bility cell gave a calibration equation (obtained as above) of $\kappa = 0.00237n + 0.4672$ with a standard deviation in κ of 0.004. This method clearly bears a larger experimental uncertainty than the first nmr method, but is particularly useful for measurements on samples containing highly volatile or reactive components (since the tubes are readily sealed) or for determinations made on powdered solids.

The density of each sample was determined in a water bath at the same temperature (within 0.1°) as the probe temperature at the time of the volume magnetic susceptibility measurement. Lipkin bicapillary pycnometers of 0.25, 0.5, and 1 ml sizes (Ace Glass Co.) were calibrated with triply distilled water and used in accordance with the procedures exhaustively discussed by other workers.[74] Density values were thus generally obtained with a precision of 0.0005 g/cc.

Solutions. Solutions for magnetic susceptibility determinations were prepared by weighing appropriate quantities of solute and solvent to the nearest 0.1 mg in 5-ml stoppered vessels. Concentrations were expressed as weight fractions. Once prepared, solutions were treated in the same manner as other liquid samples; all possible care was taken to maintain constant concentrations. The Wiedemann additivity law[13,75] was applied to determine the susceptibility of a solute from that of the solution. For the compounds of this study, the only solvent found to give deviations from Wiedemann's law was dimethyl sulfoxide.[18]

Formulas and Data. The magnetic susceptibility per gram, χ, of a pure compound is expressed by $\chi = \kappa/\rho$ where κ and ρ represent, respectively, the volume magnetic susceptibility (units of -10^{-6}) and the density (units of cm^3/g). For a solution measurement, χ_a, the per gram susceptibility of the solute, is given[18] by the equation $\chi = (\kappa/\rho) - \chi_s(1 - f_a)/f_a$ where κ and ρ are as defined above and obtained for the solution, f_a is the weight fraction of the solute, and χ_s is the per gram susceptibility of the solvent. The molar susceptibility, χ_M, is defined as $\chi_M = M\chi$ where M is the molecular weight of the substance in grams; the units of χ_M are -10^{-6} cm^3/mol. Table IV presents the data used in calculating the molar susceptibilities of several neat liquids, and Table V contains the data for solutions. In Table V two values are given for the mass susceptibility of benzene; 0.708 is the susceptibility of benzene saturated with nitrogen, and 0.702 is the value for benzene saturated with air.[13]

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The Absolute Configuration of Pinacolyl Alcohol[1]

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Abstract: The absolute configuration of (+)-pinacolyl alcohol (**1**), although widely assumed to be (*S*), has never been firmly established and there is reason to question the usual assignment. Direct chemical correlation with (+)-(*S*)-lactic acid firmly establishes that the absolute configuration usually assumed is indeed correct. The key step in the chemical correlation (Chart I) was the construction of the *t*-butyl group by hydrogenolysis of a 1-methyl-1-cyclopropane derivative (**4**).

Optically active pinacolyl alcohol (3,3-dimethyl-2-butanol, **1**) has been frequently employed in asymmetric syntheses,[2] yet its absolute configuration, though widely assumed to be (+)-(*S*) on the basis of indirect physical[3] and chemical[4] evidence, has never been rigorously established. However, the physical evidence has been termed "not entirely convincing."[5] There is at least one case on record,[6] as far as chemical evidence[4] is concerned, in which an apparent inconsistency involving **1** has been encountered: whereas methyl ketones (CH_3COR, R = C_2H_5, *i*-C_3H_7, C_6H_5) yield alcohols of

