oxygen exchange with H_2O must be considered: α-H migration from $Cp^*_2Ta(O^*)H$ to yield $[Cp^*_2Ta^{III}\text{-}O^*H]$, oxidative addition of HO-H, reductive elimination of H_2O^*, and α-H elimination to give the isotopomer $Cp^*_2Ta(=O)H$. The latter possibility is eliminated, however, by the observation that treatment of $Cp^*_2Ta(=^{18}O)H$ with excess $D_2{}^{16}O$ results in rapid exchange of oxygen isotopes but no *H/D exchange* (eq 3).[14]

$$Cp^*_2Ta(=^{18}O)H + D_2{}^{16}O \rightleftharpoons \left[Cp^*_2Ta\begin{matrix}{}^{16}OD\\ {}^{18}OD\\ H\end{matrix}\right] \rightleftharpoons Cp^*_2Ta(=^{16}O)H + D_2{}^{18}O \quad (3)$$

Significantly, the W=O bond of $Cp^*_2W{=}O$ reacts even with nonpolar σ bonds such as H-H and H-$SiMe_3$, albeit under more forcing conditions, to afford $Cp^*_2WH_2$[15] (Scheme I).[16]

In light of the d^2, W^{IV}, nature of $Cp^*_2W{=}O$, we have also investigated reactions which could result in oxidation of the tungsten center. Thus, reaction of $Cp^*_2W{=}O$ with either $H_2O_{2(aq)}$ or Me_3CO_2H results in oxygen atom transfer[17] to give the dioxo (W^{VI}) derivative, $(\eta^5\text{-}C_5Me_5)(\eta^1\text{-}C_5Me_5)W(=O)_2$[4] [$\nu(WO_2)_{sym}$ = 895 cm^{-1}, $\nu(WO_2)_{asym}$ = 935 cm^{-1}], which has been structurally characterized by X-ray diffraction methods.[18]

The clean reaction with O_2 (1 atm, 25 °C), shown in Scheme II, further illustrates the exceptional chemical reactivity of $Cp^*_2W{=}O$. The structure of the isolated product $(\eta^5\text{-}C_5Me_5)W(=O)_2(OC_5Me_5)$[4] has been determined by X-ray diffraction methods.[19] As is apparent, one of the Cp* ligands has been transferred to oxygen. IR and ^{17}O NMR studies indicate that the W-*O*-C_5Me_5 oxygen originates exclusively from O_2. These results do not allow a distinction between the two most probable pathways for the formation of $(\eta^5\text{-}C_5Me_5)W(=O)_2(OC_5Me_5)$: (i) formation of $(\eta^5\text{-}C_5Me_5)(\eta^1\text{-}C_5Me_5)W(=O)(\eta^2\text{-}O_2)$, followed by migration of the $(\eta^1\text{-}C_5Me_5)$ ligand to $(\eta^2\text{-}O_2)$, or (ii) direct attack by O_2 at the W-Cp* bond leading to a bridging peroxo species. In either case, the subsequent rearrangement of the proposed intermediate $[(\eta^5\text{-}C_5Me_5)W(=O)(OOC_5Me_5)]$ to $(\eta^5\text{-}C_5Me_5)W(=O)_2(OC_5Me_5)$ is similar to the rearrangement of $(\eta^5\text{-}C_5Me_5)_2Hf(R)(OOCMe_3)$ to $(\eta^5\text{-}C_5Me_5)_2Hf(OR)(OCMe_3)$,[20] acid-catalyzed rearrangement of $Cp^*_2Ta(\eta^2\text{-}O{-}O)CH_3$[1b] to $Cp^*_2Ta(=O)OCH_3$, and the conversion of Ti and Zr alkyls to alkoxides upon exposure to O_2.[21]

In summary, the "class b" metal-oxo nature for $Cp^*_2W{=}O$ actuates a series of interesting reactions leading to reduction of the W=O bond order via 1,2-additions of both polar and nonpolar σ bonds as well as oxidations of the metal center by H_2O_2, HO_2CMe_3, or even O_2. The product, $(\eta^5\text{-}C_5Me_5)W(=O)_2(OC_5Me_5)$, arises from insertion of an oxygen atom from O_2 into a W-$(\eta^5\text{-}C_5Me_5)$ bond. This facile oxo transfer chemistry, both to and from tungsten, augurs well for organotungsten derivatives in effecting catalytic oxidation reactions.

