address this possibility in the enzyme.

Acknowledgment. The help and guidance of Drs. K. D. Karlin and Z. Tyeklar in performing the O_2 uptake measurements is gratefully acknowledged. We are grateful to Dr. D. Hamilton for helpful discussions and the use of her equipment for the determination of the oxygen dependence. This research was supported by NIH Grant GM-38829.

Supplementary Material Available: Tables of positional parameters and their estimated standard deviations and of general displacement parameter expressions (4 pages). Ordering information is given on any current masthead page.

Tertiary Hydroxylation Using Fluorine: Activation of the C–H Bond

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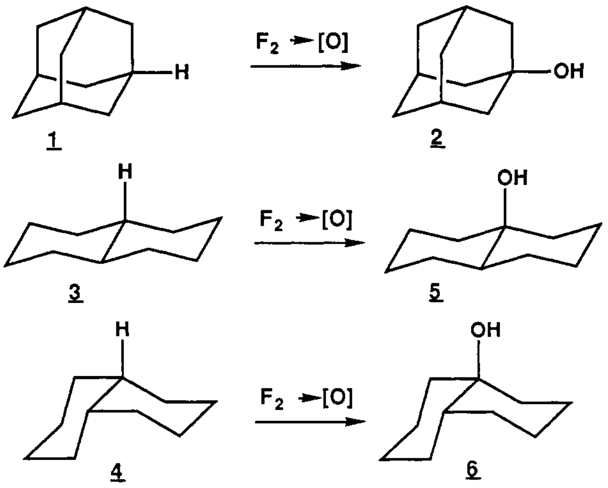
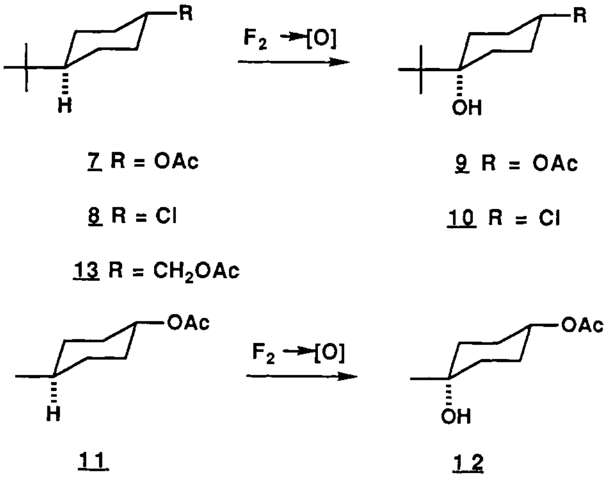
The use of F_2 as a fluorinating agent has been steadily increasing in the last decade.[1] It is clear, however, that the potential of this halogen as a synthetic tool reaches far beyond the field of fluoroorganics. Recently we have been able to demonstrate the ability of this very reactive element to take part in the synthesis of some difficult to obtain fluorine free compounds via the in situ generation of active intermediary agents. Such agents either are strongly polarized in an unusual way or create highly energetic intermediates with organic substrates thus performing some unexpected reactions.[2] We report now yet another unusual reaction involving fluorine, acetonitrile, and water whose outcome is selective hydroxylation of remote unactivated CH bonds.

Activation of paraffinic and other CH bonds far away from any functional group is a subject of many recent projects. The most conspicuous approaches are homogeneous catalysis with organometallic complexes and oxygenation processes involving the peroxide bond, including the use of O_3 or H_2O_2 with or without metal cations.[3] Regio- and stereoselective activation is of course a much more demanding process, and the two most successful approaches involve Breslow's[4] remote radical activation and electrophilic substitution of tertiary hydrogens by F_2.[5]

When fluorine is passed through wet acetonitrile at 0 °C, an oxidizing solution is formed.[6] We have already reported that this oxidizing solution is able to epoxidize olefins with unprecedented efficiency in an electrophilic mode.[7] When no olefin is present, the bonds most susceptible to electrophilic attack are the ones with the highest p-orbital contribution. These are usually the tertiary C–H bonds situated far away from any electron-withdrawing moiety. Furthermore, such an attack should inevitably take place with full retention of configuration.[5,8] Thus, when adamantane (**1**) is treated with the oxidative solution,[9] only a tertiary hydrogen is substituted, resulting in an 80% yield of 1-adamantanol (**2**). Other paraffins were also similarly hydroxylated, including *trans*- and *cis*-decalin (**3** and **4**), which gave respectively *trans*- and *cis*-9-decalol (**5** and **6**) in yields higher than 80%.



