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Kinetics of Oxidation of Aldo Sugars by Quinquevalent Vanadium Ion in Acid Medium

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The oxidation kinetics of glucose, considered as a model compound for reducing sugars, with vanadium(V) in sulfuric and perchloric acid solutions has indicated a rate-limiting bimolecular reaction between vanadium(V) and the reducing sugars leading to the formation of a free radical. There is a linear correlation between the observed rate constant k_1 and [sugar], $[H^+]^2$, and $[HSO_4^-]$. The oxidation is faster in sulfuric acid, and various correlations between the rate and acidity have been tested. The mutarotation equilibrium is immediately attained and therefore the rate of oxidation is independent of the rate of mutarotation. The linear correlation between the rates of oxidation of sugars and their concentrations present in the solution as free aldehyde helps to explain the observed reactivity of different sugars, which is in the order xylose > arabinose > galactose > mannose > glucose.

The oxidation kinetics of reducing sugars with quadrivalent cerium in the presence of 0.5 *M* sulfuric acid has been discussed in a previous communication.[1] It is, therefore, of interest to us to investigate how the oxidation mechanism of reducing sugars is affected by a change in the one equivalent oxidant. The choice of quinquevalent vanadium ion is motivated by our additional interest in studying the correlation between the acid-catalyzed oxidation rate and various acidity scales.

The mechanism of the oxidation of various organic compounds by quinquevalent vanadium has been reviewed.[2] The kinetics of vanadium(V) oxidation of glucose and xylose in sulfuric, perchloric, and hydrochloric acid solutions was reported[3] after the review[2] was published. However, this study is not conclusive and needs a reinvestigation, as no attempt was made by the authors[3] to measure the rates of oxidation of other hexoses as well as to consider the effect of mutarotation equilibrium on the rate of oxidation of reducing sugars.

Experimental Section

Ammonium metavanadate was dissolved in sulfuric or perchloric acid solutions as required. The acid concentration of the stock vanadium(V) solution was taken as the difference between the amount initially added and the amount consumed by reaction 1.

$$NH_4VO_3 + 2H^+ \longrightarrow NH_4^+ + VO_2^+ + H_2O \qquad (1)$$

The vanadium(V) solutions are quite stable. The sugar solutions were freshly prepared by direct weighing of the samples. The vanadium(V) solution was standardized against a freshly prepared standard solution of ferrous ammonium sulfate to a barium diphenylamine sulfonate end point in the presence of phosphoric acid.

The reaction has been studied in the presence of an excess of sugars and at 50° unless stated otherwise. The other experimental details for following the progress of the reaction from time to time and calculation of the observed rate constant k_1 with respect to vanadium(V) are similar to one described elsewhere.[4]

Stoichiometry and Product Analysis. The reaction mixtures had an excess of glucose or mannose to ensure that there was no appreciable reduction of vanadium(V) by the more reactive oxidation products. Arabinose and formic acid were confirmed as the oxidation products in the glucose oxidation by paper chromatography using pure samples as reference.

In another set of experiments, the completely oxidized reaction mixtures were treated with barium carbonate to remove most of the sulfuric acid. The absence of formaldehyde, gluconic acid, and glucuronic acid in the reaction mixtures was established with color reactions of chromotropic acid[5a] and β,β'-dinaphthol,[5b] respectively. The filtrate and washings were subjected to fractional distillation in an all-glass apparatus fitted with standard joints. The distillate collected at 101–102° was made to a known volume and titrated against a standard alkali to a phenolphthalein end point. The distillate was confirmed to be formic acid by using chromotropic acid[5c] and paper chromatography.

The results of few quantitative estimations for the formic acid indicated that 2 equiv of vanadium(V) are used per mole of formic acid produced. The reaction is therefore expressed as in eq 2.

$$C_6H_{12}O_6 + 2V(V) + H_2O \longrightarrow C_5H_{10}O_5 + HCOOH + 2V(IV) + 2H^+ \qquad (2)$$

Results and Discussion

The first-order dependence both in vanadium(V) and reducing sugars at any given acid concentration was established by effecting a tenfold variation in the respective concentrations at the constant concentration of the other. The rate increased with the increase in the ionic strength; lithium perchlorate was used for the purpose. (These data are available as supplementary material; see paragraph at end of paper.) There is no deviation from the first-order dependence in glucose even at 4 *M* sulfuric or perchloric acid as had been noted in the oxidation of butane-1,3-diol,[6] quinol,[7] and glycerol.[8] The linear plot (Figure 1) between the observed rate constant k_1 and [sugar] passes through the origin, thus confirming a first-order dependence in the reducing sugars.

