greater than 98% enantiomeric excess as described below.

Experimental Section

Nuclear magnetic resonance spectra were recorded on a Varian XL300 spectrometer. Infrared spectra were recorded on a Beckman 3001 instrument. Chemical ionization (CI) mass spectra were run on a Finnigan Mat-10150 spectrometer and high-resolution mass spectra on a VG 7070F spectrometer. Gas chromatographic analysis utilized a Hewlett-Packard 5880A instrument with a carbowax capillary. Melting points were obtained with a Thomas-Hoover Unimelt apparatus and are uncorrected.

(*S*)-(+)-3-Methylpiperidine. A slurry of 45.64 g (0.3 mol) of (+)-mandelic acid in 300 mL of ethyl acetate was heated to solution and treated with 29.75 g (0.3 mol) of 3-methylpiperidine in one portion. The mixture was allowed to come to room temperature before filtration. The crystalline material was washed with 400 mL of 1:1 ethyl acetate/ether and dried to give 31.38 g of optically impure salt. Two recrystallizatons of this salt from ethyl acetate gave 24.65 g (64%) of (*S*)-(+)-3-methylpiperidine mandelate, mp 122–123 °C (lit.[8] mp 122–124 °C).

(+)-*N*-Benzoyl-3-methylpiperidine. (*S*)-3-Methylpiperidine mandelate (19.3 g, 76.8 mmol) was dissolved in 200 mL of 1.0 N sodium hydroxide solution. The solution was cooled to 3 °C, and 11.25 g (80.0 mmol) of benzoyl chloride was added dropwise over 10 min. After the addition was complete, the mixture was transferred to a separatory funnel and extracted with ether (2 × 100 mL). The combined extracts were dried ($MgSO_4$) and concentrated to give 14.65 g (94%) of analytically pure amide: mp 72 °C; $[\alpha]^{23}_D$ +49.5° (*c* 1.00, CH_3OH); ^1H NMR (C_6D_6, 70 °C) δ 7.30 (d, *J* = 6 Hz, 2 H), 7.08 (m, 3 H), 4.0 (br, 2 H), 2.58 (ddd, *J* = 13.2, 10.2, 4.1 Hz, 1 H), 2.30 (dd, *J* = 12.9, 9.9 Hz, 1 H), 1.2–1.5 (m, 4 H), 0.8 (m, 1 H), 0.6 (d, *J* = 6.5 Hz, 3 H); IR (neat) 3075, 3000, 1680 cm^{-1}; mass spectrum (CI, NH_3) *m/e* 204 (M + 1). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.80; H, 8.43; N, 6.89. Found: C, 76.73; H, 8.44; N, 6.79.

(−)-2-Methyl-1,5-dibromopentane (2). A 500-mL flask holding 45.1 g (222.2 mmol) of powdered (+)-*N*-benzoyl-3-methylpiperidine was cooled to 5 °C. Phosphorus tribromide (60.1 g, 222.2 mmol) was added from a dropping funnel over 1 h with vigorous stirring. A bright yellow oily crystalline mass was formed. After the addition was complete, the cooling bath was removed, and the mixture became homogeneous upon warming to room temperature. A new dropping funnel containing 11 mL of Br_2 (222.2 mol) was attached, and the Br_2 was added dropwise over 20 min. The resulting mixture was stirred for an additional 3 h. The addition funnel was replaced with a distillation head, and the mixture was distilled under vacuum (1.0 mm) until the pot residue was sticky black. The distillate was dissolved in 100 mL of isooctane and washed successively with water (50 mL), concentrated sulfuric acid (4 × 10 mL), water (50 mL), 1.0 N NaOH solution (2 × 100 mL), and finally water (50 mL). The isooctane solution was dried ($NaSO_4$) and concentrated. The resulting oil was distilled under reduced pressure to give 26.6 g (49.9%) of (−)-2-methyl-1,5-dibromopentane: bp 111 °C (10 mm); $[\alpha]^{23}_D$ −2.99° (neat); ^1H NMR ($CDCl_3$) δ 3.41 (dt, *J* = 6.9, 1.5 Hz, 2 H), 3.35 (dt, *J* = 10.0, 5.9 Hz, 2 H), 1.8–1.95 (m, 3 H), 1.62 (m, 1 H), 1.41 (m, 1 H), 1.04 (d, *J* = 6.5 Hz, 3 H); IR (neat) 2980, 2860, 1450, 1430, 1370, 1250, 1225 cm^{-1}. Anal. Calcd for $C_6H_{12}Br_2$: C, 29.54; H, 4.96. Found: C, 29.80; H, 5.02.