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[2] (a) H. S. Mosher and E. La Combe, *J. Am. Chem. Soc.*, **72**, 3994 (1950); (b) L. M. Jackman, J. A. Mills, and J. S. Shannon, *ibid.*, **72**, 4814 (1950); (c) H. S. Mosher and E. La Combe, *ibid.*, **72**, 4991 (1950); (d) V. Prelog, E. Philbin, E. Watanabe, and M. Wilhelm, *Helv. Chim. Acta*, **39**, 1086 (1956); (e) H. S. Mosher and P. K. Loeffler, *J. Am. Chem. Soc.*, **78**, 4959 (1956); (f) V. Prelog and H. Scherrer, *Helv. Chim. Acta*, **42**, 2227 (1957); (g) P. Newman, P. Rutkin, and K. Mislow, *J. Am. Chem. Soc.*, **80**, 465 (1958); (h) W. M. Foley, F. J. Welch, E. M. La Combe, and H. S. Mosher, *ibid.*, **81**, 2779 (1959); (i) K. Mislow, R. E. O'Brien, and H. Schaefer, *ibid.*, **82**, 5512 (1960); (j) O. Červinka, *Collection Czech. Chem. Commun.*, **30**, 1684 (1965); (k) M. M. Green, M. Axelrod, and K. Mislow, *J. Am. Chem. Soc.*, **88**, 861 (1966); (l) J. Sauer and J. Kredel, *Tetrahedron Letters*, 6359 (1966); (m) O. Červinka, O. Bělovský, A. Fábryová, V. Dudek, and K. Grohman, *Collection Czech. Chem. Commun.*, **32**, 2618 (1967).

[3] Through application of the Freudenberg Displacement Rule (P. G. Stevens, *J. Am. Chem. Soc.*, **55**, 4237 (1933)).

[4] The chemical evidence has consisted of configurational correlations which, implicitly or explicitly, have involved comparisons of topographies of diastereomeric transition states in asymmetric syntheses.[2]

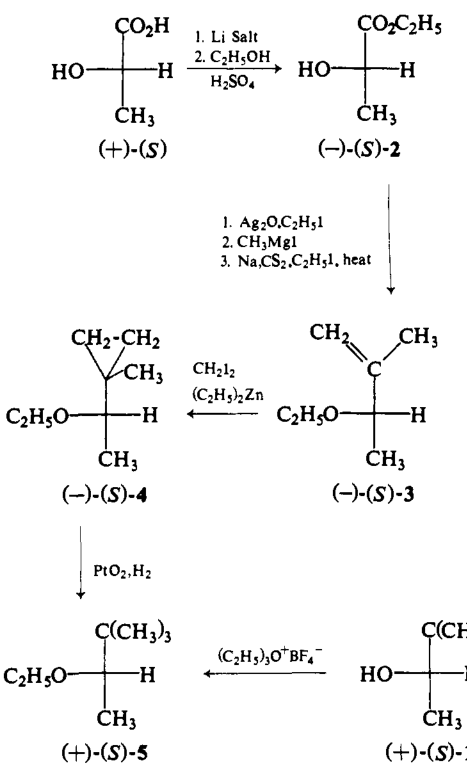
[5] J. A. Mills and W. Klyne, *Progr. Stereochem.*, 1, 206 (1954).

[6] H. C. Brown and D. B. Bigley, *J. Am. Chem. Soc.*, **83**, 3166 (1961).

the *R* configuration upon reaction with (−)-tetraisopinocampheyldiborane, methyl *t*-butyl ketone yields (*S*)-**1** upon reduction with the same reagent.[7,8]

In view of the importance of this problem, we felt it desirable to determine the absolute configuration of **1** unequivocally. This has been accomplished by the direct chemical correlation of (+)-**1** with (+)-(*S*)-lactic acid,[9] as shown in Chart I. The lithium salt of (+)-(*S*)-lactic acid was converted to 94% optically pure[12] (−)-(*S*)-ethyl lactate (**2**), which was converted to (−)-(*S*)-3-ethoxy-2-methyl-1-butene (**3**) by a known reaction sequence,[14] α^{23}D −35.9° (*l* 1, neat), presumably 94% optically pure since the reaction sequence **2** → **3** does not affect the asymmetric center.[15] A sample of (−)-(*S*)-**3** with α^{23}D −12.3° (*l* 1, neat), 32% ((12.3)(94)/35.9) optically pure, was converted to (−)-(*S*)-1-methyl-1-(1-ethoxyethyl)cyclopropane (**4**) by a modified Simmons–Smith reaction;[16] the product, $[\alpha]^{27}$D −2.71° (*c* 2.59, CCl_4), is assumed to be 32% optically pure. The key step in the reaction sequence, selective hydrogenolysis of the cyclopropane ring of **4**,[17] was effected with platinum oxide and hydrogen at 50° to yield (+)-(*S*)-pinacolyl ethyl ether (**5**) as the major reaction product, $[\alpha]^{27}$D +6.1° (*c* 1.27, CCl_4), assumed to be 32% optically pure.

