(24) C. S. Foote, R. W. Denny, L. Weaver, Y. Chang, and J. W. Peters, *Ann. N.Y. Acad. Sci.*, **171**, 139 (1970).
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(27) Note Added in Proof. We have been informed by Professor L. Miller of a serious explosion which occurred during this preparation. We have had a small fire (which we attribute to the use of a paper Soxhlet thimble). Since using an all-glass extraction apparatus, no further incidents in some 20 preparations have been encountered. Caution is advisable.

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Osmium Catalyzed Vicinal Hydroxylation of Olefins by *tert*-Butyl Hydroperoxide under Alkaline Conditions

Sir:

A better means for direct cis dihydroxylation of olefins is needed. The existing methods[1,2] all have rather serious limitations, especially when large-scale reactions are considered. The reaction of an olefin with a stoichiometric quantity of osmium tetroxide in pyridine, followed by the appropriate reductive hydrolysis, is without doubt the most reliable procedure[2b,c] for effecting this transformation. However, the great expense[3] of osmium limits the use of this method and has been responsible for the development of alternative procedures wherein osmium is employed catalytically. The two popular catalytic systems rely on metal chlorates (Hofmann)[2a] or on hydrogen peroxide (Milas)[2d,e,f] as the stoichiometric oxidant. With certain types of olefins both the Hofmann and Milas reagents give rise to over-oxidation products (e.g., ketols and compounds resulting from cleavage of the carbon-carbon bond). We reasoned that such by-products might be suppressed under alkaline conditions[4] which would favor rapid hydrolytic removal of the diol from the coordination sphere of the osmium.

We found that whereas alkaline solutions of hydrogen peroxide decomposed violently[5] (oxygen evolution) in the presence of OsO_4, solutions of *tert*-butyl hydroperoxide[6] in the presence of base and OsO_4 were stable. These latter solutions were allowed to react with a variety of olefins to give good yields of vicinal diols (Table I).

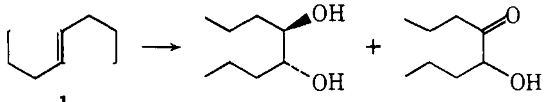
As shown in Table II for (*E*)-4-octene (**1**), this new reagent (case 1) gives more diol and less ketol than the Milas (case 3) or Hofmann (case 4) reagents. Case 2 reveals that the presence of base (Et_4NOH) is essential to the success of this new reagent.

Table I.[a] Diols from Olefins with *tert*-BuOOH, OsO_4, and Et_4NOH

Olefin	% yield[b] of diol	Olefin	% yield[b] of diol
1. 1-Decene	73	6. Cyclohexene	62
2. (*E*)-4-Octene	73	7. α-Methyl styrene	71
3. (*Z*)-4-Octene	61	8. 2-Methyl-2-butene[d]	63
4. Oleic acid[c]	70	9. 2-Methyl-2-hexene[d]	67
5. Oleyl alcohol	51	10. Tetramethyl ethylene	72
		11. 2,3-Dimethyl-2-octene[e]	69

[a] Except for oleic acid and oleyl alcohol, which were done on a 10 mmol scale, all reactions were carried out on a 100 mmol scale as described in the general procedure. [b] All yields were determined by isolation (distillation or recrystallization). [c] In this case 1 equiv of NaOH was added to titrate the acidic proton. [d] Several different modifications of the Hofmann and Milas procedures were also tried on these two trisubstituted olefins. The best yield of diol obtained with an H_2O_2 based reagent (Milas) was ~10%; ketol (~20%) was always the major product. (With these olefins our reagent gave a diol to ketol ratio of ~10:1). The ClO_3^- based methods (Hofmann) all gave principally recovered olefin and bad mixtures of oxidation products in trace amounts. [e] As in note *d* above, various modifications of the Hofmann and Milas procedures were also explored with this substrate. However, the tetrasubstituted olefin was completely inert to these reagents and was recovered unchanged.

Table II.