3-Methylcyclohexanone Dimethyl Dithioketal *S*-Oxide (3). Potassium hydride (8.00 g, 50% in oil) was placed in a dry argon-filled 250-mL three-neck flask fitted with rubber septum, argon inlet, and thermometer. The reagent was washed twice with 20 mL of isooctane to remove carrier oil and then covered with 70 mL of dry THF. After cooling the reaction flask to −10 °C, a solution of methyl (methylsulfinyl)methyl sulfide (5.08 g, 41 mmol) in THF (5 mL) was added via cannula over 2 min. After 10 min, a solution of (−)-2-methyl-1,5-dibromopentane (10 g) in THF (30 mL) was added via cannula over 5 min, keeping the reaction temperature below 20 °C. After the addition was complete, the reaction was stirred for an additional 1 h, absolute ethanol (3 mL) was carefully added, and the reaction was poured into a 500-mL separatory funnel containing water (50 mL) and ether (150 mL). The organic layer was removed, dried with $MgSO_4$, and concentrated. The crude material was filtered through a short pad of silica gel using 30% EtOAc/hexane as the eluant, and the filtrate was concentrated to give 6.09 g (78%) of the two diastereomeric dithioketals (ratio 3:5 by GC analysis): ^1H NMR ($CDCl_3$) δ 2.72 (m, 2 H), 2.67 (s, 3 H, SMe), 2.34 and 2.33 (s, 3 H, SMe), 1.6–2.2 (m, 6 H), 1.48 (dd, *J* = 13.0, 12.2 Hz, 1 H), 1.02 and 0.90 (d, *J* = 6.4 Hz, 3 H); IR (neat) 2935, 1445, 1290, 1050 cm^{-1}; mass spectrum (CI, NH_3), *m/e* 143 (M − SOMe); high-resolution mass spectrum, calcd for $C_8H_{15}S$ 143.0891, found 143.0894.

(*S*)-(−)-3-Methylcyclohexanone (4). Concentrated hydrochloric acid (6 mL) was added to a solution of **3** (8.4 g, 40.8 mmol) in methanol (35 mL) and the resulting mixture was refluxed for 15 min. The mixture was then poured into a separatory funnel containing 70 mL of 1 N NaOH solution and extracted with two 25-mL portions of ether. The combined extracts were dried ($MgSO_4$) and filtered. After removal of the solvent by distillation through a Vigreux column, the product was obtained by short-path distillation, bp 169 °C (3.8 g, 83%). The ketone obtained was in all respects (^1H NMR, MS, IR) identical with the commercially available (+)-3-methylcyclohexanone except for optical rotation [$[\alpha]^{23}_D$ −12.8° (neat)] and odor. Anal. Calcd for $C_7H_{12}O$: C, 74.95; H, 10.79. Found: C, 75.02; H, 10.81.

Determination of Optical Purity. Derivatization of commercial (*R*)-(+)-4 and the synthetic (*S*)-(−)-4 with (2*R*,3*R*)-butane-2,3-diol by the method of Plattner and Rapoport,[10] gave the corresponding diastereomeric ketals. ^{13}C NMR analysis, according to Hiemstra and Wynberg,[9] of the ketal derivative of (−)-4 revealed no diastereomeric impurity. Our sample of commercial (+)-4 was also revealed to be optically pure by this method. Addition of 1% of the (+)-4 to our sample of (−)-4, followed by derivatization and ^{13}C NMR analysis clearly showed the presence of the diastereomeric impurity. Thus, both (+)- and (−)-4 were >98% enantiomerically pure.

