be isolated by vacuum distillation. Analysis of the crude reaction mixture by gas chromatography and NMR spectroscopy showed 95% 1,1-dichloroacetone and 5% 1,1,1-trichloroacetone.

Acknowledgment. We thank P. Donahue for recording ^{13}C NMR spectra and R. May and H. Grade for the many gas chromatographic mass spectral analyses. Helpful discussions with G. Davis, G. Faler, and J. Verbicky are also greatly appreciated.

Registry No. 1,1-Dichloro-2,2-dimethoxypropane, 32730-70-4; 1,1-dichloroacetone, 513-88-2; 1,3-dichloro-2,2-dimethoxypropane, 6626-57-9; 1,3-dichloro-2-propanone, 534-07-6; 5,5-dichloro-4-heptanone, 77416-00-3; 3,5-dichloro-4-heptanone, 77416-01-4; 3,5-dichloro-4,4-dimethoxyheptane, 77416-02-5; 1-chloro-2-butanone, 616-27-3; 1-chloro-2,2-dimethoxybutane, 77416-03-6; 3-chloro-2-butanone, 4091-39-8; 2-chloro-3,3-dimethoxybutane, 77416-04-7; 1,3-dichloro-2-butanone, 16714-77-5; 1,3-dichloro-2,2-dimethoxybutane, 77416-05-8; 3-chloro-3-methyl-2-butanone, 5950-19-6; 1-chloro-3-methyl-2-butanone, 17687-63-7; 1,1-dichloro-3-methyl-2-butanone, 39140-45-9; 1,1-dichloro-2,2-dimethoxy-3-methylbutane, 77416-06-9; 1,3-dichloro-3-methyl-2-butanone, 57539-84-1; 1,3-dichloro-2,2-dimethoxy-3-methylbutane, 77416-07-0; bromoacetone, 598-31-2; 1,1-dibromoacetone, 867-54-9; 1,3-dibromoacetone, 816-39-7; 1,1-dibromoacetone dimethyl ketal, 77416-08-1; 1,3-dibromoacetone dimethyl ketal, 22094-18-4; 1,1,3-tribromoacetone dimethyl ketal, 77416-09-2; 1,1,1-trichloroacetone, 918-00-3; 2,2-dimethoxypropane, 77-76-9; 1,1-dichloro-2,2-dimethoxypropane, 2718-42-5; 2,2-bis(chloromethyl)-1,3-dioxacycloheptane, 77416-10-5; *cis*-2-(chloromethyl)-2,5-dimethyl-1,3-dioxacyclohexane, 77416-11-6; *trans*-2-(chloromethyl)-2,5-dimethyl-1,3-dioxacyclohexane, 69245-13-2; 2-methyl-2-chloromethyl-1,3-dioxacyclopentane, 4469-49-2; 2,2-bis(chloromethyl)-1,3-dioxacyclopentane, 26271-50-1; acetone, 67-64-1; 2-butanone, 78-93-3; 3-methyl-2-butanone, 563-80-4; 4-heptanone, 123-19-3.

Supplementary Material Available: Mass spectral data of α-chloro ketones and ketals (4 pages). Ordering information is given on any current masthead page.

Enantiomeric Interactions and Reaction Rates: Ketalization of (*S*)- and (*RS*)-1,2-Propanediols

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Aliphatic ketones, e.g., butanone, are converted nearly quantitatively to the corresponding dioxolanes (ketals) in neat (*S*)- or (*RS*)-1,2-propanediol containing dichloroacetic acid. The reactions follow the pseudo-first-order law at a given acid concentration, are inhibited by water, and proceed approximately twofold faster in (*RS*)-diol-$O,O\text{-}d_2$ than in undeuterated diol. No difference in rates greater than 1% could be detected between (*S*)- and (*RS*)-diols at identical temperatures, acid concentrations, and water concentrations. Thus, for a chiral diol molecule and the activated complex, free-energy differences are virtually the same in (*S*)- and (*RS*)-diols as solvents. Differences in interactions among identical and enantiomeric molecules, if any, are evidently matched by differences in the activated complexes.

Various reports over the years have called attention to differences in properties between chiral compounds and the corresponding racemic compounds,[2] e.g., tartaric acid[3] and hydrobenzoin.[4] The dramatic differences in melting points and solubilities probably originate largely from strong interactions in the solid state.

More subtle, however, is the question whether pure enantiomers behave differently from their racemates *in solution.* The environment of a given chiral molecule, denoted *R*, in a sample of neat liquid *R*, will be diastereomeric with and thus different from that in neat liquid racemic mixture, *RS*. Since all real substances behave nonideally to some extent, the possibility of at least slight differences in behavior at high concentrations must be taken seriously.

