and the residue was dissolved in CH_2Cl_2 and washed with water. After drying of the organic phase over anhydrous sodium sulfate and filtration, removal of solvent under reduced pressure yielded a viscous yellow oil, which was purified by silica gel column chromatography (eluent, hexane/ethyl acetate = 3:1 in volume). A white powder of **6** (12.2 g, 70% yield) was obtained: mp 123–128 °C; IR (KBr pelet) $\nu_{C=O}$ 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.3–2.7 (m, 15 H, $ArCH_3$), 2.7–3.4 (m, 16 H, NCH_2CH_2N), 3.81 (s, 3 H, CO_2CH_3), 4.11 (d, J = 16 Hz, 2 H, $ArCH_aH_bN$), 4.48 (d, J = 16 Hz, 2 H, $ArCH_aH_bN$), 7.2–7.5 (m, 13 H, Ar*H*, Ar*H* (Ts)), 7.5–7.9 (m, 10 H, Ar*H* (Ts)).

The detosylation of the pentatosylate **6** (1.0 g, 0.89 mmol) was achieved in 50 mL of AcOH–48% aqueous HBr (3:2 in volume) at 140 °C for 48 h. After the removal of solvent, the residue was dissolved in 50 mL of water and washed with three portions of CH_2Cl_2. The water phase was evaporated and the residue was passed through a strong anion exchange resin column (Amberlite IRA-400). The free **7** was obtained as colorless prisms (80 mg, 28% yield), recrystallized from CH_3CN: mp 134.0 °C; MS M^+ (m/e) 317; IR (KBr pelet) $\nu_{C=O}$ 1686 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.5–2.9 (m, 12 H, $HNCH_2CH_2NH$), 2.9–3.1 (m, 2 H, $HNCH_2CH_2NC{=}O$), 3.7–3.9 (m, 2 H, $HNCH_2CH_2NC{=}O$), 4.10 (s, 2 H, $ArCH_2NH$), 4.40 (s, 2 H, $ArCH_2NC{=}O$), 7.2–7.6 (m, 3 H, Ar*H*). Anal. Calcd for $C_{17}H_{27}H_5O_1{\cdot}0.2H_2O$: C, 63.60; H, 8.60; N, 21.82. Found: C, 63.64; H, 8.57; N, 21.64.

Hydrolysis of 7. Alkaline hydrolysis of the amide **7** was achieved by reflux with equivalent KOH in aqueous solution for 44 h. The reaction was monitored by silica gel TLC (eluent, CH_2Cl_2/CH_3OH/aqueous NH_3 = 25:10:1; R_f values are 0.2 for **7** and 0.5 for **9**). After evaporating the reaction mixture in vacuo, the crude product was obtained as the mixture of **7** and **9** (main product), which was supported by ^1H NMR (an equivalent benzylic protons at δ 4.35 (s) for **9**) and IR (an absorption at 1686 cm^{-1} for **9**) spectra. Attempts to neutralize the alkaline salt **9** with weak acidic solution always resulted in the formation of **7** (monitored by TLC).

Registry No. CuL, 124177-78-2; ZnL, 124199-98-0; TsN-$((CH_2)_2NTs(CH_2)_2NHTs)_2$, 99142-42-4; **5**, 56263-51-5; **6**, 124199-97-9; **7**, 124177-76-0; **9**, 124177-77-1.

Supplementary Material Available: Atomic coordinates, temperature factors, bond lengths and bond angles for **7**, and UV absorption spectral data (6 pages). Ordering information is given on any current masthead page.

Osmium Tetraoxide Catalyzed Vicinal Hydroxylation of Higher Olefins by Using Hexacyanoferrate(III) Ion as a Cooxidant

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The oxidation of olefins with osmium tetraoxide to give *cis*-diols is a well-established reaction.[1] Criegee showed that osmium tetraoxide in a stoichiometric amount could be used for effective cis hydroxylation of the olefins and that this method is more reliable than other diol syntheses,[2,3] despite its high cost and toxicity. Subsequently, a catalytic amount of osmium tetraoxide has been successfully used in the presence of suitable cooxidants like hydrogen peroxide (Milas' reagent),[4-6] metal chlorates,[7-9] *tert*-butyl hydroperoxide,[10-12] and amine *N*-oxides (such as *N*-methylmorpholine *N*-oxide, NMO).[13] These catalytic hydroxylation reagents, however, have disadvantages due to appreciable overoxidation or inertness toward hindered olefins. We report here a modification of catalytic vicinal hydroxylation using hexacyanoferrate(III) ion as a cheap and convenient cooxidant for osmium(VI).