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Registry No. **2**, 81155-94-4; **3**-(*R*), 109152-47-8; **3**-(*S*), 109278-47-9; **4**, 24965-87-5; Br_3P, 7789-60-8; Br_2, 7726-95-6; (*S*)-(−)-3-methylpiperidine mandelate, 109152-46-7; 3-methylpiperidine, 626-56-2; (+)-*N*-benzoyl-3-methylpiperidine, 109152-48-9; (methylthio)methyl ethyl sulfone, 109152-49-0.

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Metal Catalysis in Oxidation by Peroxides.[1] Anionic Molybdenum-Picolinate *N*-Oxido-Peroxo Complex: An Effective Oxidant of Primary and Secondary Alcohols in Nonpolar Solvents

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Anionic molybdenum–peroxo complexes are useful reagents in alcohol oxidations.[2] In a preliminary report

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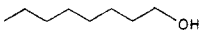
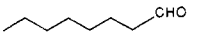
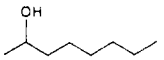
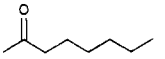
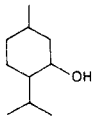
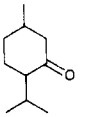
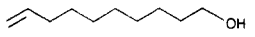
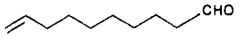
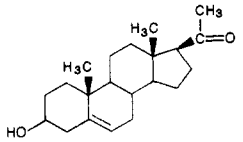
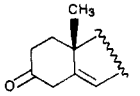
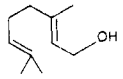
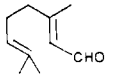
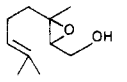
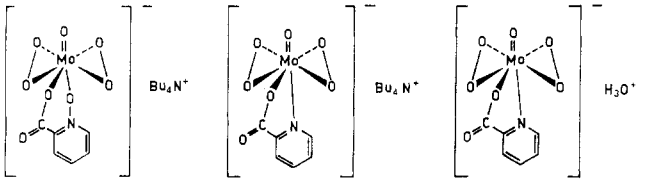
0022-3263/87/1952-5467$01.50/0

Table I. Oxidation of Various Alcohols with 1a in DCE at 50 °C; [Substrate]$_0$ = [Active Oxygen]$_0$ = 0.02 M

run	substrate	time, h	product[a]	yield, %
1		7		94
2		5		96
3		10		96
4		9		96
5		6		98
6		9		97
7		5		96
8		9		99[b]
9		3		99
10		10		96[c]
11		4		80
				20

[a] Determined by GC (see the Experimental Section). [b] Isolated yield (silica gel, CH_2Cl_2). [c] Isolated yield (silica gel, ethyl acetate–petroleum ether, 30/70).

from this laboratory,[1] we described the synthesis of complexes **1a** and **1b**, belonging to the family of oxo diperoxo complexes containing bidentate ligands studied by Mares et al.[3] In particular, they resemble (cf. the structure of



1a **1b** **1c**

1a reported in the Experimental Section) complex **1c**, which has been used in the oxidation of secondary alcohols in methanol solvent.[4] Owing to the presence of the lipophilic cation Bu_4N^+, both **1a** and **1b** are fairly soluble in nonpolar solvents such as dichloroethane (DCE), where the oxidations are faster than in protic media. Furthermore, it has been found that complex **1a** is ca. 50-fold more reactive than **1b** toward cyclohexanol.[1] Therefore, we examined the oxidation of a series of primary and secondary alcohols with **1a**. We also investigated the chemoselectivity of **1a** as far as the competition between alcohol oxidation and double-bond epoxidation is concerned. The pertinent results are collected in Table I. By using equimolar amounts of substrate and active oxygen, quantitative yields of the corresponding carbonyl compounds are obtained. Under the experimental conditions adopted, further oxidation of aldehydes to carboxylic acids does not occur. Interestingly, there is little difference in reactivity between primary and secondary alcohols, contrary to the behavior of other molybdenum-based oxidations.[2] By contrast, it is observed that cyclohexanol is oxidized faster than cyclopentanol.[2,5]

In all the examples considered, with the exception of geraniol, double-bond epoxidation does not compete at all with alcohol oxidation. Noteworthy, in geraniol oxidation, only 2,3-epoxygeraniol is formed together with geranial. This indicates that the primary alcohol oxidation predominates over the epoxidation of the highly nucleophilic, trialkyl-substituted, 6,7 double bond.[6] Accordingly, dialkyl-substituted allylic (entry 9) and homoallylic (entry 10) double bonds are not epoxidized in the presence of the alcoholic function.