Horeau has critically reviewed the available evidence concerning physical properties[5] and concluded that diastereomeric interactions between enantiomers in solution can give rise to measurable free-energy differences.

Recent reports from these laboratories[6] have discussed what are apparently the first observations of differences in *chemical reactivity.* Since the sum total of chemical entities in eq 1 and 2 are neither identical nor enantiomeric, they must be diastereomeric.

$$R \text{ isomer} \xrightarrow{\text{reagent}} \text{products} \tag{1}$$

$$RS \text{ mixture} \xrightarrow{\text{reagent}} \text{products} \tag{2}$$

Free-energy differences between the ground states and/or between the transition states could in principle lead to differences in activation energies. Evidence for such differences was manifest in differences in stereoselectivities of two coupling reactions and a ketone reduction.[6a] These differences were interpreted in terms of two effects: (1) enantiomeric recognition, the preferential reaction of a molecule with either an identical molecule or its antipode, as the case might be; (2) antipodal interaction, essentially differential solvation of a reacting molecule, which is the effect of interest in the present investigation.

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(1) To whom correspondence should be addressed at Filson Chemical Laboratories. This paper is based on work performed during this author's sabbatical leave at Groningen, 1977–1978.

(2) (a) M. L. Pasteur, *Ann. Chim. Phys.*, **28**, 56 (1850); (b) E. L. Eliel, "Stereochemistry of Carbon Compounds", McGraw-Hill, New York, 1962, e.g., pp 39–47; (c) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions", Prentice-Hall, New York, 1971.

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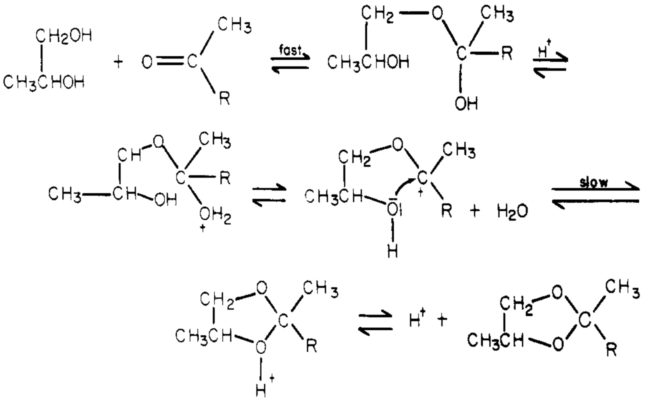
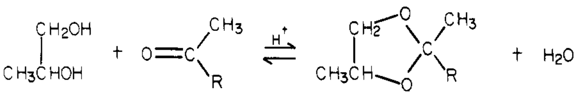
Chart I. Mechanism of Ketalization of Diols



Since all three reactions mentioned above involved metal compounds as catalysts, the possibility cannot be ruled out that complexes containing two or more chiral substrate molecules are intermediates in all three reactions.[7] In that case the antipodal interaction effect would not have been unequivocally demonstrated.

It is further clearly of interest whether differences in reaction rates can be observed directly by comparing a pure chiral compound at high concentration and its racemate.

For both these reasons we sought a reaction, not involving metallic reagents, whose rate could be very precisely measured and which involved a chiral reactant at very high concentration, preferably neat, to maximize nonbonded interactions. Reaction 3, the ketalization of


(3)

1,2-propanediol with ketones, fulfilled our criteria inasmuch as 1,2-propanediol is a liquid at ambient temperature, metallic reagents are not required, the rate might well be monitored very precisely by using the ketone n → π* band, use of neat diol might drive the equilibrium to completion, the rate should be conveniently manipulated since an acid catalyst is an absolute requirement,[8] and chiral diols do not racemize under the conditions of reaction 3. Reaction 3 appeared of further interest because of the small number of previous kinetic studies of ketalization, as contrasted with the number of studies of the hydrolysis of dioxolanes and other ketals.[8,10] We now report the results of our kinetic study of reaction 3, the rates of reaction of (*S*)- and (*RS*)-1,2-propanediols under identical conditions.