1 **2** **3**

Conditions[a]	Ratio[b] of diol **2** to ketol **3**	% yield
1. *tert*-BuOOH, *tert*-BuOH, H_2O, Et_4NOH, 0°	10	73
2. *tert*-BuOOH, *tert*-BuOH, H_2O, 0°	0.5	<10[c]
3. H_2O_2, *tert*-BuOH, H_2O, 0° (Milas reagent)	0.6	<20[c]
4. $KClO_3$, dioxane, H_2O, 50° (Hofmann reagent)	?[d]	<5[c]

[a] A catalytic amount (0.2%) of OsO_4 was used in each case. [b] We have found that yields of vicinal diols such as 2 cannot be determined by GLC due to great (30%) fluctuation in response factors. Thus the GLC determined ratios of diol to ketol reported here are of only qualitative importance. [c] In these three cases yields were estimated by GLC; the large amount of ketol and other by-products made it impractical to isolate pure diol. [d] In this case the GLC trace was too complicated (four overlapping peaks) in the diol–ketol region to allow determination of the ratio.

General Procedure. A 500-ml one-necked, round-bottomed flask was charged with 200 ml of reagent grade *tert*-butyl alcohol, 15 ml of 10% aqueous Et_4NOH[7] (ca. 10 mmol), and 100 mmol of olefin. This solution was cooled[8] to ca. 0° by stirring in an ice-salt bath and 18 ml (ca. 160 mmol) of 90% *tert*-butyl hydroperoxide[9] was added, followed by 10 ml of 0.5% OsO_4 in *tert*-butyl alcohol[10] (ca. 0.2 mmol). The resulting brownish purple solution was stirred for 2 h at 0° then stored in a refrigerator (0–5°) overnight. At this point the solution was either pale yellow or colorless, and 100 ml of 5% aqueous $NaHSO_3$ was added and the mixture was allowed to warm to room temperature while stirring. This mixture was concentrated on a rotary evaporator to remove most of the *tert*-butyl alcohol and water, and the resulting residue was extracted with ether. The organic extract was washed with saturated brine, dried ($MgSO_4$), and concentrated to afford the crude diol product. Purification was effected either by distillation or recrystallization.

Except in those circumstances where the molecule is sensitive to base, this new procedure for cis dihydroxylation of olefins generally affords better yields than the existing methods[1,2] for this transformation. In the case of mono- and disubstituted olefins the advantage of this new reagent is most apparent when the olefin (e.g., 4-octene and α-methyl styrene) is sensitive to over-oxidation; with less sensitive olefins (e.g., cyclohexene and 1-decene) the yields are comparable to those reported using the Hofmann and Milas reagents. However, in the case of tri- and tetrasubstituted olefins this new reagent is clearly superior to the Hofmann and Milas methods. These latter reagents often fail completely (e.g., case 11, Table I) with these more substituted olefins or they give only poor yields (e.g., cases 8 and 9, Table I) of ketol and diol products. Since it has been shown that the rate of reaction of osmium tetroxide with olefins is enhanced by increased alkyl substitution,[11] the low reactivity of tri- and tetrasubstituted olefins toward the Hofmann and Milas reagents is interesting. It seems likely that the osmate esters generated from highly substituted olefins could be slow to hydrolyze, thus creating a bottleneck in the catalytic sequence. The basic conditions used with our reagent probably facilitate hydrolysis[12] of such hindered osmate esters and enable a more rapid turnover of the osmium catalyst.[14]

Acknowledgment. We thank the National Science Foundation (MP57-21260) and Asahi Chemical Industry Corporation for financial support.

References and Notes

(1) MnO_4^-: (a) G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **127**, 175 (1925); (b) J. E. Coleman, C. Ricciuti, and D. Swern, *J. Am. Chem. Soc.*, **78**, 5342 (1956).

