an intense charge-transfer band at $\lambda = 318$ nm ($f = 0.32$) corresponding to the electronic excitation $(\sigma)^2(\sigma^*)^1 \rightarrow (\sigma)^1(\sigma^*)^2$, in good agreement with the maximum observed at 334 nm. Furthermore, exploratory calculations indicate that the hydrido[15] and alkyl radical[10] adducts reported previously are indeed π^*-type radicals with a fully formed N-H or N-alkyl two-electron σ bond; the weak absorption band observed at long wavelengths in, e.g., **4**, involves excitation of the π-electron system only. The electronic structures of those radicals are thus dramatically different from the σ^*-type pyridine/Cl• complexes discussed here, reflecting the relative N-X bond strengths.

Both our experimental and our theoretical studies indicate that chlorine complexes with pyridine derivatives involve a long weak bond as in **5**. When this geometry brings the chlorine near a substrate hydrogen, as it does in the steroid examples reported earlier,[3] this loose (probably flexible) complex can perform a direct hydrogen abstraction with excellent selectivity.

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Pressure Effect of the ^{1}H NMR Spectra of Organic Compounds in the Presence of Lanthanide Shift Reagents. A Formally Associative Process Characterized by Volume Expansion

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Following the successful application of hydrostatic pressure in mechanistic investigations of organic reactions[2] and taking a lead from the pioneering investigation of Hunt and Taube[3] in complex ion chemistry, chemists have launched a vigorous effort to apply this tool to substitution reactions of coordination compounds.[4] The main premise in these studies has been the connection of volume decreases (as derived from pressure-induced rate increases) with associative behavior and volume increases with dissociative characteristics. This assumption has been impartially discussed, especially by Swaddle.[5] The insertion of a water molecule into the coordination sphere of hexaaquo cations in water is considered to be the quintessential example of a neutral molecule adding to such ions; the reaction volume is estimated to be −13 to −14 cm^3/mol.

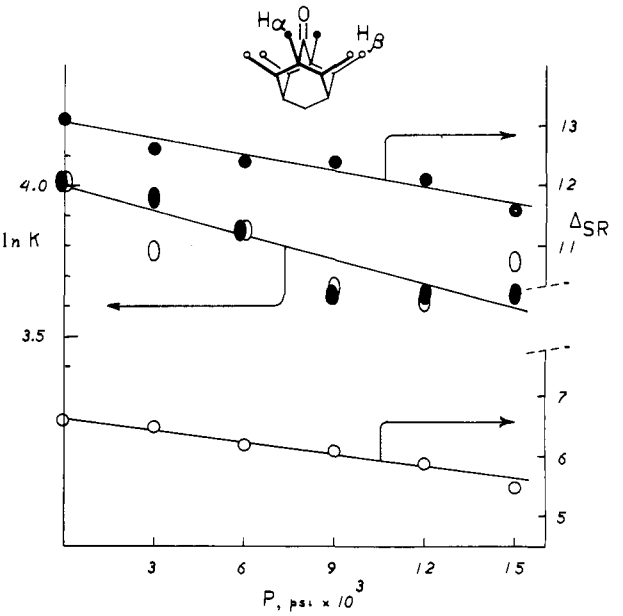

Figure 1. Pressure effects on ln K for the association of adamantanone with Eu(fod)$_3$ (left vertical axis; slope related to ΔV as in the text) and on the bound shifts of H_α and H_β (right vertical axis). Solid points refer to H_α, open ones to H_β.

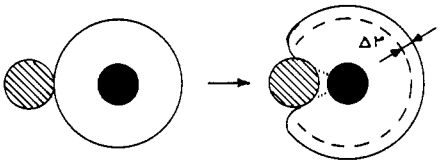

Figure 2. Schematic explanation of expansion upon association.

Accordingly, we began to study pressure effects in the NMR spectra of ketone-lanthanide combinations with the hope that the increased shifts anticipated might enhance the utility of the method, perhaps even expand its applicability to new classes of compounds. Application of the assumption quoted led us to estimate that the volume decrease could be as much as 50 cm^3/mol. But this was not to be. When a solution of adamantanone and Eu(fod)$_3$[6] in $CDCl_3$ is compressed at probe temperature, the well-known paramagnetic shifts of all adamantanone protons are *reduced*. At the same time, the slight increase in shielding of the ligand *tert*-butyl protons observed upon complexation is also reversed. This phenomenon is not an artifact of method or apparatus; it has been found with thick-walled unsupported glass capillaries in either a JEOL FX-90-Q or a Nicolet NT-300 spectrometer as well as with thin-walled capillaries inside metallic non-magnetic pressure vessels in a Bruker WP-60 instrument.[7] The effect of 100 MPa (~1000 atm) pressure is roughly equal to that of dilution by a factor of 2 or more. We soon found that the result is not restricted to this complex. 5-Phenyl- and 5-*tert*-butyladamantan-2-one, piperidine, tetrahydrofuran, and cyclopentanol also exhibited pressure-reduced lanthanide-induced shifts with Eu(fod)$_3$; Yb(fod)$_3$ and the *shielding* reagent Pr(fod)$_3$ showed the same effect with adamantanone. Solvent variations (CD_2Cl_2, CCl_4) caused minor changes in the magnitude of these shifts but did not reverse any.