The values of the second-order rate constant k_2 (Table I)

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Table I
The Second-Order Rate Constant k_2 for Various Sugars in Sulfuric And Perchloric Acid[a]

		$10^4 k_2 \pm 0.1$		
Registry no.	Sugar	Sulfuric acid (40°)	Sulfuric acid (50°)	Perchloric acid (50°)
50-99-7	D(+)-Glucose	1.3	3.7	3.3
3458-28-4	D(+)-Mannose		5.0	5.8
59-23-4	D(+)-Galactose	3.6	8.4	6.5
58-86-6	D(+)-Xylose	7.2	17.4	22.7
5328-37-0	L(+)-Arabinose		16.8	18.4
3615-41-6	L(+)-Rhamnose		4.8	
154-17-6	2-Deoxy-D(+)-glucose		8.5	

[a] $k_2 = (-d[V(V)]/dt)/[V(V)][sugar]$; [vanadium(V)] = 0.02 *M*; [acid] = 2 *M*.

Table II
The Observed First-Order Rate Constant k_1 at Different Concentrations of Sulfuric and Perchloric Acid When the Ionic Strength Is Not Kept Constant at 50°[a]

A. [Sulfuric acid], *M*	2.0	3.0	4.0	5.0	6.0
$10^4 k_1$, sec^{-1} (glucose)	1.1	2.6	5.4	13.2	33.6
$10^4 k_1$, sec^{-1} (mannose)	1.3	3.2	7.6	16.3	36.3
$10^4 k_1$, sec^{-1} (galactose)	3.1	7.3	14.9	32.8	
B. [Perchloric acid], *M*	2.0	3.0	4.0	5.0	6.0
$10^4 k_1$, sec^{-1} (glucose)	1.0	1.8	3.8	8.3	21.4
$10^4 k_1$, sec^{-1} (mannose)	0.7	1.5	3.0	8.7	28.3
$10^4 k_1$, sec^{-1} (galactose)	2.4	4.1	8.1	16.8	39.8

[a] [Vanadium(V)] = 0.02 *M*; [glucose] = 0.3 *M*; [mannose] = 0.25 *M*; [galactose] = 0.375 *M*.

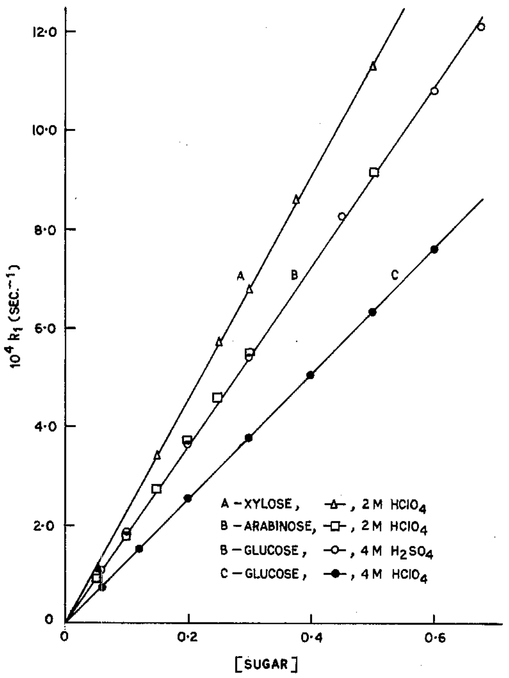

Figure 1. The linear dependence between the observed rate constant k_1 and [sugar]: [vanadium(V)] = 0.02 *M*; [sulfuric acid] = 2 *M*; *T* = 50°.

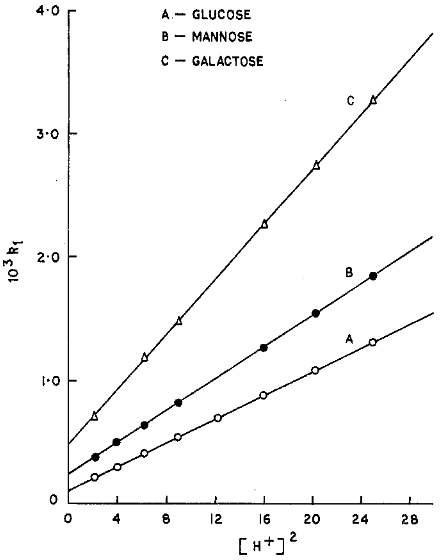

Figure 2. The linear plot between observed rate constant k_1 and $[H^+]^2$ at constant ionic strength at 50°: ($[H_2SO_4]$ + $[NaHSO_4]$) = 5 *M*; [vanadium(V)] = 0.02 *M*; [glucose] = 0.3 *M*; [mannose] = 0.3 *M*; [galactose] = 0.375 *M*; *T* = 50°.