(2) OsO_4: (a) K. A. Hofmann, *Ber. Dtsch. Chem. Ges.*, **45**, 3329 (1912); (b) R. Criegee, *Justus Liebigs Ann. Chem.*, **522**, 75 (1936); (c) R. Criegee, B. Manchard, and H. Wannorvius, *Ibid.*, **550**, 99 (1942); (d) N. A. Milas and S. Sussman, *J. Am. Chem. Soc.*, **58**, 1302 (1936); (e) N. A. Milas and S. Sussman, *Ibid.*, **59**, 2345 (1937); (f) N. A. Milas, J. H. Trepagnier, J. T. Nolan, and M. I. Iliopolus, *ibid.*, **81**, 4730 (1959).

(3) Because RuO_4 is both less expensive and less toxic than OsO_4, we attempted to control its reactions with olefins so as to produce diols rather than the usual cleavage products. Reaction of RuO_4 with *E*- and with *Z*-cyclododecene in EtOAc at −78°, followed by reduction at −78° with dimethylsulfide, afforded the threo and erythro diols, respectively (ca. 20% yield in each case). This proves for the first time that RuO_4 reacts with olefins, like MnO_4^- and OsO_4, by stereospecific cis addition to produce initially a cyclic ruthenium (VI) ester (K. B. Sharpless and A. Y. Teranishi, unpublished results). However, due to the poor yields, this is not a practical route to diols.

(4) The beneficial effect of basic conditions on the yield of diol in MnO_4^- oxidations of olefins is well known (see ref. 1b and K. B. Wiberg, "Oxidation in Organic Chemistry", Academic Press, New York, N.Y., 1965, pp. 42–43).

(5) The catalytic decomposition of H_2O_2, especially alkaline H_2O_2, by a variety of transition metals is well known (see J. A. Connor and E. A. V. Ebsworth, *Adv. Inorg. Chem. Radiochem.*, **6**, 359–360 (1964), and S. B. Brown, P. Jones, and A. Suggett, *Prog. Inorg. Chem.*, **13**, 159–204 (1970)).

(6) There is one earlier claim to the use of *tert*-butyl hydroperoxide, catalyzed by OsO_4, for the vicinal hydroxylation of an olefin (G. E. McCasland, S. Turuta, and L. J. Durham, *J. Org. Chem.*, **33**, 2835 (1968)). However, the experimental section of that paper reveals that hydrogen peroxide in *tert*-butyl alcohol (i.e., the Milas reagent), not *tert*-butyl hydroperoxide, was the oxidant actually used.

(7) Tetraethylammonium hydroxide was chosen as the base for its solubility in the organic medium. Use of sodium or potassium hydroxides resulted in heterogeneous reaction mixtures and lower yields.

(8) Cooling is more important for some olefins than for others. For example, at room temperature α-methylstyrene gives more cleavage to acetophenone and the 4-octenes afford less diol and more ketol and α-diketone.

(9) The impurities in commercial *tert*-butyl hydroperoxide are *tert*-butyl alcohol and water. Since neither of these impurities interferes with this reaction, *tert*-butyl hydroperoxide of any strength or purity can be used. By contrast, the molybdenum and vanadium catalyzed epoxidations of olefins are very sensitive to the purity of the hydroperoxide (K. B. Sharpless and R. C. Michaelson, *J. Am. Chem. Soc.*, **95**, 6136 (1973); S. Tanaka, H. Yamamoto, H. Nozaki, K. B. Sharpless, R. C. Michaelson, and J. D. Cutting, *ibid.*, **96**, 5254 (1974)).

(10) This catalyst solution was prepared as described by Daniels and Fischer (R. Daniels and J. L. Fischer, *J. Org. Chem.*, **28**, 320 (1963)) with the exception that *tert*-butyl hydroperoxide was used in place of H_2O_2 as the stabilizer. Recipe: 1 g of OsO_4, 199 ml of the specially purified *tert*-butyl alcohol, and 1 ml of 90% *tert*-butyl hydroperoxide; each milliliter contains 2×10^{-5} mol of OsO_4.

(11) K. B. Sharpless and D. R. Williams, *Tetrahedron Lett.*, 3045 (1975).