With the objective of learning whether these effects are due to a suppressed equilibrium population or to a reduction in the bound shift of the complex, we measured the spectra for a series

(1) (a) At Buffalo. (b) At Stony Brook. (c) At Lausanne. (d) At Kobe.
(2) For reviews, see: (a) le Noble, W. J.; Kelm, H. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 841. (b) Isaacs, N. S. *Liquid Phase High Pressure Chemistry*; Wiley: New York, 1981. For a much more complete listing, see: Matsumoto, K.; Sera, A.; Uchida, T. *Synthesis* **1985**, 1.
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(4) (a) Kelm, H. *High Pressure Chemistry*; Reidel: Dordrecht, 1978. (b) van Eldik, R. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*. (c) *Inorganic High Pressure Chemistry: Kinetics and Mechanisms*; van Eldik, R., Ed.; Elsevier: Amsterdam, 1986.
(5) For example: Swaddle, T. W. *Adv. Inorg. Bioinorg. Mech.* **1983**, *2*, 95 (see p 112). Swaddle, T. W. *Inorg. Chem.* **1980**, *19*, 3203; **1983**, *22*, 2663.
(6) Tris-6,6,7,7,8,8,8-heptafluoro-2-dimethyl-3,5-octanedionatoeuropium (III).
(7) For a review of the technology, see: Ando, I.; Webb, G. A. *Magn. Reson. Chem.* **1986**, *24*, 557.

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of equimolar solutions of adamantanone and $Eu(fod)_3$ in $CDCl_3$ and used the Bouquant–Chuche equation to calculate both.[8] Reasonable agreement with known atmosphere pressure data was obtained;[9] our results are shown in Figure 1. Assuming a linear relation between ln K and P, we have calculated the reaction volume $\Delta V^\circ_{ass.} = -RT\,\partial \ln K/\partial p$ to be $+8 \pm 2$ cm^3/mol at 21 °C. At the same time, the bound shift of H_α is reduced by 100 MPa from 13.1 to 11.6 and that of $H_{\beta/syn}$ from 6.6 to 5.5. In the free ligand, the resonances appear at $\delta_\alpha = 2.50$ and $\delta_\beta = 2.00$ ppm;[10] hence these reductions amount to 15–20%. Evidently, *both* the equilibrium concentration and the bound shift of the complex decline as the pressure is raised. Both of these effects are almost unique.

One possible explanation is that the metal–fod bonds may be lengthened somewhat as room is made for the additional ligand (Figure 2). The volume increase resulting from such lengthening by Δr would to a first approximation equal the volume of a spherical shell of radius r_{av} ($=^1/_2 (r_0 + r_i)$) and thickness Δr; i.e., $4\pi\Delta r r_{av}^2$. In other words, it is proportional to the square of the radius. With small ligands and first-series transition-metal ions, this contribution to the volume change should therefore be modest; there is no reason to suppose that it compromises the many solvent exchange studies under pressure that have been reported, for example. But in the present case, even if half of the adamantanone molecule is buried in the coordination sphere, an increase of just 0.1 Å in the Eu–O distances would be enough to negate the hoped-for contraction.[11] X-ray data show that ionic radii do indeed increase by small amounts upon expansion of the number of ligands in the coordination sphere of virtually all monatomic cations.[12]

Alternatively, it is conceivable that these reactions have some feature unsuspected heretofore, in spite of the highly refined analyses that have been made of the shifts observed. Thus, if a substantial fraction of the uncomplexed shift reagent were in an oligomeric form, this could in principle also account for our observations.[13] Still another possibility is that $Eu(fod)_3$ in the absence of any other base in chloroform is strongly bound to the solvent, though evidence for such binding has been vainly sought by Raber.[14] Finally, pressure-induced geometric changes in the shift reagent itself[15] or in the solvent surrounding it[16] can also not be ruled out.

Acknowledgment. We gratefully acknowledge support by the Japanese Ministry of Education (travel grant to H.Y.) and the Swiss and U.S. National Science Foundations for support of this study (A.E.M. and W.J.leN.)

(8) Bouquant, J.; Chuche, J. *Tetrahedron Lett.* **1973**, 493. Alternative approaches have been evaluated: Raber, D. J.; Hardee, L. E. *Org. Magn. Reson.* **1982**, *20*, 125. Our approach is dictated by experimental constraints.

