16) For a review of monomeric late-metal alkoxides, see: (a) Bryndza, H. E.; Tam, W. *Chem. Rev.* **1988**, 1163 and references therein. Also see: (b) Hartwig, J. F.; Andersen, R. A.; Bergman, R. G. *J. Organomet. Chem.* **1990**, *394*, 417. (c) Komiya, S.; Tane-Ichi, S.; Yamamoto, A.; Yamamoto, T. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 673.

(17) For a review including some metallapinacols, see: (a) Kahn, B. E.; Rieke, R. D. *Chem. Rev.* **1988**, *88*, 733. Other monomeric metallapinacols have been prepared in our lab and other labs: (b) McCallum, J. S.; Glueck, D. S.; Bergman, R. G. unpublished results. (c) Andrews, M. A.; Gould, G. L. *Organometallics* **1991**, *10*, 387.

(18) For saturated late transition metal bis(thiolates), see: Klein, D. P.; Kloster, G. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 2022 and references therein.

(19) A dimer for **8** would be expected to show two *tert*-butyl resonances (terminal and bridging).

A Neutral, Water-Soluble, α-Helical Peptide: The Effect of Ionic Strength on the Helix–Coil Equilibrium

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Short, alanine-based peptides that are made water-soluble by insertion either of glutamic acid and lysine residues[1] or of lysine alone[2] can adopt an α-helical structure in aqueous solution. A recent calorimetric study[3] suggests that the α-helical polypeptide backbone itself is responsible for the stability of the helix in water. These and other peptides are being used to study the helix propensities of amino acids by substitution experiments.[4-7] Introduction of an uncharged reference peptide could be a significant advance, particularly for determining helix propensities of charged amino acids. We report the synthesis and characterization of such an uncharged helix-forming peptide that contains naturally occurring amino acids.[8] The 16-residue peptide contains three blocks of the simple repeat[11] AAQAA; four alanine residues separate successive glutamine residues. The peptide sequence is Ac-$(AAQAA)_3Y(NH_2)$. The single tyrosine residue allows accurate measurement of peptide concentration by tyrosine absorbance.[2] The acetyl and amide blocking groups eliminate the charges on $\alpha\text{-}NH_3^+$ and $\alpha\text{-}COO^-$ groups, respectively. Insertion of three glutamine residues provides water solubility; the poly-L-alanine sequence is not soluble.

The circular dichroism (CD) spectrum of the peptide (Figure 1) shows the two minima at 222 and 208 nm and the maximum close to 190 nm that are characteristic of mixtures of α-helix and random coil structures,[12] and the helix unfolds with increasing temperature (Figure 1), like other alanine-based peptides.[1-3] The value of $-[\theta]_{222}$ at 0 °C in 0.1 M NaCl (16 500 deg cm^2 dmol^{-1}) is somewhat lower than the values reported[2] (~22 000) for some different 16-residue, alanine-based peptides that contain three lysine residues. Thermal-unfolding curves are coincident over a broad range of peptide concentration (from 8.5 to 119 μM), which shows that helical stability is not concentration dependent and therefore the helix is probably monomeric. An earlier study of

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(8) Peptide synthesis was performed by standard solid-phase methods.[9,10] Peptide purification was performed by using HLPC as described.[3] Peptide purity was determined by amino acid analysis and FABMS (calculated MW 1458.73, found $(M + H)^+$ 1459.46, $(M + Na)^+$ 1481.18). Coincidence of the electrophoretic mobilities of the peptide at pH 5.0 and 2.8 was used to confirm that the glutamine side chains had not hydrolyzed to glutamic acid during the synthesis or purification of the peptide.

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(11) Abbreviations used: A, L-alanine; Q, L-glutamine; Y, L-tyrosine; CD, circular dichroism.

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