Acknowledgment. We acknowledge helpful discussions with Drs. Yasumasa Tsukitani and Hiroyuki Kikuchi of Fujisawa Pharmaceutical Co., Ltd. Tokyo, Japan. We are greatly indebted to Drs. Takashi Iwashita and Hideo Naoki of Suntory Institute for Bioorganic Research (SUNBOR) for the 360-MHz NMR measurements. Furthermore, the ^{13}C NMR spectra were measured by Drs. Masaaki Toda (Ono Pharmaceutical Co., Ltd., Japan) and Katsuhiko Kushida (Varian Instruments Ltd., Japan). We express our thanks to them. This research was supported by the Foundation for the Promotion of Research on Medical Resources.

Supplementary Material Available: 1D and 2D spectra of **1–3**, the ^{13}C NMR spectrum (75.4 MHz) of **1**, table of ^{1}H and ^{13}C NMR data of **1**, and table of atomic coordinates, temperature factors, and bond lengths and angles of **2** (23 pages). Ordering information is given on any current masthead page.

Simple ^{31}P NMR Method for the Determination of Enantiomeric Purity of Alcohols Not Requiring Chiral Auxiliary Compounds

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Essential to stereochemical analyses of asymmetric processes and chemical conversions of chiral compounds are facile methods for the determination of enantiomeric purities. NMR and chromatographic methods based on the formation of diastereomeric complexes or derivatives are widely used.[1] All these methods rely on chiral auxiliary compounds. Horeau[2] was the first to recognize the potential of using the intrinsic differences in chirality of an enantiomerically pure and (partly) racemic substance for enantiomeric excess (ee) determinations. The method depends on coupling of enantiomers (*R*,*S*) via achiral agent A resulting in diastereoisomers *R*-A-*R* (*S*-A-*S*) (a *d*,*l*-pair) and *R*-A-*S* (*S*-A-*R*) (a meso compound) (eq 1).

$$\underset{\text{R,S}}{\text{R-A}} + \text{A} \longrightarrow \underset{\text{(S-A-S)}}{\text{R-A-R}} + \underset{\text{(S-A-R)}}{\text{R-A-S}} \qquad (1)$$

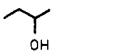
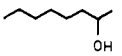
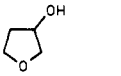
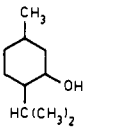
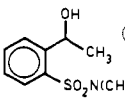
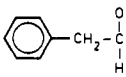
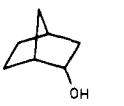
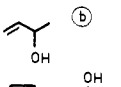
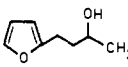
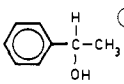
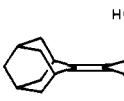
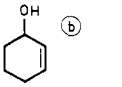
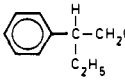
A few applications of this coupling reaction for ee determinations have been demonstrated.[2] The differences in properties between the diastereoisomers (eq 1) can be used in a new and practical method for ee determination if coupling via agent A proceeds in quantitative yield; A contains an unique atom that makes analysis of each diastereoisomer via a *single* NMR absorption possible; no deviation from statistical ratio's of coupled products via "chiral self-recognition"[3] occurs, and chemical shift differences are large enough for accurate integration. On the basis of these considerations and with the knowledge that ^{31}P NMR shows great advantages in ee determinations using chiral derivatizing agents,[4] we have developed a method for ee determination that requires no chiral auxiliary substance. Using PCl_3 as a dimerization agent, alcohols are converted into phosphonates in a fast and quantitative reaction (Scheme I).[5,6]

Application of this reaction for the determination of ee's of alcohols is illustrated for 2-octanol (Scheme I). Racemic **1** should

Table I. Determination of ee's of Optically Active Alcohols[8,9]

alcohol	% ee by weight	% ee by rotation	% ee by ^{31}P NMR
d-2-octanol		100	100
d-2-octanol	49.5	51	51
d-2-octanol	76	76	78
l-menthol		100	100
l-*N*,*N*-dimethylmandelicamide		48	48
l-ethyl lactate	39		41

Table II. ^{31}P NMR Data of Phosphonates from Racemic Alcohols and PCl_3[a,8]

alcohol	δ(meso) Hz	δ(meso) Hz	δ(d,l-pair) Hz	ratio meso : d,l
	454	387	425	49.5 : 50.5
	432	365	401	49.2 : 50.8
	481	447	464	49.1 : 50.9
	459	309	413	49.4 : 50.6
	368	329	346	50.0 : 50.0
	471	362	449	50.0 : 50.0
	525	515	518	(a)
	393	349	369	50.6 : 49.4
	449	395	433	50.4 : 49.6
	416	344	370	50.0 : 50.0
	337	291	330	50.0 : 50.0
	450	416	432	50.0 : 50.0
	652	590	623	50.0 : 50.0

[a] (a) approximately 50:50 (no base-line separation); (b) 3 equiv of pyridine added prior to addition of PCl_3.