Acknowledgment. We thank Professors Jack Faller, Peter Legzdins, and Bob Bergman for providing information prior to publication and David Wheeler for measuring ^{17}O NMR spectra. This work was supported by the National Science Foundation (Grant No. CHE-8600875) and by Shell Companies Foundation, which are gratefully acknowledged. G.P. acknowledges support through a NATO Postdoctoral Fellowship administered through the Science and Engineering Research Council (U.K.).

Supplementary Material Available: Experimental details describing the synthesis of $Cp^*_2W{=}O$, $(\eta^5\text{-}C_5Me_5)(\eta^1\text{-}C_5Me_5)W(=O)_2$, and $(\eta^5\text{-}C_5Me_5)W(=O)_2(OC_5Me_5)$ (1 page). Ordering information is given on any current masthead page.

(14) Similarly, the reaction of $Cp^*_2Ta(=NPh)H$ with D_2O yields $Cp^*_2Ta(=O)H$ and $PhND_2$.

(15) Cloke, F. G. N.; Green, J. C.; Green, M. L. H.; Morley, C. P. *J. Chem. Soc., Chem. Commun.* **1985**, 945-946.

(16) In the reaction with H_2, the yield of $Cp^*_2WH_2$ is approximately 50%; C_5Me_5H is also formed, presumably as a product of the secondary reaction of water with $Cp^*_2WH_2$ and/or $Cp^*_2W{=}O$. In the reaction with $HSiMe_3$, $Cp^*_2WH_2$ is obtained in >90% yield together with $(Me_3Si)_2O$; however, some H/D exchange with benzene-d_6 accompanies the reaction under the reaction conditions (220 °C, 12 h).

(17) Surprisingly, N_2O does not cleanly transfer an oxygen atom to generate $(\eta^5\text{-}C_5Me_5)(\eta^1\text{-}C_5Me_5)W(=O)_2$, unlike that observed in other systems, e.g.: (a) Vaughan, G. A.; Rupert, P. B.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1987**, *109*, 5538-5539. (b) van Asselt, A.; Parkin, G.; Whinnery, L. L.; Trimmer, M. S.; Bercaw, J. E. Unpublished results.

(18) Schaefer, W. P.; Parkin, G.; Bercaw, J. E. Manuscript in preparation.

(19) Parkin, G.; Schaefer, W. P.; Marsh, R. E.; Bercaw, J. E. *Inorg. Chem.* **1988**, *27*, 3262-4.

(20) van Asselt, A.; Santarsiero, B. D.; Bercaw, J. E. *J. Am. Chem. Soc.* **1986**, *108*, 8291-8293.

(21) (a) Blackburn, T. F.; Labinger, J. A.; Schwartz, J. *Tetrahedron Lett.* **1975**, 3041. (b) Lubben, T. V.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1985**, *107*, 701-703. (c) Lubben, T. V.; Wolczanski, P. T. *J. Am. Chem. Soc.* **1987**, *109*, 424-435.

Fluoride-Induced Trifluoromethylation of Carbonyl Compounds with Trifluoromethyltrimethylsilane ($TMS\text{-}CF_3$). A Trifluoromethide Equivalent[1]

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Although the literature abounds with examples of introducing perfluoroalkyl groups into carbonyl compounds through organometallic reagents of zinc,[2] calcium,[3] manganese,[4] magnesium,[5] silver,[4] and lithium,[6] the procedures are seldom applicable to trifluoromethylation. The trifluoromethide anion (CF_3^-) or its metalloorganic equivalents generally show great tendency for fluoride elimination. On the other hand, trifluoromethylation of aromatics is achieved rather readily with a variety of methods most notable using trifluoromethylcopper (CF_3Cu),[7] sodium trifluoroacetate,[8] trifluoromethyl triflate,[9] bis(trifluoromethyl)mercury ($(CF_3)_2Hg$),[10] and other related reagents.[11]

We wish to report now a very efficient nucleophilic trifluoromethylation reaction for carbonyl compounds using easily prepared trifluoromethyltrimethylsilane ($TMS\text{-}CF_3$).[12] Over the years

(1) Synthetic Methods and Reactions. 141. Part 140, see: Olah, G. A.; Wu, A.; Farooq, O. *J. Org. Chem.* **1988**, *53*, 5143.

