mL of 2 N KOH was heated at 80 °C with stirring for 3 h. This basic solution was cooled to room temperature and the title compound isolated according to the procedure of Rich.[10e] The basic solution was acidified with Dowex 50 W×8 (H^+ form; 100–200 mesh) to pH <4 and heated again for 5 min at 80 °C. The mixture of Dowex H^+/water was filtered through ca. 30 mL of Dowex 50 W×8 (H^+ form: 100–200 mesh). The desired amino acid was finally eluted with 200–250 mL of an aqueous 1.5 N NH_3 solution. The desired fractions (ninhydrine-active) were combined and evaporated in vacuo to dryness. The colorless residue was then taken up twice in some water and each time concentrated to dryness. The residue[18] was recrystallized from MeOH/H_2O to yield 194 mg (76%) of very fine crystals of MeBmt in diastereomerically and enantiomerically pure form: $[\alpha]_D$ 12.3 (c 0.43, phosphate buffer Titrisol pH 7.00 from Merck) [lit.[10f] $[\alpha]_D$ = 13.5 (c 0.50, phosphate buffer Titrisol pH 7.00 from Merck); lit.[10a] $[\alpha]_D$ 11.4 (c 0.50, phosphate buffer Titrisol pH 7.00 from Merck)]; mp 243–245 °C dec (lit.[10f] mp 240–241 °C; lit.[10a] mp 242–243 °C). The spectroscopic data (IR, ^1H NMR) of this compound were in good agreement with reported ones:[10a,f] ^{13}C NMR (100 MHz, D_2O) δ 18.06, 19.88, 35.26, 36.33, 38.20, 69.33, 76.80, 130.60, 131.43, 174.73. Anal. Calcd for $C_{10}H_{19}NO_3$: C, 59.68; H, 9.52; N, 6.96. Found: C, 59.57; H, 9.65; N, 6.81.

Acknowledgment. Financial support from the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung (project No. 20-25276.88, to S.Y.K.) is gratefully acknowledged. The work described here was started during a postdoctoral collaboration with S.Y.K. (1987–1989; present address: Sandoz Institute for Medical Research, 5 Gower Place, GB-London WC1E 6BN). It is part of the Ph.D. Thesis of D. B., ETH Dissertation No. 9527, ETH Zürich, 1991.

Registry No. (*R*)-**2a**, 119323-03-4; **3**, 104372-54-5; **4**, 135646-39-8; **4** (C1′-epimer), 135684-43-4; **5**, 135646-40-1; **6**, 135646-41-2; **7a**, 81135-60-6; **7a** (C1′-epimer), 135684-44-5; **8**, 104324-29-0; **8** (C1′-epimer), 122090-71-5; **9**, 59865-23-5.

A Versatile Transformation of *vic*-Diols into α-Hydroxy Ketones with Hydrogen Peroxide Catalyzed by Peroxotungstophosphates

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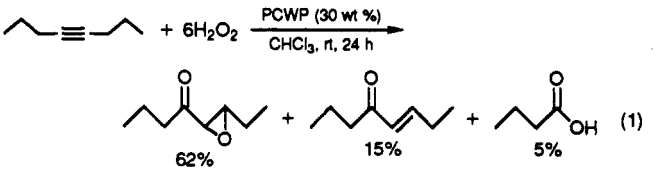
Received March 12, 1991

α-Hydroxy ketones (α-ketols), which are versatile starting materials in organic synthesis, are classically synthesized by the acyloin condensation of esters,[1] but this method suffers from a serious limitation in the preparation of cyclic and unsymmetrical aliphatic α-ketols. In order to overcome this limitation, a number of synthetic methods have been developed for the preparation of cyclic α-ketols (e.g., oxidation of silyl enol ethers with *m*-CPBA,[2] treatment of *vic*-diols with Fetizon reagent[3] or Corey–Kim reagent,[4] or permanganate oxidation of olefins[5]) and for aliphatic α-ketols (e.g., mercuric-assisted hydrolysis of α-hydroxy alkyl dithioketals,[6a] hydration of propargylic alcohols,[5b,7] oxidation of ketones with iodosobenzene,[8] DMSO oxidation of oxiranes,[9] treatment of iodocarbonates with fluoride anion on polymeric support,[10] or Ni(II)-catalyzed oxygenation of silyl enol ethers[11]). In general, Swern oxidation of diols results in formation of dicarbonyl compounds.[12]