Chart I[a,b]



[a] Configurations are given as Fischer projections. [b] The sign of rotation refers to 589 nm (sodium D line).

Pinacolyl alcohol ($[\alpha]^{28}$D +7.8° (neat), 99% optically pure[18]) was treated with triethyloxonium tetrafluoroborate[19] to yield (+)-(*S*)-**5** with $[\alpha]^{21}$D +21.9° (*c* 3.7, CCl_4). Assuming an optical purity of 99%, the maximum rotation of (+)-**5** is thus $[\alpha]^{21}$D +22.4° (*c* 3.7, CCl_4); corrected to optical purity, (+)-**5** produced from (+)-lactic acid has $[\alpha]^{27}$D +19.1° (*c* 1.2, CCl_4). Consequently, the over-all extent of racemization in the sequence (+)-(*S*)-**2** → (+)-(*S*)-**5** is insignificant.

The correlation of (+)-pinacolyl alcohol with (+)-(*S*)-lactic acid unequivocally establishes the configuration of (+)-**1** as *S*.

The determination of the absolute configuration of pinacolyl alcohol by direct chemical correlation has not been accomplished before, presumably because of the lack of a suitable method of constructing the *t*-butyl group. Recently, it has been recognized that a general method—the hydrogenolysis of 1-methyl-1-cyclopropyl derivatives—is available for such purposes.[17] The success of the present experiments illustrates again the synthetic utility of such hydrogenolyses.

Experimental Section[20]

(−)-(*S*)-Ethyl lactate (2) was prepared by a modification of a previously reported procedure.[21] A slurry of 48 g (0.5 mol) of the lithium salt of (+)-(*S*)-lactic acid[9] (Miles Laboratories, Elkhart, Ind.) in 58 ml of absolute ethanol and 52 ml of benzene was cooled as 14 ml of concentrated sulfuric acid was added. The resulting slurry was heated and 90 ml of distillate was removed *via* a Dean–Stark trap. The pot temperature reached ~90° during the final stages of the distillation. The reaction mixture was cooled, poured into 500 ml of 10% aqueous sodium bicarbonate, and the resulting mixture was extracted with ether. The ether extract was dried over anhydrous magnesium sulfate and filtered, and the solvent was removed under reduced pressure. The residue was distilled at 82–84° (72 mm) to give 22 g of (−)-(**2**): $[\alpha]^{23}$D −10.8° (neat)

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(7) Because of this discrepancy, Brown and Bigley[6] called attention to the earlier observation of Mills and Klyne,[5] referred to above, questioning the security of the configurational assignment.

(8) Morrison has suggested that a change in mechanism in the asymmetric hydroboration may account for this discrepancy (J. D. Morrison in "Survey of Progress in Chemistry," Vol. 3, A. F. Scott, Ed., Academic Press, New York, N. Y., 1966, p 171). Most recently, however, K. R. Varma and E. Caspi, *Tetrahedron*, **24**, 6365 (1968), have obtained results at variance with those reported by Brown and Bigley:[6] reduction of ethyl and isopropyl methyl ketones with (+)-tetraisopinocampheyldiborane yields *R* alcohols; reduction of isopropyl and *t*-butyl methyl ketones with (−)-tetraisopinocampheyldiborane yields *S* alcohols. This observation casts doubt on the experimental basis for the discrepancy reported by Brown and Bigley.

(9) (+)-Lactic acid has been correlated with (−)-glyceraldehyde and (−)-tartaric acid,[10] both of which are known to have the *S* configuration on the basis of anomalous X-ray diffraction.[11]

(10) K. Freudenberg, *Chem. Ber.*, **47**, 2027 (1914).

(11) J. M. Bijvoet, A. F. Peerdeman, and A. J. von Bommel, *Nature*, **168**, 271 (1951).

(12) The maximum rotation reported[13] for **2** is $[\alpha]^{20}$D 11.5° (neat); material employed in this study had $[\alpha]^{23}$D −10.8° (neat).

(13) K. Mislow and K. Bleicher, *J. Am. Chem. Soc.*, **76**, 2825 (1954).

(14) P. G. Stevens, *ibid.*, **54**, 3732 (1932).

(15) Based on the data of Stevens,[14] the absolute $[\alpha]$D of **3** is calculated to be 36.5–40.9° (neat).