Results and Discussion

Pilot experiments immediately confirmed the above expectations about reaction 3. Thus, solutions of 1 drop (ca. 10 mg, ca. 0.14 mmol) of butanone in 2.5 mL of either 1,2-ethanediol, 1,2-propanediol, or 2,3-butanediol (mixture of *dl*- and *meso*-diols) gave a λ_{max} of ca. 280 nm and absorbance values (*A*) of ca. 1.0 ± 0.2 which did not decrease until acid was added. Acids which caused decreases in absorbance at ambient temperature included acetic, formic, chloro- and dichloroacetic, methanesulfonic, and *p*-toluenesulfonic acids, in order of both increasing strength and rate. *A* generally dropped to less than 5% of its initial value within a few hours. Addition of ca. 0.5 M water after *A* had become constant caused a significant increase in *A*, as expected if the equilibrium of reaction 3 was displaced to the left. Finally, a preparative-scale experiment afforded 2-ethyl-2,4-dimethyl-1,3-dioxolane from butanone and excess neat (*RS*)-1,2-propanediol in 79% crude yield.

Table I. Effect of Acid Concentration on the Rate of the Butanone-(*RS*)-Propanediol Reaction at 21.0 °C

run	[AH],[a] M	$10^2 k_{obsd}$,[b] min^{-1}	$k_{obsd}/[AH]$	$k_{obsd}/[AH]^{1/2}$
10[c]	0.0805	3.50	0.434	0.123
10[c]	0.120_4	4.45	0.370	0.128
10[c]	0.160_1	5.63	0.352	0.141
10[c]	0.201_5	7.14	0.354	0.159
14[d]	0.0817	4.35 ± 0.03[e]	0.533	0.152
14[d]	0.1650	7.80 ± 0.26[e]	0.472	0.192
24[d]	0.1244	5.62 ± 0.12[e]	0.452	0.160
24[d]	0.2113	8.53 ± 0.15[e]	0.404	0.186

[a] Concentration of Cl_2CHCO_2H. [b] From plots of eq 5. [c] Solutions weighed in cuvettes. [d] Solutions weighed in flasks and divided between two cuvettes. [e] Mean value ± deviation from mean of duplicates.

Kinetics. Reaction 3 is expected to show the rate law of eq 4, on the basis of the mechanism in Chart I, with ring

$$\frac{-d[\text{ketone}]}{dt} = k[\text{diol}][\text{H}^+][\text{ketone}] \tag{4}$$

closure being rate determining.[8a] Both forward and reverse reactions are reported to be specific-acid catalyzed;[8] this leads to dependence on $[HA]^{1/2}$. The reverse reaction is faster in D_2O than in H_2O.[8,11] With neat diol, the forward rate should be pseudo first order in ketone. If the diol contains more water than ketone, the reverse reaction will also be pseudo first order in ketal, and the kinetics should conform to the approach to equilibrium of reaction A ⇌ B (eq 5, where $k_{obsd} = k_f + k_r$). At lower water concentrations the reaction would be better represented by A ⇌ B + C (cf. ref 12).

$$2.303 \log (A_t - A_0) = -k_{obsd}t + c \tag{5}$$

In general, plots of kinetics data according to eq 5 were linear for 1,2-ethanediol and 1,2-propanediol but never for 2,3-butanediol. Plots for propanediol showed a slight upward curvature which may have arisen both from (a) a slight warming of the solution during addition of ketone and (b) an increase in the water concentration during approach to equilibrium. Treatment of the data by the equation appropriate for A ⇌ B + C decreased the curvature but hardly altered the rate constants. We ultimately adopted the simpler expedient of manipulating $[H_2O]$, vide infra.

The kinetic order in acid depended on concentration. Some early results appeared consistent with dependency on $[HA]^{1/2}$, but in more careful, later experiments (cf. Table I) the order appeared to change from half-order at low [AH] (0.14 M) to first order at higher [AH]. The incursion of general-acid catalysis at higher [AH] would explain these results. This matter was not considered a serious disadvantage, since comparisons of chiral and racemic diols were to be made at acid concentrations as

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Table II. Reproducibility of Rate Measurements at 21.0 °C

run[a]	[AH],[b] M	10^2k_{obsd},[c] min^{-1}	$k_{obsd}/[AH]^{1/2}$
18	0.1156	5.46 ± 0.05	0.161 ± 0.002
	0.1201	5.90 ± 0.07	0.170 ± 0.002
20	0.0954	4.90 ± 0.05	0.159 ± 0.002
	0.0981	5.05 ± 0.10	0.161 ± 0.003
22	0.1219	5.90 ± 0.01	0.169$_0$ ± 0.0002
	0.1241	5.97 ± 0.01	0.169$_5$ ± 0.0002

[a] Solutions weighed in flasks and divided between two cuvettes; in a given run, both solutions were prepared from the same sample of diol. [b] Concentration of Cl_2CHCO_2H. [c] Mean value ± deviation from mean of duplicates from eq 5.