The ability to activate paraffins, either in a radical or in an ionic mode, is common to most of the few existing hydroxylation reagents. Similar reactions on heteroatom-containing derivatives are extremely rare however, since the heteroatom represses a chain reaction in a radical process or lowers the electron density of the CH bonds to such an extent that they are practically immune to attack by the known peroxy reagents. Although our oxidative agent is also somewhat affected by the proximity of a deactivating heteroatom group, it still can substitute a tertiary hydrogen in such compounds. Thus, when *trans*-acetoxy- or *trans*-chloro-4-*tert*-butylcyclohexane (**7** or **8**) is reacted, the simple but previously inaccessible trans 4-hydroxy derivatives are obtained in 50% and 30% yields, respectively.[10]



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[1] For some reviews on the use of F_2 in fluoroorganic synthesis, see: Rozen, S. *Acc. Chem. Res.* **1988**, *21*, 307. Purrington, S. T.; Kagen, B. S.; Patrick, T. B. *Chem. Rev.* **1986**, *86*, 997. Mann, J. *Chem. Soc. Rev.* **1987**, *16*, 381. Haas, A.; Lieb, M. *Chimia* **1985**, *39*, 134. Vyplel, H. *Chimia* **1985**, *39*, 305.

[2] Rozen, S.; Brand, M.; Lidor, R. *J. Org. Chem.* **1988**, *53*, 5545. Rozen, S.; Zamir, D.; Menahem, Y.; Brand, M. *J. Org. Chem.* **1988**, *53*, 1123. Rozen, S.; Hebel, D. *Heterocycles* **1989**, *28*, 249.

[3] Burk, M. J.; Crabtree, R. H. *J. Am. Chem. Soc.* **1987**, *109*, 8025. Barton, D. H. R.; Boivin, J.; Lelandais, P. *J. Chem. Soc., Perkin Trans. 1* **1989**, 463. Giamalva, D. H.; Church, D. F.; Pryor, W. A. *J. Org. Chem.* **1988**, *53*, 3429. Fish, R. H.; Fong, R. H.; Vincent, J. B.; Christau, G. *J. Chem. Soc., Chem. Commun.* **1988**, 1504.

[4] Breslow, R.; Brandl, M.; Hunger, J.; Adams, A. D. *J. Am. Chem. Soc.* **1987**, *109*, 3799.

[5] Rozen, S.; Gal, C. *J. Org. Chem.* **1987**, *52*, 2769. Rozen, S.; Gal, C. *J. Org. Chem.* **1987**, *52*, 4928.

[6] It is reasonable to assume that first a fast reaction between F_2 and water takes place to form HOF (Appelman, E. H.; Jache, A. W. *J. Am. Chem. Soc.* **1987**, *109*, 1754.) The next step is either a stabilization of the HOF by the acetonitrile or a reaction between the two compounds to form yet another oxidizing material. We will publish later our ongoing studies, in collaboration with Appelman's group, which already indicate that the oxidant contains fluorine and does not have a peroxy moiety.

[7] Rozen, S.; Brand, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 554.

[8] Olah, G. A.; Prakash, G. K. S.; Williams, R. E.; Field, L. D.; Wade, K. *Hypercarbon Chemistry*; Wiley: New York, 1987.

[9] A mixture of 10% F_2[11] in N_2 was bubbled through a cold (−10 °C) mixture of CH_3CN/H_2O (95:5) till a concentration of 0.1–0.2 M oxidizing solution (checked iodometrically) was obtained. The organic substrate (5–15 mmol) was dissolved in $CHCl_3$, cooled to 0 °C, and added in one portion to the above solution. Usually an excess of about 10 mol/equiv of the oxidizing agent was used, and the progress of the reaction was monitored by GC or TLC. At 0 °C, the half-lifetime of the oxidizing agent is more than 10 h. In some difficult hydroxylations, more oxidizing solution had to be added. Usually, after 70–100% conversion, the reaction mixture was added to a large amount of water, extracted with chloroform, washed until neutral, and dried and the solvent evaporated. If necessary, the reaction mixture was chromatographed.

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To emphasize the electrophilic character of the reagent, some competitive experiments were also performed. When an equimolar mixture of 4-methylcyclohexanol acetate (**11**) and methyl cyclohexane were treated with the oxidative solution made from F_2, the latter reacted about 8 times faster. This is largely due to the difference in the tertiary CH electron density, which is lower in **11** because of the proximity of the electron-withdrawing group.[5] If the distance between such a group and the tertiary hydrogen increases as in the pair (4-*tert*-butylcyclohexyl)methyl acetate (**13**) and **7**, again, in accordance with the electrophilic nature of the reaction, the former reacts considerably faster.

Of some importance is the use of this reaction to introduce the ^{18}O isotope into organic molecules. The most convenient source for this isotope is $H_2{}^{18}O$, and since, unlike any other hydroxylation method, the oxygen in the above process comes from water, introducing ^{18}O becomes a relatively simple task. For example, when adamantane is treated with the oxidizing solution originated from $F_2/CH_3CN/H_2{}^{18}O$, [^{18}O]-1-hydroxyadamantane was obtained in higher than 80% yield.

We are thus hopeful that F_2, now accepted by many fluorine chemists as an important fluorinating reagent, will also be considered by the general chemical community as a reagent that can perform some uncommon reactions leading to fluorine-free and difficult to obtain derivatives.

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(10) The spectral properties as well as the microanalyses of the new compounds are in excellent agreement with the proposed structures.