(16) J. Furukawa, N. Kawabata, and J. Nishimura, *Tetrahedron Letters*, 3353 (1966); 3495 (1968); *Tetrahedron*, **24**, 53 (1968).

(17) The use of this method for the synthesis of *t*-carbon atoms has been emphasized recently by C. W. Woodworth, V. Buss, and P. von R. Schleyer, *Chem. Commun.*, 569 (1968); Z. Majerski and P. von R. Schleyer, *Tetrahedron Letters*, 6195 (1968), and references cited therein.

(18) Based on the highest reported[28] rotation, $[\alpha]^{29}$D +7.88° (neat).

(19) Modification of a procedure for the preparation of hindered ethers, see H. Meerwein, G. Hinz, P. Hofmann, E. Kroning, and E. Pfeil, *J. Prakt. Chem.*, 147, 257 (1937). Attempted preparations of the ether with silver oxide and ethyl iodide were unsuccessful.

(20) Nmr spectra were recorded on a Varian A-60A spectrometer in ~10% solution, unless otherwise indicated. Rotations were measured on a Schmidt and Haensch visual polarimeter or on a Cary 60 recording spectropolarimeter. Mass spectra were measured on an AEI MS-9 high-resolution mass spectrometer. We would like to thank the National Science Foundation for providing the funds for the purchase of the mass spectrometer under Grant No. GP-5200.

(21) W. Gerrard, J. Kenyon, and H. Phillips, *J. Chem. Soc.*, 153 (1937).

(lit.[21] bp 54–56° (11 mm), α^{18}D −11.15° (*l* 1, neat); lit.[22] $d^{18.9}{}_4$ 1.0345); nmr in $CDCl_3$, $C\mathit{H}_3CH_2$, t, τ 8.71, *J* = 7.2 Hz, 3 H; $C\mathit{H}_3CH$, d, τ 8.58, *J* = 7.0 Hz, 3 H; $CH_3C\mathit{H}_2$, q, τ 5.76, *J* = 7.2 Hz, 2 H; $CH_3C\mathit{H}$, q, τ 5.71, *J* = 7.0 Hz, 1 H; $O\mathit{H}$, s, τ 6.76, 1 H.

(−)-(*S*)-Ethyl-O-ethyl lactate (6), prepared from **2** by a previously reported procedure,[14] had bp 81–83° (70 mm), $[\alpha]^{24}$D −65.9° (neat) (lit.[23] $[\alpha]^{20}$D 79.69° (neat), $d_4{}^{20}$ 0.9355; lit.[14] $[\alpha]^{24}$D +3.48° (neat) from ethyl lactate with $[\alpha]^{27}$D +0.52° (neat)).

(+)-(*S*)-2-Methyl-3-ethoxy-2-butanol (7), prepared from **6** (above) by a previously reported procedure,[14] had bp 140–141°, α^{23}D +37.6° (*l* 1, neat) (lit.[14] bp 140.0–140.5°, $[\alpha]^{29.5}$D −1.84° (neat) from **6** with $[\alpha]^{24}$D +3.48° (neat)).

(−)-(*S*)-2-Methyl-3-ethoxy-1-butene (3), prepared from **7** (above) by a previously reported procedure,[14] had bp 95–99°, α^{23}D −35.9° (*l* 1, neat) (lit.[14] bp 99°, $[\alpha]^{27.5}$D +1.65° and $[\alpha]^{25.5}$D +1.85° (neat) from **7** with $[\alpha]^{29}$D −1.84° (neat)); nmr in $CDCl_3$, $C\mathit{H}_3CH_2$, t, τ 8.83, *J* = 7.0 Hz; CH_3CH, d, τ 8.75, *J* = 7.0 Hz; CH_3CC, m, τ 8.32; $CH_3C\mathit{H}$, m, τ 6.62; $CH_3C\mathit{H}_2$, q, τ 6.2, *J* = 7.0 Hz; $C\mathit{H}_2{=}C$, m, τ 5.1.