(1) Chiral shift reagents: Sullivan, G. R. In "Topics in Stereochemistry"; Eliel, E. L., Allinger, N. L., Eds.; Wiley-Interscience: New York, 1978, p 287. Chiral solvents: Pirkle, W. H.; Hoover, D. J. "Topics in Stereochemistry"; Eliel, E. L., Allinger, N. L., Eds.; Wiley-Interscience: New York, 1982; p 263. Diastereomeric derivatives: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(2) Vigneron, J. P.; Dhaenens, M.; Horeau, A. *Tetrahedron* **1973**, *29*, 1055.

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(6) To prevent byproduct formation, decomposition, and/or racemization equimolar quantities of pyridine were added in the case of acid-sensitive alcohols, e.g., allylic and benzylic alcohols. Excess pyridine or pyridine salts do not influence the ^{31}P NMR determination.

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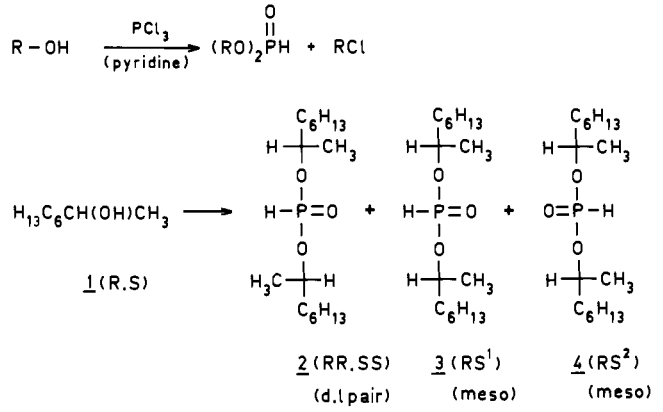
Scheme I



yield a mixture of phosphonates **2** (*RR*,*SS*), **3** (*RS*[1] meso), and **4** (*RS*[2] meso) in a 2:1:1 ratio and ^{31}P NMR of the reaction mixture shows three well-separated singlets in that ratio.[6,7] Enantiomerically pure (*S*)-(−)-**1** yields exclusively (*SS*)-**2**, as is demonstrated by the absence of the two absorptions due to meso isomers **3** and **4**.

The method described in this paper is especially advantageous for chiral compounds with complicated ^{1}H or ^{13}C NMR spectra, e.g., the phosphonate of enantiomerically pure 3-hydroxyandrost-5-en-17-one shows a single ^{31}P NMR absorption at δ 4.30. Byproducts (if present) either gave no ^{31}P NMR absorption or singlets well separated from the phosphonate absorptions.

Table I summarizes data on optically pure or partially enriched alcohols and compares ee's determined by weight and by rotation with results obtained by the ^{31}P NMR method.[8,9] These results show that during derivatization no racemization of the alcohols occurs and it is also shown that the "loss" of part of the alcohol as the halide does not influence the accuracy of the ee determination. The results of this technique with several racemic alchols are summarized in Table II.[8]

The present method tolerates large variations in alcohol structure, e.g., primary and secondary benzylic and allylic alcohols and α-hydroxy amides and esters. Chiral recognition during the coupling reaction is negligible as is illustrated by the small deviations from 50/50 in the *RR* (*SS*) to meso ratio's in Table II and the accuracy of the calculated and measured ee's (Table I). Chemical shift differences compare favorably with those obtained using chiral derivatizing agents, e.g., for 2-butanol $\Delta\delta$ 0.0056 (C_6D_6)[4c] and 0.20 ($CDCl_3$)[4b] were reported whereas $\Delta\delta$ 0.35 and 0.46 ($CDCl_3$) were obtained by the present method. In contrast to prior results with chiral reagents[4b] our method did not give satisfactory results for the enantiomeric excess determination of amines so far. Application of this technique for the determination of enantiomeric purities at submilligram scale is currently under investigation since ^{31}P NMR lends itself admirably to this purpose.