(9) A recent report gives $K = 63$ or 51 dm^3 mol^{-1} at 30 °C (two methods): Horská, A.; Hajek, M.; Trška, P. *P. Chem. Soc., Perkin Trans. 2* **1985**, 1523. An earlier value of 316 (Raber, D. J.; Johnston, M. D.; Janks, C. M.; Perry, J. W.; Jackson, G. F., III *Org. Magn. Reson.* **1980**, *14*, 32) has been revised to 94 (Raber, D. J.; Peters, J. A. *Magn. Reson. Chem.* **1985**, *23*, 621). Our value cannot be put on a par with the reported ones as our resolution is not as good, our signals are broader, and we cannot take small concentrations of other complexes such as LS_2 or L_2S into account. However, the main sources of error should cancel in our treatment of the pressure induced *changes* in K.

(10) Literature values (ref 9): 13.1 or 14.0 and 6.9 or 7.2 (two methods) and 15.4 and 7.5, revised to 15.2 and 7.5, respectively. The other protons change too little and/or overlap too much to be useful in the calculations.

(11) We assumed a molar volume of 135 cm^3 for the adamantanone, and 8 Å for r_{av}.

(12) Shannon, R. D. *Acta Crystallogr.* **1976**, *A32*, 751. Huheey, J. E., Ed. *Inorganic Chemistry: Principles of Structure and Reactivity*, 3rd ed.; Harper and Row: New York, NY, 1983; Chapter 3. We thank Prof. J. Drenth (University of Groningen) for acquainting us with this literature.

(13) Such oligomerization appears to be substantial in CCl_4 (Bruder, A. H.; Tanny, S. R.; Rockefeller, H. A.; Springer, C. S. *Inorg. Chem.* **1974**, *13*, 880) but not in chloroform (Desreux, J. F.; Fox, L. E.; Reilley, C. N. *Anal. Chem.* **1972**, *44*, 2217).

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(15) Inagaki, F.; Miyazawa, T. *Prog. Nucl. Magn. Reson.* **1981**, *14*, 67.

(16) Electrostriction changes in reactions involving neutral species alone are usually considered to be negligible; however, see: Kelm, H.; Palmer, D. A. ref 4a, p 302. Whalley, E. *J. Chem. Phys.* **1963**, *38*, 1400.

Registry No. $Eu(fod)_3$, 17631-68-4; $Yb(fod)_3$, 18323-96-1; $Pr(fod)_3$, 17978-77-7; adamantanone, 700-58-3; 5-phenyladamantan-2-one, 38584-33-7; 5-*tert*-butyladamantan-2-one, 84454-67-1; piperidine, 110-89-4; tetrahydrofuran, 109-99-9; pentanol, 96-41-3.

Supplementary Material Available: Graphs showing the effect of pressure on the chemical shifts of several substrates in the presence of shift reagents in several solvents and tabular summaries (14 pages). Ordering information is given on any current masthead page.

Metallocene Antitumor Agents. Unusual $Mo(\eta^5\text{-}C_5H_5)_2Cl_2$ Nucleotide/Nucleobase Aqueous Coordination Chemistry

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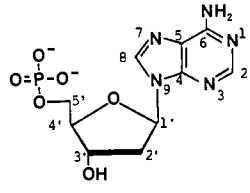
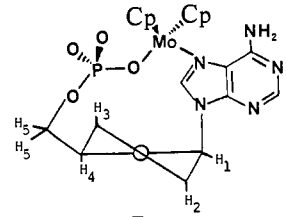
The complexes Cp_2MX_2 (M = Ti, V, Mo; X = halide or pseudohalide) exhibit antineoplastic activity against a wide spectrum of murine and human tumors,[1,2] with the key cellular target proposed to be DNA.[1,3] We have previously shown[4] that in aqueous solution near physiological pH, Cp_2TiCl_2 and Cp_2VCl_2 suffer more rapid and extensive chloride aquation than does *cis*-$Pt(NH_3)_2Cl_2$ (cisplatin)[5] and that the Ti-C_5H_5 ligation is hydrolytically unstable. In contrast to cisplatin, the binding of $Cp_2VCl_{2(aq)}$ to nucleotides is labile on the NMR time scale and predominantly phosphate-centered,[6] with minimal disruption of Watson–Crick base pairing.[6] We now report that $Cp_2MoCl_{2(aq)}$ exhibits an unusual nucleotide/nucleobase coordination chemistry which differs significantly from that of the aforementioned titanium and vanadium complexes.

As indicated by techniques described elsewhere,[4] Cp_2MoCl_2 (**1**) suffers more rapid ($t_{1/2} < 30$ min) and extensive (>98%) chloride aquation than does Cp_2TiCl_2 and Cp_2VCl_2. There is no detectable Mo–C_5H_5 protonolysis over a period of several weeks at pD 7.6. Titration of Na_2(5′-dAMP) (A) with **1** in D_2O at pD



A



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