(12) It is well known that osmium(VI) glycol esters are often reluctant to hydrolyze. For this reason we believe that, in these catalytic systems, the osmium(VI) ester is first oxidized to an osmium(VIII) ester which then undergoes hydrolysis. Considerations of pK_a indicate that the principal base in our system will be the *tert*-butyl hydroperoxide anion. In addition to facilitating hydrolysis, this anion might also be expected to increase the rate of oxidation of osmium(VI) to osmium(VIII).

(13) Camille and Henry Dreyfus Teacher–Scholar Grant recipient; Alfred P. Sloan Fellow, 1973–1975.

(14) Note Added in Proof. A group at Upjohn has discovered a mild osmium catalyzed oxidation of olefins to vicinal diols using amine N-oxides as the oxidant (V. Van Rheenen, R. C. Kelly, and D. Y. Cha, *Tetrahedron Lett.*, in press). We are grateful to Dr. Robert Kelly for informing us of their results prior to publication.

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Free Energies of Hydration and Hydrolysis of Gaseous Acetamide

Sir:

Despite widespread interest in the biochemical properties of the acylamido function in aqueous solution, there seems to be little thermodynamic information about the strength of interaction between amides and solvent water. An absolute measure of the hydrophilic character of a solute is provided by its equilibrium of distribution between dilute solution and the dilute vapor phase, in which intermolecular forces are absent. This is to report that the hydrophilic character of acetamide, which is apparently the first amide to have been studied in this way, far surpasses that of other simple uncharged organic compounds which have been measured before.[1,2]

Initial attempts to measure the partial pressure of aqueous acetamide by conventional methods were in vain. Analysis by mass spectrometry showed that acetamide was not present at detectable levels (ca. 10^{-3} Torr) in samples removed from the gas space over stirred solutions of acetamide (1 M) in water at 25°. It was therefore necessary to resort to a dynamic technique, similar to that first developed by Shaw and Butler[3] for use with more volatile solutes, and use radioactivity as a means of detection.

In a typical experiment, water-pumped nitrogen was passed (at a rate of 40 ml/min) through a glass train consisting of a series of three wash bottles with fritted glass disks, each containing 100 ml of acetamide-*1*-^{14}C (0.01 M, 0.03 Ci/mol) in dilute KOH (0.01 M). The alkali was added to trap acetic acid, which was found to be generated in trace quantities during long-term experiments. Continuing through a spray trap, the effluent gas then passed through a second series of three wash bottles, each containing water (150 ml). At intervals, samples were removed from these traps for analysis of radioactivity accumulated as a function of the volume of gas passed through the train. Of the radioactivity transferred, more than 96% appeared in the first two receiving vessels, indicating the efficiency of the trapping system. The chemical nature of the radioactive substance transferred was determined by measuring its distribution coefficient between water, containing either HCl (0.05 M) or KOH (0.05 M), and 1-octanol at 25°. In both acidic and basic systems, the radioactive substance exhibited $K_d = 0.070$ toward octanol, identical with values measured with samples of authentic acetamide in separate experiments (and similar to a value extrapolated from the observed behavior of butyramide[4]). In contrast, the possible contaminant acetic acid gave $K_d = 0.60$ from 0.05 M HCl to octanol, and $K_d \leq 0.001$ from 0.05 M KOH to octanol (consistent with literature values[4]).

The rate of transfer of radioactive acetamide was found to be proportional to the rate of flow of gas, and to the concentration of radioactivity in the equilibrating vessels. The rate was unaffected by varying the concentration of nonradioactive acetamide in the equilibrating vessels in the range from 0.001 to 0.01 M (consistent with the known monomeric nature of acetamide in water[5]), or by increasing the volume and number of equilibrating vessels containing radioactive acetamide in solution (indicating that equilibration was complete under these conditions). The observed rate of transfer corresponded to an absolute distribution coefficient of 7.6×10^{-8} (with a standard deviation of 2.5×10^{-8} in eight experiments) from water to the vapor phase at 25°.

The most hydrophilic of simple organic compounds studied previously, acetic acid, gave $K_d = 1.1 \times 10^{-5}$ for distribution from aqueous solution (0.05 M) to the vapor phase by the present method, in good agreement with earlier de-