The nature of the solvent, likely its donicity,[7] appears to play a role in determining the chemoselectivity of geraniol epoxidation. Preliminary experiments, not reported

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in the table, indicate that in passing from CH_3NO_2 to DMF the yield in geranial is raised from 68 to 95%.

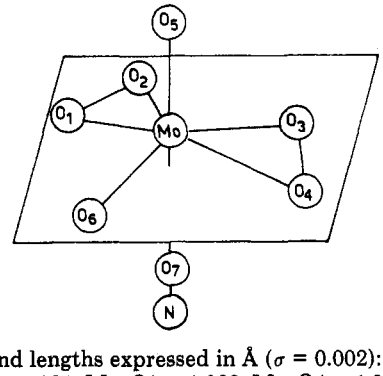
While mechanistic studies are in progress to elucidate the peculiar features shown by **1a**, our efforts are also directed toward the development of a catalytic process based on picolinate *N*-oxido-molybdenum complexes.

Experimental Section

Materials. All alcohols are high-purity materials further purified by distillation or crystallization. 1,2 Dichloroethane, nitromethane, and *N,N*-dimethylformamide were also purified by standard procedures. All other chemicals are commercially available products used as received. The products of oxidation were identified on the basis of their spectral properties and by comparison with authentic samples.

Preparation of $[MoO(O_2)_2C_5H_4N(O)COO]^-R_4N^+\cdot H_2O$ (R = Me, Bu). $Na_2MoO_4\cdot 2H_2O$ (3.36 g, 14 mmol) was dissolved in 10 mL of water, and the acidity of the solution was adjusted at pH 2 with H_2SO_4 (50%). Then 7 mL of H_2O_2 (36%, w/v) was added, and the resultant solution was diluted to 20 mL with water (solution A). Picolinic acid *N*-oxide (2.14 g, 15 mmol) was dissolved in 10 mL of an aqueous solution of tetramethylammonium hydroxide (1.5 M), and the resultant mixture was diluted to 20 mL with water (solution B). In an ice-cold bath, under vigorous stirring, 20 mL of solution A was added to 18 mL of solution B, maintaining the acidity of the media at pH 2 by adding 50% H_2SO_4. After 30 min, the formation of a bright yellow precipitate (4.06 g, 10 mmol, 71%) was complete. The solid was filtered off and washed several times with ether. The product was recrystallized from DCE. The water molecule may be removed by keeping the complex overnight in the dark at 0.1 mmHg in the presence of P_2O_5. The dehydrated complex is a very stable material, which may be stored for several weeks: iodometric titration, [active oxygen] ≡ 2[**1a**] = 98%; mp 183-184 °C dec (uncorrected); IR (KBr) ν(Mo=O) 950, ν(O—Mo—O) 586, 524, ν(C=O), 1660, ν(N→O) 1240 cm^{-1}. Anal. Calcd for $C_{10}H_{18}MoN_2O_9$: C, 29.50, H, 4.01; N, 6.89. Found: C, 29,48; H, 3.97; N, 6.82.

Suitable crystals for X-ray analysis were obtained by slow crystallization at -3 °C in DCE. The crystal system was obtained with an automatic Phillips PW 1100/16 with standard software: cell parameters a = 10.290, b = 21.476, c = 6.982 Å; β = 94.65°; Z = 4; space group $P2_1/a$. The structure was solved with the Patterson method and refined to factor R = 0.023 by using 2319 reflections with $I \geq 3\sigma(I)$. See the paragraph at the end of paper about supplementary material.



Selected bond lengths expressed in Å (σ = 0.002): Mo-O1 = 1.967, Mo-O2 = 1.931, Mo-O3 = 1.923, Mo-O4 = 1.947, Mo-O5 = 1.675, Mo-O6 = 2.256, Mo-O7 = 2.075, N-O7 = 1.329. Selected bond angles in degrees (σ = 0.1): O1-Mo-O^2 = 44.6, O3-Mo-O4 = 44.4, O5-Mo-O1 = 100.6, O5-Mo-O4 = 101.2, O7-Mo-O1 = 89.3, O7-Mo-O4 = 87.9, O7-Mo-O5 = 92.1, O5-Mo-O6 = 168.1.