(11) Fluorine is of course a strong oxidizer and a very corrosive material. An appropriate vacuum line made from copper or Monel in a well-ventilated area should be constructed for working with this element. The reactions themselves can be carried out in glass vessels. If elementary precautions are taken, work with fluorine is relatively simple, and we have had no bad experiences working with it.

Additions and Corrections

X-ray Structures of Cubylcubane and 2-*tert*-Butylcubylcubane: Short Cage–Cage Bonds [*J. Am. Chem. Soc.* **1988**, *110*, 7232]. RICHARD GILARDI,* MICHELE MAGGINI, and PHILIP E. EATON

Page 7232, second paragraph: the intercage bond length for *tert*-butylcubylcubane is misstated as 1.464 (5) Å. The correct intercage distance is 1.474 (5) Å as shown in Figure 2b.

Nephelauxetic Effect in Paramagnetic Shielding of Transition-Metal Nuclei in Octahedral d^6 Complexes [*J. Am. Chem. Soc.* **1988**, *110*, 8341]. NENAD JURANIC

Page 8343: The last equation in the Appendix should read:

$$B(\zeta_i,\zeta_j) = 4180\ \zeta_i a^2\{1 - {}^{25}\!/_3 a^2[1 - (1 + a^{-1})^{-2}] + {}^{50}\!/_3 a(1 + a^{-1})^{-3} + {}^{1}\!/_3(1 + a^{-1})^{-4}[72 + 88(1 + a)^{-1} + 95(1 + a)^{-2} + 90(1 + a)^{-3} + 70(1 + a)^{-4} + 35(1 + a)^{-5}]\}$$

Multiphoton Ionization of Acetone Clusters: Metastable Unimolecular Decomposition of Acetone Cluster Ions and the Influence of Solvation on Intracluster Ion–Molecule Reactions [*J. Am. Chem. Soc.* **1989**, *111*, 6035]. W. B. TZENG, S. WEI, and A. W. CASTLEMAN, JR.*

Page 6039: The two sentences before the paragraph head (B) Studies of Metastable Processes, "When water is present... on site B in structure II. As a result, ... is quenched." should read "When water is present in the system, it can bond to either site A or site B. However, the dehydration reaction of the protonated acetone cluster is quenched if the water molecule is bonded to site A in structure II."

Ligand Oxidation in a Nickel Thiolate Complex [*J. Am. Chem. Soc.* **1989**, *111*, 5974–5976]. MANOJ KUMAR, ROBERTA O. DAY, GERARD J. COLPAS, and MICHAEL J. MARONEY*

Page 5975, Figure 1: In the figure caption the data refer to an oxidation (not a reduction) of **1** at −190 mV employing 0.1 M supporting electrolyte.

Oxidation and Reaction of Trolox c, a Tocopherol Analogue, in Aqueous Solution. A Pulse-Radiolysis Study [*J. Am. Chem. Soc.* **1989**, *111*, 3315]. MICHAEL J. THOMAS* and BENON H. J. BIELSKI

Page 3316: The NMR and IR data for **5** and **6** are consistent with those previously reported by Cohen et al.[1] The melting point of **3** is identical with that reported by Cort et al.[2]

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(1) Cohen, N.; Lopresti, R. J.; Saucy, G. *J. Am. Chem. Soc.* **1979**, *101*, 6710.

(2) Cort, W. M.; Scott, J. W.; Araujo, M.; Mergens, W. J.; Cannalonga, M. A.; Osadca, M.; Harley, H.; Parrish, D. R.; Pool, W. R. *J. Am. Oil Chem. Soc.* **1975**, *52*, 174.

Computer Software Reviews

MassSpec. A Graphics-Based Mass Spectrum Interpreter. Version 1.0. Trinity Software: P.O. Box 960, Campton, NH. List Price $60.00.

MassSpec is a utility designed to aid in interpretation of mass spectra by identifying potential fragments from a user-entered chemical structure of up to 255 atoms. The program is available in both MS-DOS and Macintosh versions, which offer identical options and results with the exception of slight differences in the main menu structure. The MS-DOS system requires 256K RAM, mouse, and graphics card (CGA, EGA, or HGA) and a math coprocessor is recommended. The Macintosh version requires 512 K RAM and an 800K disk drive. Each version is supplied on a single disk along with a 29-page User's Manual. The Macintosh version was evaluated for this review.

The MassSpec utility can be broken down into two main functions: a structure editor and a fragment generator/locater. After starting the program, the user is given a blank work area in which a structure can be created, loaded, or saved to disk. Structures are created using menu options that include Ring (3–10 member and benzene), Bond (single, double, triple, and π circle), and Group, which can be any combination of elements up to atomic number 94, deuterium, tritium, a + or − charge, or a radical center. Options are also included to allow modification of various portions of a structure. After a structure is created, the user can make use of the Generate option to produce and display potential fragments based on up to three simultaneous cleavages. Only single bonds are selected for cleavage except for aromatic compounds with a molecular