Table III. Effect of Water Concentration on Reaction Rate at 21.0 °C

run	[AH],[a] M	$[H_2O]$,[b] M	10^2k_{obsd}, min^{-1} [c]	$k_{obsd}/[AH]^{1/2}$	$A_\infty - A_0$ [d]
32	0.1165	*e*	5.56 ± 0.20	0.163	0.03
	0.1223	*f*	3.65 ± 0.05	0.104	0.09
48	0.1235	0.015	6.05 ± 0.01	0.172	0.020
	0.1147	0.015	5.68 ± 0.01	0.168	0.020
56	0.1006	0.015	4.84 ± 0.02	0.153	0.013
62	0.1203	0.03	4.51 ± 0.01	0.130	0.034
66	0.1324	0.05	4.43 ± 0.01	0.122	0.032
58	0.1285	0.13	3.83 ± 0.05	0.107	0.04$_5$
70	0.1341	0.19	3.16 ± 0.02	0.086$_3$	0.061

[a] Concentration of Cl_2CHCO_2H. [b] By GC; cf. Experimental Section. [c] From plots of eq 5; mean values ± deviations of duplicates from mean. [d] Difference between final absorbance at 280 nm and that before addition of 2-butanone. [e] Not analyzed by GC; $k_{obsd}/[AH]^{1/2}$ corresponds to $[H_2O] \approx 0.020$ M. [f] Not analyzed by GC; $k_{obsd}/[AH]^{1/2}$ corresponds to $[H_2O] \approx 0.13$ M.

nearly equal as possible. To compare runs with slightly different acid concentrations, we adopted the practice of dividing k_{obsd} by $[AH]^{1/2}$ to obtain apparent pseudo-three-halves-order rate constants k_{app}.

The precision of the kinetics experiments was very good, as shown by the pairs of results in Table II. Thus, when two solutions were prepared from a given sample of diol and closely similar amounts of acid were added, values of $k_{obsd}/[AH]^{1/2}$ differed from their mean by less than 1.0% in two of three cases.

The influence of water concentrations was indeed serious and necessitated careful control. Table III shows that when $[H_2O]$ was monitored by gas chromatography, different samples of (*RS*)-diol containing the same $[H_2O]$ gave the same rate constant. Before this was done, a discouragingly large range of values was obtained for different samples. Some of these diol samples were analyzed for water, and its influence can also be seen in the increase of A_∞ with $[H_2O]$ (cf. Table III). It is clear that, at a given acid concentration, k_{app} varies inversely with $[H_2O]$. Finally, deliberate addition of water to the diol decreased the curvature of simple first-order kinetics plots, because the water concentration now remained more nearly constant throughout a run.

Solvent Isotope Effect. A determination of the solvent deuterium isotope effect was undertaken, since no mention of such a measurement for ketalization could be found in the literature. At [AH] = 0.123–0.126 M and slightly different water concentrations, $10^2k_D = 10.8$, $10^2k_H = 6.2$ min^{-1}, and $k_D/k_H = 1.75$. If a value of $k_H = 5.0 \times 10^{-2}$ min^{-1} is assumed for undeuterated propanediol containing 0.030 M water, then $k_D/k_H = 2.2$. This result is similar to and consistent with several reported for hydrolyses,[8] if the equilibrium constant is independent of the isotope.

Table IV. Comparison of Reaction Rates of (*S*)- and (*RS*)-Propanediol at 21.0 °C

run	diol	[AH],[a] M	$[H_2O]$, M	10^2k_{obsd}, min^{-1}	$k_{obsd}/[AH]^{1/2}$
56	*RS*	0.1006	0.017	4.84 ± 0.01	0.153 ± 0.000$_3$
56	*S*	0.1026	0.030	4.51 ± 0.10	0.141 ± 0.003
62	*RS*	0.1203	0.030	4.51 ± 0.01	0.130 ± 0.000$_3$
62	*S*	0.1142	0.030	4.12 ± 0.01	0.122 ± 0.000$_3$
66	*RS*	0.1324	0.050	4.44 ± 0.02	0.122 ± 0.001
66	*S*	0.1272	0.050	4.27 ± 0.01	0.120 ± 0.000$_5$
68[c]	*RS*	0.1324	0.050	7.30 ± 0.01	0.201 ± 0.000$_4$
68[c]	*S*	0.1272	0.050	7.00 ± 0.01	0.196 ± 0.000$_4$
58	*RS*	0.1285	0.13	3.83 ± 0.05	0.107 ± 0.001
58	*S*	0.1285	0.13	3.88 ± 0.01	0.108 ± 0.000$_3$
70	*RS*	0.1341	0.19	3.16 ± 0.01	0.086$_3$ ± 0.000$_4$
70	*S*	0.1323	0.19	3.02 ± 0.01	0.083$_0$ ± 0.000$_4$
74[d]	*RS*	0.1341	0.19	6.50 ± 0.06	0.178 ± 0.001
74[d]	*S*	0.1323	0.19	6.65 ± 0.06	0.183 ± 0.001