The complex with R = Bu has been obtained according to the same procedure by using tetrabutylammonium hydroxide: active oxygen 98%; mp 144-145 °C dec (uncorrected); IR (KBr), ν(Mo=O) 947, ν(O—Mo—O) 582, 528, ν(C=O) 1663 ν(N→O) 1238 cm^{-1}. Anal. Calcd for $C_{22}H_{40}MoN_2O_8$: C, 47.48; H, 7.25; N, 5.03. Found: C, 47.71; H, 7.37; N, 5.01.

Due to its higher solubility in DCE, it has been used in all the oxidations described in this paper.

Procedures. In a typical run, 5 mL of DCE containing 0.3 mmol of substrate was added to a DCE solution (10 mL) containing the complex (0.15 mmol) and an internal GC standard in a glass reactor maintained at 50 °C. After complete consumption of active oxygen (absence of iodometric titer), the yield was calculated by GLC analysis on a FFAP 3% (0.5-m) or on a Carbowax 20 M 10% (1.5-m) column, both on Chromosorb WAW-DMCS, with a Varian 3700 or a Varian 6000 instrument equipped with a Varian CDS 401 or a Shimatzu C-R3A.

Registry No. **1a**, 105194-63-6; $[MoO(O_2)_2C_5H_4N(O)COO]^-Me_4N^+$, 110316-47-7; Na_2MoO_4, 7631-95-0; $H_3C(CH_2)_7OH$, 111-87-5; $H_3C(CH_2)_6CHO$, 124-13-0; $PhCH_2OH$, 100-51-6; PhCHO, 100-52-7; $H_3C(CH_2)_5CH(OH)CH_3$, 123-96-6; $H_3C(CH_2)_5COCH_3$, 111-13-7; $PhCH(OH)CH_3$, 98-85-1; $PhCOCH_3$, 98-86-2; $H_2C{=}CH(CH_2)_8OH$, 13019-22-2; $H_2C{=}CH(CH_2)_7CHO$, 39770-05-3; $(H_3C)_2C{=}CH(CH_2)_2C(CH_3){=}CHCH_2OH$, 624-15-7; $(H_3C)_2C{=}CH(CH_2)_2C(CH_3){=}CHCHO$, 5392-40-5; picolinic acid *N*-oxide, 824-40-8; cyclopentanol, 96-41-3; cyclopentanone, 120-92-3; cyclohexanol, 108-93-0; cyclohexanone, 108-94-1; 5-methyl-2-(1-methylethyl)cyclohexanol, 1490-04-6; 5-methyl-2-(1-methylethyl)cyclohexanone, 10458-14-7; cyclohexen-3-ol, 822-67-3; cyclohexen-3-one, 930-68-7; 3-methyl-3-(4-methyl-3-pentyl)oxiranemethanol, 50727-94-1; 3-hydroxypregn-5-en-20-one, 38372-24-6; pregn-5-ene-3,20-dione, 1236-09-5.

Supplementary Material Available: Tables of atomic coordinates, bond distances, and bond angles and the full structure of compound 1 (R = Me) (4 pages). Ordering information is given on any current masthead page.

A Simple Transformation of Carminic Acid into Kermesic Acid

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Carminic acid (**1a**) is the principal component of the food dye cochineal, obtained from the insect *Dactylopius coccus*, possessing a significant inhibitory activity against ascites tumors in Jensen rats[1,2] due to its structural similarity to the antitumor agent shikonin and the anthracyclines[3] with the merit that it is not toxic and does not bind to DNA.[4] In a previous paper we reported chemical and spectroscopic evidence that the C-glycosyl bond of carminic acid possesses the β-configuration.[5,6] This result was more recently confirmed by a complete ^1H and ^{13}C NMR study.[7]

The aglycon moiety of carminic acid is represented by kermesic acid (**1b**), the coloring matter of kermes,[8] the most ancient dyestuff on record. Kermesic acid is at present not commercially available and has been syn-

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