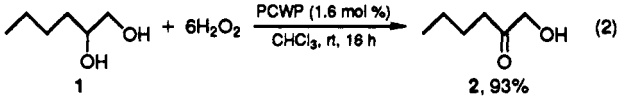
The application of metal reagents such as chromium(IV) or permanganate, which are often used for ketonization of alcohols, to the oxidation of *vic*-diols led to carbon–carbon bond scission to form carboxylic acids.[13] Periodate[14] or lead tetraacetate oxidations[15] of *vic*-diols are well-known methods leading to aldehydes. On the other hand, *vic*-diols have been cleaved to carboxylic acids by hydrogen peroxide under the influence of WO_4^{3-}/PO_4^{3-},[16] $[Me(CH_2)_{15}C_5H_5N]_3PW_{12}O_{40}$ (CWP),[17] or H_2WO_4.[18] However, the oxidative dehydrogenation of *vic*-diols into α-hydroxy ketones has been difficult to achieve in satisfactory yields.

In a preceding paper,[19] we reported that peroxotungstophosphate (PCWP), which can be readily prepared by treating 12-tungstophosphoric acid (WPA) in aqueous hydrogen peroxide with cetylpyridinium chloride (CPC), catalyzed a novel oxidation of internal alkynes into α,β-epoxy ketones and α,β-unsaturated ketones with 35% H_2O_2 in a biphasic system using chloroform as the solvent (eq 1).



(1)

We now report the transformation of *vic*-diols into α-hydroxyketones via a catalytic process employing the PCWP–H_2O_2 system. The reaction was achieved by the use of 35% H_2O_2 (6 equiv) in the presence of PCWP (1.6 mol %) in a biphasic system using chloroform as the solvent (eq 2, Table I).



(2)

Primary–secondary diols were dehydrogenated with high chemoselectivity to form 1-hydroxy-2-alkanones in good

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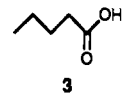
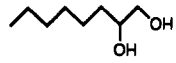
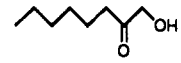
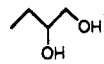
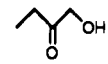
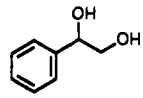
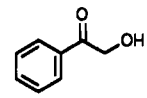
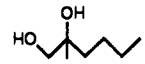
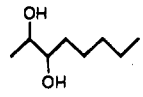
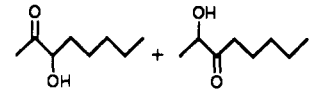
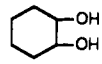
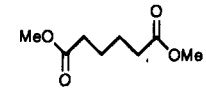
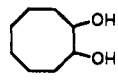
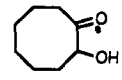
Table I. Oxidation of *vic*-Diols to α-Ketols by PCWP-H_2O_2 System[a]

run	diol	catalyst	product	yield[b] (%)
1	1	PCWP	2	93 (72)[c]
2[d]		PCWP	 3	68
3		CWP	2	16
4		PCMP	2	18
5	 4	PCWP	 5	90
6	 6	PCWP	 7	43
7	 8	PCWP	 9	92
8	 10	PCWP	no reaction	
9	 11	PCWP	 12a 12b	85[e]
10	 13	PCWP	 14	54[f]
11	 15	PCWP	 16	32

[a] Diol (3 mmol) was allowed to react with 35% H_2O_2 (6 equiv) in the presence of catalyst (1–1.6 mol %) under refluxing temperature of chloroform (15 mL) for 16 h. [b] Determined by GC based on the diols used. Conversion of diols was more than 90% except for runs 3 and 4 whose conversion was up to 30%. [c] H_2O_2 of 3 equiv was used. [d] *t*-BuOH was used as solvent. [e] Ratio of **12a**/**12b** = 2/3. [f] Isolated yield after methyl esterification.