[a] Concentration of Cl_2CHCO_2H. [b] Mean values ± deviation of duplicates from mean. [c] Substrate was 2-propanone. [d] At 30.0 °C.

Preparation of (*S*)-(+)-1,2-Propanediol. This chiral material has been prepared by several methods,[13] including resolution of the racemate.[13a,b] The method thought at the time to be best suited to large-scale work was adopted,[13c,g] viz., acetylation of (*S*)-(−)-ethyl lactate, followed by LAH reduction of the acetate and aqueous workup. The (*S*)-(+)-diol had to be isolated by continuous extraction with ether; the crude yield of 56% was less than the reported 87%,[13c] but the product had a high rotation (cf. Experimental Section). The product contained a UV-absorbing impurity which could be removed by extraction from an aqueous solution with dichloromethane, followed by distillation. This procedure, performed three times, gave the diol as transparent at 280 nm as the (±)-diol purified similarly. Consistent with the literature report,[8] the optical rotation of the (*S*)-(+)-diol used in kinetics experiments was unchanged after the diol, containing dichloroacetic or *p*-toluenesulfonic acid, was allowed to stand several weeks.

Comparison of Reaction Rates of Chiral and Racemic Diols. Table IV records the pseudo-three-halves-order rate constants determined in duplicate for the two diols reacting with butanone, as well as one set of runs with acetone; cf. the Experimental Section for the conditions and procedure. The first run listed merely shows that a higher water concentration decreases the rate. In four of the remaining runs, the racemic diol appeared to react slightly faster than the chiral diol, but in the remaining two, the reverse held true. In four runs the rate constant pairs differed from their means by only 1%. The data provide no basis for believing that the rates of reaction of chiral and racemic diols in reaction 3 differ by more than 1%.

In the formalism of state functions, $\Delta G^\ddagger$ is the same in each solvent, or $\Delta\Delta G^\ddagger = 0$ for transfer of the reaction from one solvent to the other. It follows that any change in free energy of the reactants, on changing from (*S*)- to (*RS*)-diol, is matched by the change in free energy of the activated complex. Interactions among molecules in this system predominantly involve hydrogen bonding, and since the activated complex still contains a hydroxyl group, these

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[13] (a) W. L. Howard and J. D. Burger, U. S. Patent 3 737 463 (1973); *Chem. Abstr.*, **79**, P31497 (1973); (b) J. L. Norula, *Chem. Era*, 11, 21 (1975); (c) M. Sanz-Burata, J. Irurre-Perez, and S. Julia-Arechaga, *Afinidad*, **27**, 693 (1970); (d) J. P. Guetté, N. Spassky, and D. Boucherot, *Bull. Soc. Chim. Fr.*, 4217 (1972); (e) J. Gombos, E. Haslinger, and U. Schmidt, *Chem. Ber.*, **109**, 2645 (1976); (f) C. Melchiorre, *Chem. Ind.* (*London*), 218 (1976), and references cited. (g) The one-step diborane reduction of (*S*)-lactic acid[13f] would now appear to be the method of choice.

interactions are still strong at that stage. The nul result of our experiment suggests, but by no means proves, that the interactions among identical and enantiomeric 1,2-propanediol molecules are very closely similar. It is not clear how one might design an experiment to enhance any such differences, but moderately strong intermolecular interactions seem essential if reaction rate differences are to be detected.

Experimental Section

Materials. Acetone was reagent grade (Fluka) and used as received. Butanone (reagent grade) was distilled at atmospheric pressure, bp 80.0 °C. Dichloroacetic acid (reagent grade) was distilled: bp 86 °C (12 mm); neutralization equivalent 129.2 ± 0.5 g mol^{-1} (theory 128.96). (±)-1,2-Propanediol (Baker reagent grade) was vacuum distilled: bp 88 °C (12 mm), 90 °C (15 mm), 94 °C (18 mm); n^{23}_{D} 1.4327 (distilled); $d^{21.5}$ 1.036$_0$ (lit.[14] *d* 1.036).