(2) (a) Kitazume, T.; Ishikawa, N. *Chem. Lett.* **1981**, 1679; **1982**, *137*, 1453. (b) O'Reilly, N. J.; Maruta, M.; Ishikawa, N. *Chem. Lett.* **1984**, 517.

(3) (a) Santini, G.; Le Blanc, M.; Reiss, J. G. *J. Organomet. Chem.* **1977**, *140*, 1. (b) Santini, G.; Le Blanc, M.; Riess, J. G. *J. Chem. Soc., Chem. Commun.* **1975**, 678.

(4) Kitazume, T.; Ishikawa, N. *Nippon Kagaku Kaishi* **1984**, 1725.

(5) (a) Stacy, M.; Tatlow, J. C.; Sharpe, A. B. *Adv. Fluorine Chem.* **1963**, *3*, 19. (b) Stone, F. G. A.; West, R. *Adv. Organomet. Chem.* **1964**, *1*, 143. (c) Denson, D. D.; Smith, C. F.; Tamborski, C. *J. Fluorine Chem.* **1973/1974**, *3*, 247. (d) Smith, C. F.; Soloski, E. J.; Tamborski, C. *Ibid.* **1974**, *4*, 35. (e) McBee, E. T.; Roberts, C. W.; Meiners, A. F. *J. Am. Chem. Soc.* **1957**, *79*, 335. (f) Thoai, N. *J. Fluorine Chem.* **1975**, *5*, 115. (g) Von Werner, K.; Gisser, A. *Ibid.* **1977**, *10*, 387.

(6) (a) Haszeldine, R. N. *J. Chem. Soc.* **1949**, 2952. Pierce, O. R.; McBee, E. T.; Judd, G. F. *J. Am. Chem. Soc.* **1954**, *76*, 474. (b) Johncock, P. *J. Organomet. Chem.* **1969**, *19*, 257. (c) Gassmann, P. G.; O'Reilly, N. J. *Tetrahedron Lett.* **1985**, 5243. This is the most definitive paper to generate in situ pentafluoroethyllithium. However, the method is not applicable for the generation of trifluoromethyllithium. (d) Also, see: Gassman, P. G.; O'Reilly, N. J. *J. Org. Chem.* **1987**, *52*, 2481.

(7) Wiemers, D. M.; Burton, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 832.

(8) (a) Kobayashi, Y.; Nakazato, A.; Kumadaki, I.; Filler, R. *J. Fluorine Chem.* **1986**, *32*, 467 and references cited therein. (b) Matsui, K.; Tobita, E.; Ando, M.; Kondo, K. *Chem. Lett.* **1981**, 1719.

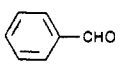
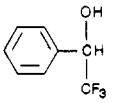
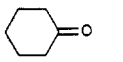
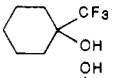
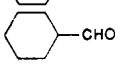
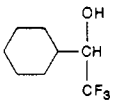
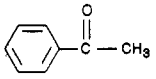
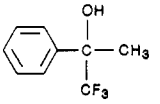
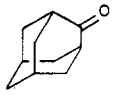
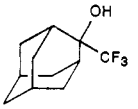
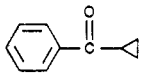
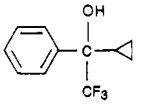
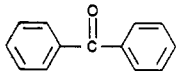
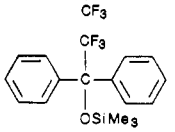
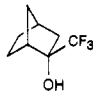
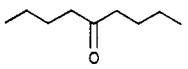
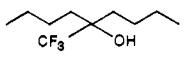
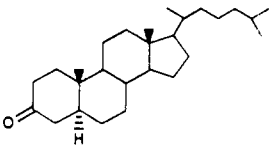
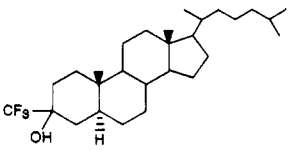
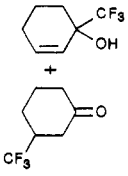
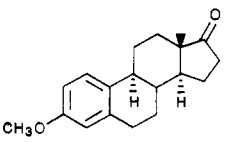
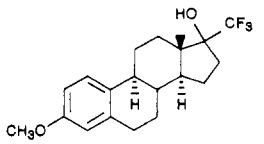
(9) Olah, G. A.; Ohyama, T. *Synthesis* **1976**, 319.