Although hexacyanoferate(III) ion has previously been used in examining the kinetics of osmium tetraoxide oxidations,[14-17] these studies were limited to the oxidation of lower molecular weight organic compounds in an aqueous strong alkaline medium. The higher molecular weight olefins do not react with an entirely aqueous solution of hexacyanoferrate(III) ion in the presence of OsO_4. In the present study we have found that, by employing an aqueous *tert*-butyl alcohol, it is possible to obtain vicinal diols in good yields (Table I). We also examined acetone and acetonitrile as a cosolvent, but both were inferior to *tert*-butyl alcohol. In addition, this procedure gives only a low yield of the dihydroxylation product from cholesterol. It has been reported that this may be due to the formation of a stable osmate ester.[12] It was also reported by Criegee that the rate of formation of the osmate ester could be enhanced by the addition of an excess of tertiary amine, such as pyridine,[3] and more recently, by Sharpless that dihydroquinidine ester accelerated the catalytic dihydroxylation of styrene using NMO as cooxidant.[18] Accordingly, we have tried the osmium tetraoxide catalyzed oxidation of cholesterol by our procedure in the presence of various tertiary amines (Table II).

Addition of an equimolar amount (1.7×10^{-2} M) of quinuclidine or 1,4-diazabicyclo[2.2.2]octane (DABCO) to cholesterol dramatically accelerated the catalytic hydroxylation, resulting in an increased yield of diol (**6**). In order to make a qualitative measurement of the acceleration of the reaction, we chose 1-decene as a substrate instead of cholesterol and studied the rate enhancement of the hydroxylation of these added amines. Consequently, it was found that quinuclidine and DABCO accelerated the half-life rate by 13- and 7.8-fold, respectively. These results indicate a striking contrast with those of Sharpless. They reported that, although dihydroquinidine ester could accelerate the reaction, quinuclidine strongly retarded catalysis.[18,19] They argued that the rate acceleration in

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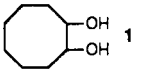
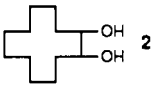
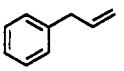
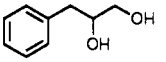
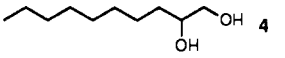
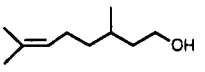
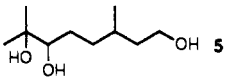
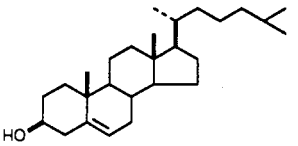
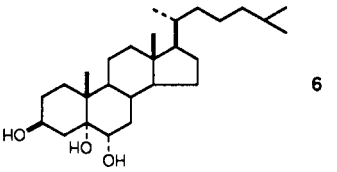
Table I. Catalytic Cis Hydroxylation of Alkenes with Osmium Tetraoxide and Potassium Hexacyanoferrate(III)

entry	substrate	product	yield,[a] %
1		 1	94
2		 2	71
3		 3	80
4		 4	89
5		 5	88
6		 6	19[b,c]

[a] Isolated yield by column chromatography. [b] A catalytic amount of OsO_4 (0.05 equiv) was used. [c] See Experimental Section.

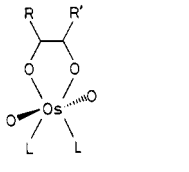
Table II. Influence of the Amine on the Oxidation of Cholesterol with OsO_4 and $K_3Fe(CN)_6$

amine[a]	yield,[b] %
pyridine	28
2,2′-dipyridyl	17
triethylamine	–[c]
N,N,N′,N′-tetraethylethylenediamine	–[c]
morpholine	21
piperazine	–[c]
quinuclidine	49
1,4-diazabicyclo[2.2.2]octane (DABCO)	74
hexamethylenetetramine	25

[a] The procedure was the same as in entry 6, Table I (see also, the Experimental Section). [b] Isolated yield. [c] No significant change in yields.

the presence of dihydroquinidine ester is accounted for by facilitation of the initial osmylation step.[20] But in our case, it appears that DABCO or quinuclidine promotes the hydrolysis of the osmate ester rather than the osmylation of olefins; many workers who studied oxidative reactions with Os(VIII) support that the decomposition of the osmate ester is rate determining.[15,17,21,22] Forming an extremely stable osmate complex, cholesterol could not undergo hydroxylation in the catalytic process.