(−)-(*S*)-1-Methyl-1-(1-ethoxyethyl)cyclopropane (4). Over a period of ∼1 hr 21 g (78 mmol) of methylene iodide was added under a static nitrogen atmosphere to a solution of 3.8 g (33 mmol) of **3** (α^{23}D −12.3° (*l* 1, neat)) and 6.9 g (55 mmol) of diethylzinc in 40 ml of anhydrous ether. After stirring for 30 hr under reflux the reaction mixture was cooled to room temperature and 40 ml of ether was added, followed by ∼50 ml of 1% aqueous hydrochloric acid. The ethereal layer was washed with water, three 50-ml portions of 10% aqueous potassium bicarbonate, and two 50-ml portions of water. The ethereal layer was dried over anhydrous sodium sulfate and filtered, and the solvent was removed by distillation through a Vigreux column. The residue was fractionated through a short column and the fraction with bp 102–115° (4.5 g containing 80–90% **4**; partial decomposition occurs at the boiling point) was purified by preparative vapor phase chromatography (50-ft FFAP column at 90°) to give **4** which was more than 97% chemically pure by vpc analysis; $[\alpha]^{27}$D −2.71° (*c* 2.59, CCl_4); nmr (neat, external TMS), cyclopropyl, m, τ 9.93, 4 H; $C\mathit{H}_3C$, s, τ 9.21, 3 H; $C\mathit{H}_3CH_2$, t, τ 9.08, *J* = 7.2 Hz, 3 H; $C\mathit{H}_3CH$, d, τ 9.07, *J* = 6.0 Hz, 3 H; $CH_3C\mathit{H}$, q, τ 7.46, *J* = 6.0 Hz, 1 H; $CH_3C\mathit{H}_2$, m, τ 6.71, 2 H; mol wt (mass spectral): calcd for $^{12}C_8{}^1H_{16}{}^{16}O$, m/e^+ 128.120109; found, 128.120090.

(+)-(*S*)-Pinacolyl Ethyl Ether (5). A. By Hydrogenolysis of (−)-4. A solution of 1.5 g (11.7 mmol) of **4**, $[\alpha]^{27}$D −2.71° (*c* 2.59, CCl_4), in 24 ml of glacial acetic acid was stirred at 50° in the presence of 356 mg of platinum oxide under hydrogen at 3.4 atm pressure for 48 hr. The reaction mixture was cooled to room temperature and ∼50 ml of *n*-pentane was added. The solution was filtered and washed with 50 ml of water, three 50-ml portions of 10% aqueous potassium bicarbonate, and an additional 50 ml of water. The pentane layer was dried over anhydrous sodium sulfate and filtered, and most of the solvent was removed by distillation through a short Vigreux column. The residue was purified by preparative vapor phase chromatography (50-ft FFAP column at 75°) to give **5** which was more than 98% chemically pure by vpc analysis; $[\alpha]^{27}$D +6.1° (*c* 1.27, CCl_4); nmr in CCl_4, $(C\mathit{H}_3)_3C$, s, τ 9.13, 9 H; $C\mathit{H}_3CH$, d, τ 8.96, *J* = 7.0 Hz, 3 H; $C\mathit{H}_3CH_2$, t, τ 8.83, *J* = 7.5 Hz, 3 H; $CH_3C\mathit{H}$, q, τ 7.02, *J* = 7.0 Hz, 1 H; $CH_3C\mathit{H}_2$, m, τ 6.52, 2 H.

B. From (+)-Pinacolyl Alcohol. A solution of 2.0 g (20 mmol) of pinacolyl alcohol ($[\alpha]^{28}$D +7.8° (neat)) and 4.75 g (25 mmol) of triethyloxonium tetrafluoroborate in 10 ml of methylene chloride was allowed to stand at 0° for 3 days. The reaction mixture was poured into water and the methylene chloride layer was separated, dried over anhydrous magnesium sulfate, and distilled. The fraction with bp 110–111° was subjected to preparative vapor phase chromatography (20-ft FFAP column at 150°) to give **5** which was more than 99% chemically pure by vpc analysis; $[\alpha]^{21}$D +21.9° (*c* 3.7, CCl_4). The nmr spectrum of this material was identical with that reported above; mol wt (mass spectral): calcd for $^{12}C_8{}^1H_{18}{}^{16}O$, m/e^+ 130.135758; found, 130.135135.

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[22] C. E. Wood, J. E. Such, and F. Scarf, *J. Chem. Soc.*, **123**, 600 (1923).

[23] T. Purdie and J. C. Irvine, *ibid.*, **75**, 483 (1899).