A typical procedure to prepare an NMR sample to determine enantiomeric composition follows: The appropriate alcohol (0.75 mmol) was dissolved in 2 mL of $CDCl_3$ and pyridine (0.75 mmol) was added, if necessary.[6] To the stirred solution was added PCl_3 (0.25 mmol) dissolved in 2 mL of $CDCl_3$. The mixture was stirred at room temperature for 10 min and subsequently transferred, without the necessity of any workup or further purification, into a 10-mm NMR tube and the ^{31}P NMR spectrum recorded.

(7) The formation of two meso phosphonates **3** and **4** is due to the "pseudoasymmetric" character of the phosphorus center: it is a stereogenic-achirotopic center; for a recent discussion, see: Mislow, K.; Siegel, J. *J. Am. Chem. Soc.* **1984**, *106*, 3319.

(8) All the spectra were obtained in $CDCl_3$ at 80.988 MHz on a Nicolet 200NT spectrometer using 10-mm tubes; chemical shift values are given in hertz with 85% H_3PO_3 (δ 0.0) as an external standard.

(9) The enantiomeric purity (p) was calculated from the integrated peak area's Q and Q' of the *RR* (*SS*) isomer and the meso isomers, respectively (with RR (SS)/meso ratio $K = Q/Q'$) using Horeau's formula $p^2 = (K - 1)/(K + 1)$ (see also ref 2).

Excited-State Nitrosyl Bending and Metal Oxidation in $K_2[Fe(CN)_5NO]$ Determined by Excited-State Raman Spectroscopy

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The geometries and the formal oxidation states of metal nitrosyl complexes are proposed to undergo large changes in MLCT excited states.[1-3] A linear $M^nN{\equiv}O^+$ unit can bend to form bent $M^{n+2}N{=}O^-$ when the metal to nitrosyl charge-transfer state is populated. The driving force for the geometry change is the population of the totally π antibonding orbital of the MNO group in the linear geometry and the stabilization upon bending of a σ nonbonded orbital on the nitrogen.[3] A *formal* two-electron oxidation of the metal accompanies the bending. (This valence bond description represents a formal upper limit for the highly covalent system.)[3] The excited-state geometry and oxidation-state changes are indirectly supported by the photochemical reactivity of metal nitrosyls.[1,2,4] Ground-state changes caused by putting in or taking out electrons from the π antibonding orbital have been well documented, e.g., the change from linear to bent MNO when a pair of electrons is added to $Co(das)_2NO^{2+}$ by addition of a ligand and the bent to linear change with a formal one-electron reduction of the metal when $Fe(das)_2NOX^+$ is oxidized by one electron.[3,5] We report here direct vibrational spectroscopic evidence for both the excited-state linear to bent geometry change and for the oxidation state increase in $Fe(CN)_5NO^{2-}$ by using excited-state resonance Raman spectroscopy.

Raman spectra of metal complexes in excited electronic states have been obtained by using either pulsed or CW lasers to produce a near-saturation yield of excited states and to simultaneously provide the probe beam for Raman scattering from the excited molecule.[6-11] The pioneering studies of Woodruff et al. showed that the method could probe electronic changes in the MLCT excited state of $Ru(bp)_3^{2+}$.[6] In the experiments reported here, excited-state Raman spectra were obtained by exciting and probing with 406-nm, 9-ns pulses at a 40-Hz repetition rate from a excimer pumped dye laser (Lambda Physik EMG 102E and FL2001). The absorption band at 400 nm has been assigned by Gray et al. to the 6e ($d_{xz,yz}$) to 7e (Π^*_{NO}) MLCT transition.[12] The Raman scattered light was passed through a Spex double monochrometer, detected by using a C31034 photomultiplier and recorded with an electrometer and strip chart recorder. An aqueous solution (~1 M) of $K_2[Fe(CN)_5NO]$ was pumped through a needle to produce a roughly 200-μm-diameter jet stream at the laser focus. Each laser pulse irradiated a fresh 10^{-11}-L volume of solution.

The Raman spectra taken at three different pulse energies are shown in Figure 1. The lowest trace (Figure 1) was taken at the lowest pulse energy and is the spectrum of the ground-state molecule. The upper two traces (Figure 1b,c) show both the ground- and excited-state Raman peaks. Four new peaks are observed which grow in intensity as the laser pulse energy increases. The intensities of all of the new peaks show a nonlinear dependence on the laser pulse energy. Plots of the log of the

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