Purification of Diols. In early work some diol samples were found to absorb strongly around 280 nm with doubly distilled water or absolute ethanol as references; these included 2,3-butanediol, (*S*)-(+)-1,2-propanediol (below), 1,3-propanediol, and even 1,2-ethanediol. Reasoning that these impurities were hydrophobic led to the following purification procedure, which greatly decreased the absorbance in each case. The diol (50–150 g) was dissolved in 2–4 volumes of distilled water in a separatory funnel and shaken with three or four 50-mL portions of distilled dichloromethane. Evaporation of dichloromethane left residues of less than 0.5 g/50 mL of dichloromethane. The aqueous layer was vacuum distilled, the diol being collected after the bulk of the water and a suitable forerun.

Determination of Water in 1,2-Propanediol. Since Karl Fischer titrations would have consumed gram quantities of diols, water was determined by gas chromatography on a 6 ft × $^1/_4$ in. column of Chromosorb 101 at 180 °C (injection port 250 °C, TC detector 250 °C, He flow rate of ca. 50 mL min^{-1}). Injection of 5.0 μL of several 1,2-propanediol samples gave in each case a small peak at 1.0 min, the height varying with the sample, and a large peak at 5.5 min assigned to diol. The small peak was enhanced by addition of water to the diol. Acetone, used to clean the syringe, appeared at ca. 2 min. Quantitative analysis was performed by using either peak heights or areas estimated by triangulation; absolute concentrations were established by analysis of a sample to which a weighed amount of water had been added. The lowest water concentration thus determined was ca. 0.015 M, corresponding to ca. 0.03%.

(*S*)-(−)-Ethyl *O*-Acetyllactate. (*S*)-(−)-Ethyl lactate [Aldrich "98%", $[\alpha]^{22}_{D}$ −10.65° (1-dm cell length, neat, *d* 1.042; lit.[15] $[\alpha]^{14}_{D}$ −10.3°); 354.5 g, 3.00 mol] was added dropwise over 5 h to acetyl chloride (281 g, 3.58 mol) contained in a 2-L, three-necked flask fitted with a reflux condenser. To the condenser was connected via vinyl tubing a funnel inverted over a beaker of water. The solution was stirred magnetically and warmed to 35 °C, and HCl was evolved. After completion of the addition, the solution was warmed at 50 °C for 1 h, transferred to a 1-L flask, and distilled at water pump pressure. Following acetyl chloride and HCl, three fractions were collected: fraction 1 (29.4 g) had a boiling point of 70–73 °C (13 mm) and smelled of acetic acid; fraction 2 (289.0 g) had a boiling point of 73–76 °C (13 mm); fraction 3 (153.9 g) had a boiling point of 72–75 °C (11 mm). The yield of fractions 2 and 3 was 442.9 g (2.765 mol, 92.3%): ^{1}H NMR (Varian A-60; CCl_4 plus Me_4Si) δ 1.25 (t, 3 H, CH_3CH_2), 1.42 (d, 3 H, CH_3CH), 2.05 (s, 3 H, CH_3CO_2), 4.17 (q, 2 H, CH_3CH_2), 4.96 (q, 1 H, CH_3CH); $[\alpha]^{22}_{D}$ −49.1° (1-dm cell length, neat, *d* 1.051; lit.[15] $[\alpha]^{14}_{D}$ −49.9°).