(10) Kondratendok, N. V.; Vechirko, E. P.; Yaguploskii, L. M. *Synthetis* **1980**, 932.

(11) For a recent review of other methods, see: Hewitt, C. D.; Silvester, M. J. *Aldrich. Chim. Acta* **1988**, *21*, 3.

0002-7863/89/1511-0393$01.50/0

Table I. Fluoride Ion Induced Trifluoromethylation of Carbonyl Compounds with Trifluoromethyltrimethylsilane

carbon compd	product	conditions[a] trifluoro-methylation	hydrolysis of the ether	overall isolated yield[b] (%)	bp/mmHg (mp)[c] °C	^{19}F NMR[d]	mass spectra data,[e] *m/e*
		1 h/rt	0.5 N HCl/ 1 h, rt	85	64–65/5.0	−79.2 (d, $^3J_{F-H}$ = 7.1 Hz)	176 (M^+, 33), 107 (100)
		1 h/rt	1.0 N HCl/ 1 h, rt	77	72–73/40 (59–61)	−86.0	168 (M^+, 0.1), 99 (100)
		1 h/rt	0.5 N HCl/ 1 h, rt	80	60–61/5.0	−76.6 (d, $^3J_{F-H}$ = 7.6 Hz)	182 (M^+, 0.1), 113 (1.7), 83 (100)
		1 h/rt	1.0 N HCl/ 6 h, rt	74	69–70/4.6	−81.8	190 (M^+, 29), 121 (100)
		24 h/rt	1.0 N HCl/ 15 h, rt	72	(117–118)	−76.6	200 (M^+, 0.9), 151 (100)
		1 h/rt	1.0 N HCl/ 15 h, rt	81	82–84/3.0	−79.5	216 (M^+, 1.4), 188 (100), 147 (34.5)
		1 h/rt		88	104–106/1.1	−73.5	324 (M^+, 0.9), 255 (100)
		1 h/rt	1.0 N HCl/ 4 h, rt	92	47–49/4.5	−81.4	180 (M^+, 2.9), 111 (12), 68 (100)
		1 h/rt	1.0 N HCl/ 26 h, rt	87	65–66/3.3	−80.7	212 (M^+, 0.1), 143 (46), 43 (100)
		2 h/rt	1.0 N HCl/ 26 h, rt	83[f]	(127–128)	−79.6	456 (M^+, 6), 387 (0.8), 301 (100)
		1 h/rt	1.0 N HCl/ 15 h, rt	60		−83.4 major −75.5 (d, $^3J_{F-H}$ = 7.1 Hz), minor	166 (M^+, 0.3), 97 (100)
		24 h/rt	1.0 N HCl/ 15 h, rt	62[g]		−76.0	354 (M^+, 47), 252 (37), 55 (100)

[a] All the reactions were initially started at 0 °C. [b] All are isolated yields of the pure compounds unless otherwise stated. Majority of these compounds are new and all of them gave satisfactory H-1 and C-13 NMR. [c] The boiling points and melting points are uncorrected. [d] In ppm, ^{19}F shifts and referenced from $CFCl_3$ (upfield). [e] Mass spectrum was obtained on a Finnigan Mat Model INCOS-50 GC-MS Instrument, only selected data are shown. [f] Only one stereoisomer was obtained. [g] Obtained as a mixture of 90% product (one isomer) and 10% starting ketone: 2.4 equiv of silane and 2 equiv of TBAF were used.