Griffith reported that the reaction of osmium tetraoxide with alkenes in the presence of an excess of quinuclidine yields a complex **7**.[23] Quinuclidine is bound strongly in this complex.[18] If one takes the trans influence into account, the bonds between osmium(VI) and oxygen are thought to be weakened by this ligand.[24] Since hexacyanoferrate(III) ion unlike NMO can oxidize the reduced metals by an outer-sphere, electron-transfer mechanism,[25] we think that the reoxidation of Os(VI) does not be retarded by the coordinated quinuclidine.



7 (L = quinuclidine)

Experimental Section

^1H NMR spectra ($CDCl_3$ or pyridine-d_5) were recorded on a JEOL FX-90Q FT spectrometer or a JEOL GSX-400 spectrometer (Me_4Si as an internal standard). IR spectra were recorded with a JASCO IRA-2 spectrophotometer. GLC analyses were carried out with a Shimadzu Model GC-4C equipped with a DC-550 on Chromosorb W column (3 mm × 3 m) at 120 °C, He being used as a carrier gas.

A solution of OsO_4 was prepared by dissolving OsO_4 (1 g) in reagent-grade *tert*-butyl alcohol (80 mL) followed by addition of several drops of 70% *t*-BuOOH. Each milliliter should contain OsO_4 (12.5 mg, 0.05 mmol).

General Procedure for the Vicinal Hydroxylation of Olefins (Entries 1–5, Table I). To a solution of an olefin (2 mmol) in *tert*-butyl alcohol (15 mL) and water (15 mL) was added $K_3Fe(CN)_6$ (1.980 g, 6 mmol), K_2CO_3 (0.830 g, 6 mmol), and the OsO_4 solution (0.5 mL, 0.0125 equiv). The reaction mixture was stirred for 24 h at ambient temperature. To this solution was then added a proper quantity of Na_2SO_3, and stirring was continued for additional several hours. The pale blue solution obtained was concentrated to dryness under reduced pressure, and the residue was extracted with three portions of ether. The combined extracts were dried ($MgSO_4$) and evaporated. The residual oil was purified by column chromatography (silica gel, hexane–ether).

1,2-Cyclooctanediol (1): ^1H NMR (90 MHz, $CDCl_3$) δ 4.03–3.77 (m, 2 H), 2.00–1.33 (m, 14 H); IR (KBr) 3300 (O–H) cm^{-1}.

1,2-Cyclododecanediol (2): ^1H NMR δ 3.89–3.60 (m, 2 H), 1.69–1.26 (m, 22 H); IR (KBr) 3300 (O–H) cm^{-1}.

3-Phenyl-1,2-propanediol (3): ^1H NMR δ 7.47–7.07 (m, 5 H), 3.91 (ddt, J = 6.6, 6.3, and 3.6 Hz, 1 H), 3.65 (dd, J = 11.7 and 3.6 Hz, 1 H), 3.43 (dd, J = 11.7 and 6.3 Hz, 1 H), 2.73 (d, J = 6.6

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Hz, 2 H); IR (neat) 3300 (O–H) cm^{-1}.

2,6-Dimethyl-2,3,8-octanetriol (5): ^1H NMR δ 3.11 (t, J = 5.7 Hz, 2 H), 2.91–2.71 (m, 1 H), 1.45–1.07 (m, 7 H), 1.05 (s, 3 H), 0.95 (s, 3 H), 0.78 (d, J = 5.1 Hz, 3 H); IR (neat) 3300 (O–H) cm^{-1}.

Cholestane-3,5,6-triol (6) (Entry 6, Table I). A reaction mixture consisting of cholesterol (1 mmol), $K_3Fe(CN)_6$ (10 mmol), K_2CO_3 (10 mmol), and OsO_4 (0.05 equiv) all dissolved in *tert*-butyl alchol (30 mL) and water (30 mL) was stirred for 24 h at 40 °C. After workup as above the residue was purified by column chromatograpy (silica gel, ether–acetone, 5:1) to give **6** in 19% yield: ^1H NMR (400 MHz, pyridine-d_5) δ 4.72 (tt, J = 12 and 6 Hz, 3α-H), 4.00 (dd, J = 12 and 4 Hz, 6-H), 3.02 (dd, J = 12 and 4 Hz, 4α-H), and 2.11 (td, J = 12 and 2 Hz, 4β-H);[26] IR (KBr) 3300 (O–H) cm^{-1}.

Influence of the Amine on the Oxidation of Cholesterol. The procedure was the same as that described above except the added amine (1 mmol) to the reaction mixture (see Table II).