yields. For instance, 1,2-hexanediol (**1**) and 1,2-octanediol (**4**) were converted into 1-hydroxy-2-hexanone (**2**) and 1-hydroxy-2-octanone (**5**), respectively, in 93% and 90% yields. The primary hydroxy function of **1** or **4** was not oxidized by the present catalyst–oxidant system. Similar chemoselectivity has been observed in the oxidative dehydrogenation of 1,3-diols having both primary and secondary alcohol functions by the CWP-H_2O_2 system.[17] By use of 3 equiv of 35% H_2O_2, the yield of **2** was lowered to 72%. The oxidation of 1,2-butanediol (**6**) proceeded less selectively than that of **1** to form 1-hydroxy-2-butanone (**7**) in moderate yield (43%). The decrease in the yield of **6** to **7** is believed to be due to the overoxidation to the carboxylic acid, since diol **6** is soluble in the aqueous phase where further oxidation can take place. In fact, under homogeneous conditions employing *tert*-butyl alcohol as the solvent, **1** was cleaved to pentanoic acid (**3**) (run 2). These observations suggest that the biphasic system for the selective oxidation of *vic*-diols into α-ketols is essential to prevent overoxidation to carboxylic acids. 1-Phenyl-1,2-ethanediol (**8**) afforded 2-hydroxy-1-phenylethanone (**9**) in excellent yield (92%).[20] The primary–tertiary diol, 2-methyl-1,2-hexanediol (**10**), was not oxidized by the present system, and starting diol was recovered unchanged.

In contrast to the oxidation of 1,2-diols where the dehydrogenation occurs regioselectively at the secondary hydroxy group, secondary–secondary diols such as 2,3-octanediol (**11**) afforded a 2:3 regioisomeric mixture of 2-hydroxy-3-octanone (**12a**) and 3-hydroxy-2-octanone (**12b**)[21] in which the internal hydroxyl group was preferentially oxidized.

Although the oxidation of *trans*-1,2-cyclohexanediol (**13**) was examined under several reaction conditions, only adipic acid (**14**) was produced without the formation of the desired α-ketols. However, 1,2-cyclooctanediol (**15**) was converted into the corresponding α-ketols **16** in moderate yield (32%) along with a considerable amount of suberic acid. These results show that cyclic α-ketols are much more susceptible to overoxidation to carboxylic acids than aliphatic ones with the present system.

The CWP catalyst, which showed high activity for the oxidative dehydrogenation of 1,3-diols,[17] was less efficient for the oxidation of 1,2-diols (run 3). The corresponding molybdenum peroxo complex (PCMP), prepared from 12-molybdophosphoric acid (MPA) in the place of WPA,

(20) Ketol **9** has been prepared from acetophenone with iodosobenzene[8] or styrene oxide by DMSO oxidation[9] in 60% and 63% yields, respectively.

(21) The ratio of **12a**/**12b** was determined by ^1H NMR (400 MHz). The methyl protons of the C-1 position of **12a** and **12b** appeared in δ 2.22 (s, 3 H) and 1.38 (d, 3 H), respectively.

was ineffective for this purpose (run 4), and about 60% of the starting diol 1 was recovered.

In conclusion, we have found the first practical transformation of *vic*-diols into α-ketols using hydrogen peroxide. This method possesses several advantages: (1) the reaction is carried out catalytically using a cheap and clean oxidant (35% H_2O_2), and the isolation of α-ketols is accomplished easily since the reaction is carried out in a biphasic system; (2) the reaction is particularly useful for oxidation of terminal diols to afford acyloins which are difficult to prepare by conventional methods; and (3) the preparation of α-ketols from *vic*-diols offers a wider range of substrate opportunities.

Experimental Section

GLC analyses were performed employing a thermal conductivity detector using a 2.6 mm × 5.4 m column (5% silicon OV-7 on Chromosorb W). Infrared spectra were measured as KBr pellets (4-cm^{-1} resolution). ^1H and ^{13}C NMR were measured at 400 MHz in $CDCl_3$ using $MeSi_4$ as the internal standard. The yield of products was estimated from peak areas based on an internal standard.

Preparation of Peroxotungsten Complex (PCWP). PCWP was prepared by the method reported previously.[19] The active oxygen content of PCWP was estimated to 3.7–3.9 mmol/g (theoretical 3.8 mmol/g) from iodometry improved by Venturello.[16] PCWP: IR (KBr/Nujol) 2900, 2850, 1633, 1486, 1466, 1090, 1055, 957, 842, 774, 722, 684, 648, 625, 571, 552, 524 cm^{-1}. Anal. Calcd for $C_{63}H_{114}N_3O_{24}PW_4$ (PCWP): C, 36.66; H, 5.57; N, 2.04. Found: C, 36.41; H, 5.47; N, 2.01.