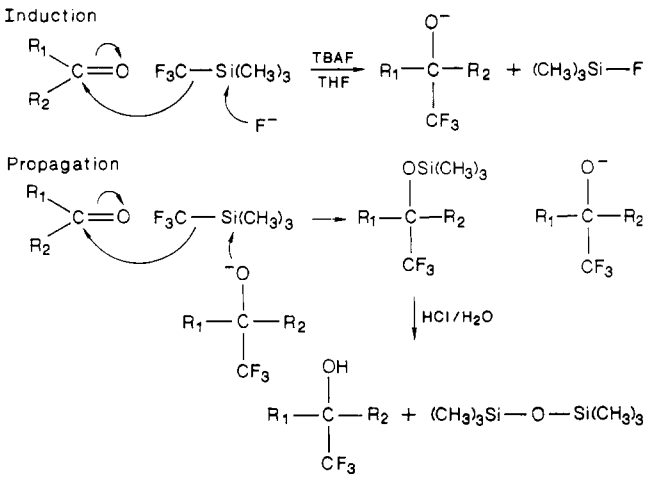
trimethylsilyl compounds substituted with electron-withdrawing substituents such as -CN, I, Cl, Br, N_3, -NCO, -CNO, etc. have been used as synthetic reagents to attach these substitutents to electron-deficient centers.[13] These reagents generally act based on the hard–soft reactivity principle[14] with the silicon atom attached to the substituent significantly bearing electropositive and the substituent negative character. Accordingly, the bond between the pseudohalide trifluoromethyl and trimethylsilyl center should be sufficiently polarized with the trifluoromethyl group bearing substantial negative charge. Consequently we have embarked on a study of trifluoromethyltrimethylsilane (TMS-CF_3)[12] as a potential reagent for introducing the trifluoromethyl group into

(12) Trifluoromethyltrimethylsilane (bp 45 °C) can be readily prepared by using readily available bromotrifluoromethane, hexaethylphosphorus triamide, and chlorotrimethylsilane in about 65–70% yield following the published procedure: Rupport, I.; Schlich, K.; Volbach, W. *Tetrahedron Lett.* **1984**, 2195.

(13) (a) Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983. (b) Colvin, E. *Silicon in Organic Synthesis*; Butterworths: London, 1980.

(14) Ho, T. L. *Hard and Soft Acids and Bases Principles in Organic Chemistry*, Academic Press: New York, 1977.

Scheme I



carbonyl compounds and have found a long sought after simple and efficient trifluoromethide equivalent reagent.

Reaction of an equimolar excess of TMS-CF_3 with cyclohexanone under nucleophilic catalysis[15] with a catalytic amount of tetrabutylammonium fluoride (TBAF) in tetrahydrofuran solution generally in an hour gave quantitatively the trifluoromethylated siloxy adduct (i.e., no trace of starting cyclohexanone was observed by GC analysis). In a typical reaction, a mixture of carbonyl compound (10 mmol) and TMS-CF_3 (12 mmol) in 25 mL of tetrahydrofuran cooled to 0 °C in an ice bath is treated with 20 mg of TBAF. Instantaneously a yellow color develops with the initial evolution of fluorotrimethylsilane, and the reaction mixture is brought to ambient temperature and stirred. The mixture is periodically analyzed by GC for the completion of the reaction. The trifluoromethylated siloxy compound is then hydrolyzed to the corresponding alcohol with aqueous HCl.[16] The reaction works equally well with a wide array of aldehydes, ketones, enones, etc. and is generally unaffected by moisture.[17] The obtained yields (of isolated free alcohols) are good to excellent (see Table I). In the case of hindered ketones such as tricyclic 2-adamantanone and tetracyclic estrone methyl ether[18] the reaction is sluggish. Nevertheless, trifluoromethylated adducts were obtained on prolonged stirring (see Table I). In the case of cyclohexenone 1,2-addition predominates (>90%).

Concerning the mechanism, the reaction is induced by fluoride ion (indicated by the irreversible formation of fluorotrimethylsilane in the initial stage of the reaction) and then further catalyzed by the in situ formed trifluoromethylated oxyanion adduct. The reaction also works under alkoxide anion catalysis.[19] The mechanism is depicted in Scheme I.