(*S*)-(+)-1,2-Propanediol. To 50 g of $LiAlH_4$ (Merck, 95%, freshly opened) in a 3-L flask was added 1.5 L of ether freshly distilled from NaH, and vigorous effervescence occurred. (*S*)-(−)-Ethyl *O*-acetyllactate (184.0 g, 1.15 mol) in 180 mL of dried ether was added dropwise over 3 h to the solution, agitated by a paddle stirrer to maintain reflux. The solution, containing a gray precipitate, was refluxed 1 h more, and 40 mL of 96% ethanol was added to destroy excess $LiAlH_4$ followed by 200 mL of concentrated HCl, 100 mL of water, and 200 mL of concentrated HCl. Most of the ether was decanted, the remaining ether and aqueous layers were transferred to a separatory funnel, 100 mL of concentrated HCl was added, the funnel was shaken, and the aqueous layer was withdrawn. Filtration through Celite to remove the fine white precipitate failed. Half of the aqueous phase was transferred to a continuous extractor and extracted for ca. 25 h with 300 mL of the ether layer from the reaction. All the aqueous liquors had now become transparent and colorless. The ether extract was removed, 300 mL more of ether (from the reaction) was added, 100 mL of the aqueous layer was added to the extractor, and the extraction was resumed for ca. 40 h, after which the distilling flask contained a lower layer (presumably aqueous diol). The remaining aqueous liquor was partially neutralized with ca. 20 mL of 25% NaOH solution, 30 g of NaCl in 100 mL of water added, and the solution extracted with the remaining ether for 24 h. The ether extracts were combined and evaporated, and the residue was distilled to afford a first fraction [bp 86–87 °C (12 mm)] which was opaque at 280 nm. The distillate and remaining material were dissolved in 100 mL of water and washed with dichloromethane (5 × 50 mL), and the aqueous layer was distilled to afford (*S*)-(+)-1,2-propanediol: 49.2 g (0.648 mol, 56.4%); $[\alpha]^{22}_{D}$ +16.45° (1-dm cell length, neat; lit.[13f] $[\alpha]_{D}$ +15.84°); n^{22}_{D} 1.4327; bp 83–84 °C (10 mm). This material was, however, also opaque at 280 nm (*A* = 2.0; 1 cm, neat) and was repurified as above to afford material of boiling point 84 °C (10 mm) and $[\alpha]^{22}_{D}$ +16.34° (1-dm cell length, neat). The absorbance (280 nm) = 0.096 vs. that of (*RS*)-diol as a reference.

More diol could probably have been recovered by further continuous extraction. A control extraction for 88 h with 80 g of (*RS*)-diol gave 80% recovery after distillation. The (*S*)-(+)-diol was recycled at least twice after a series of kinetics runs, and its absorbance at 280 nm approached 0.00.

(*RS*)-1,2-Propanediol-*O*,*O*-d_2. Distilled racemic diol (36.0 g, 0.475 mol) was weighed into a pear-shaped flask, 100 mL of D_2O (Merck, 99.75%) added, and the water distilled in vacuo [26 °C (15–17 mm); 84 mL collected] until the diol just began to distill. A second 100 mL of D_2O was added, 81 mL of water collected by vacuum distillation, the condenser dried, and the diol distilled: bp 90–92 °C (15–18 mm); 27.5 g; transparent at 280 nm. Because addition of 1 drop of 2-butanone gave an absorbance that fell by $^1/_4$ in 4 h, the product was redistilled from 210 mg of anhydrous K_2CO_3. This distillate contained no acid, since the *A* value of added butanone was constant. The product showed only ca. 2% OH via ^{1}H NMR analysis.

2-Ethyl-2,4-dimethyl-1,3-dioxolane. Into a 500-mL Erlenmeyer flask were weighed (±)-1,2-propanediol (258.5 g, 3.40 mol) and dichloroacetic acid (4.11 g, 0.0318 mol), and the mixture was swirled. The propanediol was found (Cary 14 spectrophotometer) to be transparent from 300 to 240 nm; the dichloroacetic acid solution showed end absorption to ca. 280 nm; butanone in the diol showed a broad maximum at ca. 274 nm. To the ca. 0.25 L of solution was added distilled butanone (2.04 g, 0.028 mol), the solution was swirled, and after 5 min a 2.5-mL aliquot was transferred to a quartz cuvette for monitoring at 274 nm vs. dichloroacetic acid solution. The absorbance fell in 0.5 h from ca. 1.8 to 0.6 and after 3 h to 0.09, implying 95% reaction; a scan showed broad absorption (λ_{max} ca. 274 nm). After 12 h additional butanone (2.08 g, 0.029 mol; total 4.12 g, 0.057 mol) was added to the flask, the aliquot from the cuvette returned to the bulk of solution, and a new aliquot removed for monitoring. Absorbance declined over 2.5 h from 1.8 to 0.3, again implying greater than 90% reaction overall; a scan again showed λ_{max} ca. 274 nm.