General Procedure for Oxidation of *vic*-Diols. To a stirred solution of PCWP (0.1 g, 0.048 mmol) and 35% H_2O_2 (18 mmol) in chloroform (15 mL) was added the *vic*-diol (3 mmol), and the mixture was refluxed for 16 h. The reactant was treated with a solution of 10% $NaHSO_3$ (20 mL) to decompose unreacted H_2O_2 and extracted with $CHCl_3$. The products were purified by silica gel column chromatography (hexane/ethyl acetate (10–20/1)). Spectral data of the products were identical with those reported.[1b,5,6,9,10]

Registry No. 1, 6920-22-5; 2, 73397-68-9; 3, 109-52-4; 4, 1117-86-8; 5, 7019-19-4; 6, 584-03-2; 7, 5077-67-8; 8, 93-56-1; 9, 582-24-1; 10, 56255-50-6; 11, 20653-90-1; 12a, 52279-26-2; 12b, 52279-26-2; 13, 1460-57-7; 14, 124-04-9; 15, 4277-32-1; 16, 496-82-2; H_2O_2, 7722-84-1.

Supplementary Material Available: Spectral data for acyloins in Table I (2 pages). Ordering information is given on any current masthead page.

Synthesis of Functionalized Endocyclic α,β-Unsaturated and α-Methylene Eudesmanolides[1]

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Although a number of sesquiterpenes possessing C_{12}-functionalized endocyclic α,β-unsaturated γ-lactones such as A (X = CH_3, CH_2OH, CH_2OAc, CHO)[3] and 7-hydroxy-α-methylene γ-lactones[4] such as B (Figure 1) have been reported, efficient methodology for synthesis of these functional groups has not yet been reported.[5] In the course of our studies of sesquiterpene lactones, we were interested in the syntheses of compounds possessing these functional groups because of literature reports concerning their biological activities.[6] In this paper we report the

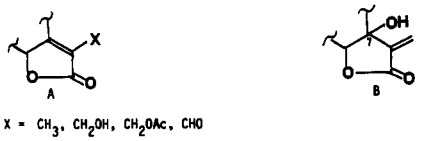
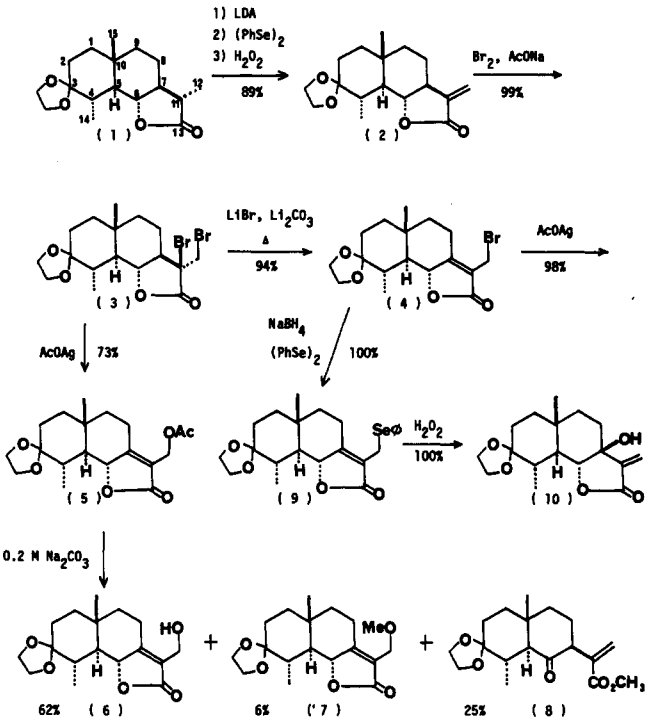
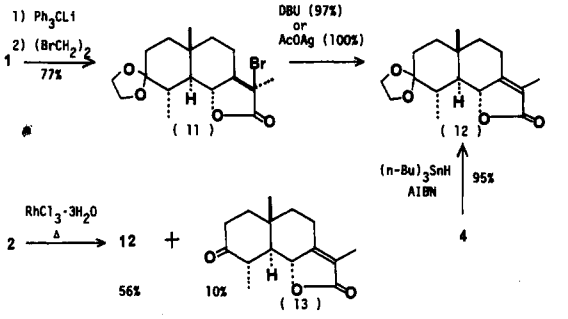


Figure 1.

Scheme I



Scheme II



(1) Studies on the Syntheses of Sesquiterpene Lactones. 13. Preliminary reports of this work were presented at the 26th and 31th Symposium on the Chemistry of Terpenes, Essential Oils, and Aromatics, Yamagata, Oct 1982; Abstract pp 224–227 and Kyoto, Sept 1987, pp 137–139.

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