Qualitative Kinetic Studies of the Vicinal Hydroxylation of 1-Decene in the Presence of Quinuclidine and DABCO. To each of *tert*-butyl alcohol–water (1:1 v/v, 40 mL), which contains 1-decene (0.281 g, 2 mmol), $K_3Fe(CN)_6$ (1.980 g, 6 mmol), K_2CO_3 (0.830 g, 6 mmol), and undecane (0.100 g, as an internal standard), was added quinuclidine (0.0556 g, 0.5 mmol), DABCO (0.0560 g, 0.5 mmol), or none (a standard solution). Initiation of the hydroxylation was brought about by mixing each solution with the OsO_4 solution (0.5 mL, 0.0125 equiv). The reaction mixture was kept at 25 ± 1 °C. Progress of the reaction was monitored by the decrease of 1-decene (vs undecane) in a given intervals (10 min) by GLC analysis. The required reaction times at 50% conversion were 30 min (quinuclidine), 50 min (DABCO), and 390 min (no added amine), respectively.

Registry No. 1, 27607-33-6; 2, 4422-05-3; 3, 17131-14-5; 4, 1119-86-4; 5, 31558-25-5; 6, 35089-25-9; DABCO, 280-57-9; $PhCH_2CH{=}CH_2$, 300-57-2; $H_2C{=}CH(CH_2)_7CH_3$, 872-05-9; OsO_4, 20816-12-0; $K_3Fe(CN)_6$, 13746-66-2; cyclooctene, 931-88-4; cyclododecene, 1501-82-2; 3,7-dimethyl-6-octenol, 106-22-9; cholesterol, 57-88-5; quinuclidine, 100-76-5.

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Difluorination of Esters. Preparation of α,α-Difluoro Ethers

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Due to the extraordinary biological, physical, and chemical properties of organofluorine compounds,[1] methods for the tactical placement of fluorine into organic structures are of considerable interest. Since many of the available fluorinating agents are difficult to handle and/or require specialized apparatus, much of organofluorine chemistry remains outside the mainstream of synthetic methodology. The development and subsequent commercial availability of diethylaminosulfur trifluoride (DAST)[2] and its relatives has opened the field of organic fluorination to the general synthetic community, since these materials can be handled using standard techniques and apparatus.

A particularly useful transformation effected by DAST is the geminal difluorination of aldehydes and ketones under mild conditions. An analogous reaction with esters would provide easy access to α,α-difluoro ethers, but DAST does not react readily with esters. The more reactive sulfur tetrafluoride converts certain perfluorinated esters to the corresponding ethers, but hydrocarbon esters are cleaved to trifluoromethyl species.[3] The conversion of esters to α,α-difluoro ethers has been accomplished with chlorine monofluoride,[4] but overfluorination interferes, and ClF is an inconvenient reagent for general use. We describe here a mild, efficient, and general procedure for the geminal difluorination of esters.

We reasoned that the nonreactivity of esters toward DAST was due to the lowered electrophilicity of the carbonyl system which inhibits transfer of nucleophilic fluorine. Thioesters are much more electrophilic than are esters; moreover, fluorodesulfurization has ample precedent.[5] Indeed, we have found that thione esters react readily with DAST under mild conditions to provide cleanly and in good yield the corresponding α,α-difluoro ethers. The results are gathered in Table I.

The thioesters were prepared from the carboxylic esters using the Lawesson[6] reagent in refluxing toluene (see table for reaction time). Best results were obtained with material prepared according to the reported procedure[7] and stored in a dessicator. In several cases, a small amount of the starting material remained even after prolonged reflux, presumably due to decomposition of the thionating agent under the reaction conditions. Since large excesses of Lawesson reagent did not improve the conversion enough to justify the increased effort necessary for purification of the thione esters, the reactions were run with 1 mol (2 equiv) of Lawesson reagent per mole of ester. After the prescribed reaction period, any unreacted ester was removed from the less polar thioester by flash chromatography. In the case of 2-naphthyl acetate (entry 8), the lone enol ester studied, the conversion was low even after prolonged reflux and could not be improved by addition of fresh Lawesson reagent. Nevertheless, the reaction is clean, and the unconsumed starting material could be recovered efficiently. We made no special effort to optimize the conditions for this reaction. For the THP-protected ethyl β-hydroxybutyrate (entry 10), no thione ester was obtained. Instead, the starting material decomposed slowly to unidentified products. Similar difficulty in preparing thioesters when other oxygen-containing functional groups are present has been noted previously.[8] For some of the esters, notably α-benzyl-γ-butyrolactone (entry 9) and, to a lesser extent, (trimethylsilyl)methyl cinnamate (entry 7), thionation is accompanied by partial rearrangement to the thiol ester. Subsequent thionation then leads to the corresponding dithioester as a major side product, accounting for nearly one quarter of the reaction

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