The solution was poured into 600 mL of water containing 4.1 g of sodium bicarbonate, swirled, and extracted with dichloromethane (3 × 50 mL), and the extracts were dried over $MgSO_4$, decanted, and distilled through a 30-cm column packed with stainless-steel wool. The product distilled at 124–124.5 °C (lit.[16] bp 122.5–123.4 °C): n^{15}_{D} 1.4095 (lit.[16] n^{20}_{D} 1.4064); yield 2.35 g. Simple distillation of the residue afforded a second fraction: bp 110–128 °C; yield 3.52 g. The total yield was 5.87 g (0.045 mol,

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79%). Fraction 1 showed a small infrared peak at 1720 cm^{-1} but no OH absorption; fraction 2 showed a small, broad OH peak at 3500 cm^{-1} but no carbonyl absorption. Both fractions had a terpene-like aroma. Both showed complex ^{1}H NMR spectra: δ 0.9 (t, J = 7 Hz, CH_3CH_2), 1.2 (d, J = 3 Hz, 4-CH_3), 1.3 (s, 2-CH_3), 1.6 (br q, J = 7 Hz, CH_3CH_2), complex multiplets at 3.3 and 4.0 assigned to the ring protons (C-4 and C-5). The ratio of high-field to low-field integrals was 3.25 for fraction 1 and 3.58 for fraction 2 (calcd, 11/3 = 3.67).

Procedure for Kinetics. Except for the very first exploratory experiments, all solutions were prepared by weighing to $\pm 1 \times 10^{-4}$ g. At first, reagents were weighed directly into quartz cuvettes (1 cm square, capacity ca. 2.5 mL), but the viscosity of propanediol and the relatively small air space hindered mixing and may have been the cause of unsatisfactory precision (±5% or more). For prevention of another conceivable mixing problem, cuvettes were used only if their caps fitted flush with the inside of the cuvette.

Solutions were prepared in 10- or 25-mL, round-bottomed flasks, weighing in first the diol and then the acid, stoppering, and swirling for at least 10 min. The solution was divided equally between two cuvettes, and these were stoppered and allowed to equilibrate for at least 1 h in the thermostated cuvette compartment of the spectrophotometer. For each run, each cuvette was briefly withdrawn, 1 drop of ketone was added, and the cuvette was again tightly stoppered, shaken for ca. 1 min, and replaced in the compartment. Measurement was begun as soon as all cuvettes were ready.

Absorbances were measured via a Beckman automatic recording spectrophotometer. With the wavelength set at 280 nm, the instrument moved each cuvette into the sample beam for a chosen dwell time, usually 15–20 s, and repeated the cycle of measurements over a chosen interval, usually 1.5–2 min in this work. The absorbance of each cuvette at each time appeared as a dot on the chart. Measurements were continued until A for each cuvette had become constant. The absorbance of each cuvette was monitored for at least 30 min prior to addition of ketone. Absorbances were treated as described in the Results and Discussion, rate constants being determined graphically.

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Registry No. (*S*)-(−)-Ethyl *O*-acetyllactate, 20918-91-6; (*S*)-(−)-ethyl lactate, 687-47-8; (*S*)-(+)-1,2-propanediol, 4254-15-3; (±)-1,2-propanediol, 4254-16-4; (±)-1,2-propanediol-*O*,*O*-d_2, 77080-53-6; 2-ethyl-2,4-dimethyl-1,3-dioxolane, 2916-28-1; butanone, 78-93-3.

Studies on the Conformation of Some Substituted 4-Selenanols

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The second-order rate constants for acetylation with acetic anhydride in pyridine have been measured at 40 °C for seven pairs of epimeric 4-selenanols, and the conformations of these compounds were determined from the kinetic data. ^{1}H NMR and ^{13}C NMR spectra were also recorded and analyzed. The ^{1}H chemical shift of the carbinol protons and ^{13}C chemical shift of the carbinol carbons are analyzed in the light of previously established correlations. Carbon-13 chemical shift data suggest that 2,2-dimethyl-*trans*-6-(*p*-chlorophenyl)selenan-*r*-4-ol exists in a nonchair conformation.

The kinetics of acetylation of epimeric alcohols[2-4] has been one of the well-devised methods to elicit corroborative evidence concerning the configuration of the hydroxyl group. Although the rates of acetylation of 4-piperidinols[5] and 4-thianols[6] are on record, no systematic investigation of a series of 4-selenanols has appeared nor have there been many studies[7] of the conformational analysis of functionalized selenium heterocycles. We report a conformational study of some epimeric pairs of substituted 4-selenanols based on the rates of acetylation as well as ^{1}H and ^{13}C NMR spectral analysis.

Table I. Composition of the Products from the Reduction of 4-Selenanones

selenanone	% total crude product	% unreduced selenanone	yield of epimeric selenanols, %	
			axial	equatorial
		Reduction with MPV		
5a	98	3	63 (**1a**)	15 (**2a**)
5b	96	4	53 (**1c**)	15 (**2c**)
5c	93	4	75 (**3b**)	14 (**4b**)
		Reduction with $LiAlH_4$		
5a	98	3	11	84
5b	97	4	12	68
5c	96	3	47	44

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