In conclusion we have developed a versatile new trifluoromethylation method for carbonyl compounds using TMS-CF_3. Further studies are underway to exploit the scope of TMS-CF_3 as a nucleophilic trifluoromethylating agent.

Acknowledgment. Support of our work by the National Science Foundation is gratefully acknowledged.

(15) For an excellent review, see: Furin, G. G.; Vyazankina, O. A.; Gostevsky, B. G.; Vyazankin, N. S. *Tetrahedron* **1988**, *44*, 2675. The reaction did not work under Lewis acid (BF_3:OEt_2, ZnI_2, $TiCl_4$, etc.) catalysis.

(16) The hydrolysis of trimethylsiloxytrifluoromethylated adducts to the corresponding alcohols posed some difficulties. In the case of benzophenone the siloxy adduct was found to be extremely stable.

(17) The tetrabutylammonium fluoride contains three molecules of H_2O, and this did not pose any serious problems in the reaction. However, when used in large quantities under prolonged stirring hydrolysis of the silane is a competing reaction which generates CF_3H. However, in no case generation of difluorocarbene($:CF_2$) was observed.

(18) In the case of sterically hindered estrone methyl ether, more than 1 equiv amount of fluoride was used.

(19) The trifluoromethylation reaction also works equally well when potassium *tert*-butoxide was used as the initiator clearly supporting our proposed mechanism.

^{113}Cd NMR Studies of a 1:1 Cd Adduct with an 18-Residue Finger Peptide from HIV-1 Nucleic Acid Binding Protein, p7

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A central issue in bioinorganic chemistry concerns the relevance and feasibility of zinc binding to putative "zinc fingers" in *RNA-binding* retroviral nucleic acid binding proteins (NABPs).[1] Without exception, retroviral NABPs (and their *gag* precursor proteins) contain the conserved amino acid finger sequence -C-X_2-C-X_4-H-X_4-C- (C = cysteine, H = histidine, X = variable amino acids).[2-4] Although related sequences found in DNA-binding proteins bind Zn^{2+} tightly,[5-10] experiments aimed at measuring the zinc content and the affinity of zinc for retroviral NABPs indicate that zinc binds weakly to these proteins,[11,12] and this has led to the conclusion that zinc is not a structural component of at least one retroviral NABP.[11] On the other hand, recent site-directed mutagenesis experiments involving murine leukemia virus provide indirect evidence that Zn binding is necessary for correct protein function.[13] In these experiments, single and double point mutations, which resulted in replacement of the conserved Cys residues by Ser, afforded mutant viral particles that appeared normal in all respects except that (1) they were noninfectious and (2) they contained cellular RNA instead of viral RNA.[13]

We have prepared Zn^{2+} and Cd^{2+} adducts with the 18-residue peptide comprising the amino acid sequence of the first finger (residues 13 through 30) of NABP p7 from HIV-1 (the causative agent of AIDS). ^1H NMR experiments indicate that the synthetic peptide ($p7^{13-30}$) forms 1:1 metal adducts that are stable in aqueous solution (pH 7, ambient T) for at least a month. Additional Cd^{2+} does not bind to $Cd(p7^{13-30})$ and precipitates from solution as hydroxides at pH 7. Additional Zn^{2+} produces very minor changes in the ^1H NMR spectrum of $Zn(p7^{13-30})$ at pH 7. Except for a few broad ^1H NMR signals observed in the spectrum of the ^{113}Cd adduct (particularly the His-H_2 and -H_4 signals), the ^1H spectra of $Zn(p7^{13-30})$ and $^{113}Cd(p7^{13-30})$ are very similar in appearance. The broader signals of the ^{113}Cd adduct narrow considerably on cooling to -5 °C.

Of the 17 backbone amide protons in $Zn(p7^{13-30})$, 12 protons exhibit resolved multiplets (due to NH-CHα scalar coupling) in the ^1H spectrum obtained at 30 °C (Figure 1). This is in contrast to the broad, unresolved NH signals observed for metal-free $p7^{13-30}$ and reflects the formation of a single, highly stable tertiary structure upon coordination of Zn^{2+}. Many NH ^1H NMR signals

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