are the average values from the slopes of the linear plots between rate k_1 and respective [sugars]. The reaction is catalyzed by mineral acids and the rate is faster in sulfuric acid. The effect of sulfuric or perchloric acid of varying ionic strength on the reaction rate is reported in Table II. The effect of hydrogen ion at constant ionic strength is also given in Table III. The ionic strength was adjusted with sodium perchlorate or sodium hydrogen sulfate depending on the acid used. The linear plot (Figure 2) between the observed k_1 and $[H^+]^2$ with intercept on the rate axis indicates that at least one term in the rate law is independent of hydrogen ion. The rate also increased with the increase in bisulfate ion at constant concentration of the hydrogen ion. The linear plot (Figure 3) between k_1 and HSO_4^- (Table IV) is similarly interpreted. The effect of sulfate ion (Table V) was so investigated that the sum total concentrations of sodium sulfate and sodium hydrogen sulfate remained constant. The rate decreased with increasing sulfate ion, indicating that sulfate complexes of vanadium(V) are unreactive. The mechanism of the oxidation of sugars as effected by the various vanadium(V) species, viz., VO_2^+, $VO_2 \cdot HSO_4$, and VO^{3+} in sulfuric acid, and the rate law consistent with the effects of hydrogen and hydrogen sul-

Table III
The Dependence of the Observed Rate Constant k_1 on [H$^+$] at Constant Ionic Strength

A. [Vanadium(V)] = 0.02 M; [HSO_4^-] = 5 M; [Glucose] = [Mannose] = 0.3 M; [Galactose] = 0.375 M; T = 50°

[H$^+$], M	1.5	2.0	3.0	4.0	4.5	5.0
10^4 k_1, sec^{-1} (glucose)	2.1	3.0	5.4	8.8	10.8	13.2
10^4 k_1, sec^{-1} (mannose)	3.8	5.0	8.0	12.7	15.4	19.5
10^4 k_1, sec^{-1} (galactose)	7.2	9.2	14.7	22.6	27.4	32.8

B. [Vanadium (V)] = 0.02 M; [ClO_4^-] = 6 M; [Glucose] = 0.26 M; [Mannose] = 0.3 M; [Galactose] = 0.3 M

[H$^+$], M	1.0	2.0	3.0	4.0	5.0
10^4 k_1, sec^{-1} (glucose)	2.3	3.8	5.7	8.9	13.2
10^4 k_1, sec^{-1} (mannose)	2.2	3.9	6.2	10.2	18.2
10^4 k_1, sec^{-1} (galactose)	6.1	8.8	13.3	19.6	28.2

Table IV
The Dependence of the Observed Rate Constant k_1 on [HSO_4^-] at Constant Acidity[a]

[HSO_4^-], M	1.0	2.0	3.0	4.0	5.0
10^4 k_1, sec^{-1} (glucose)	8.9	10.0	11.0	12.1	13.2
10^4 k_1, sec^{-1} (mannose)	11.1	13.2	15.2	17.2	19.5
10^4 k_1, sec^{-1} (galactose)	21.8	24.6	27.4	30.0	32.8

[a] [Vanadium(V)] = 0.02 M; [glucose] = 0.3 M; [galactose] = 0.375 M; [mannose] = 0.3 M; [H$^+$] = 5 M; T = 50°.

Table V
The Dependence of the Observed Rate Constant k_1 on [Sodium Sulfate] When the Sum Total Concentrations of Sodium Sulfate and Sodium Hydrogen Sulfate Are Constant[a]

[Na_2SO_4], M	0.0	0.25	0.5	0.75	1.0	1.35
10^4 k_1, sec^{-1}	1.9	1.7	1.6	1.5	1.4	1.2

[a] [Vanadium(V)] = 0.02 M; [$NaHSO_4$] + [Na_2SO_4] = 1.35 M; [sulfuric acid] = 2 M; [glucose] = 0.3 M; T = 50°.

fate ions on the rate is available as supplementary material (see paragraph at end of paper).

Rate of Mutarotation. The rate of mutarotation is known to be catalyzed by an acid or a base. The rate of mutarotation, k_m (min^{-1}), of glucose in the presence of an acid at 25° can be calculated[9] from eq 3. The value so calculated in 2 M acid is 0.00876 sec^{-1}.

$$k_m = 0.0096 + 0.258[H^+] \qquad (3)$$

Assuming that the equilibrium constant K for the mutarotation equilibrium, shown in eq 4, has a value of 1.77 at

$$\alpha\text{-glucose} \underset{k''}{\overset{k'}{\rightleftharpoons}} \beta\text{-glucose} \qquad (4)$$

$$\log k^1 - \log k^2 = \frac{E}{4.576}\left(\frac{1}{T_2} - \frac{1}{T_1}\right) \qquad (5)$$

25°, the value of k' calculated from the known value of k_m ($k' + k''$) in 2 M sulfuric acid is 0.005605 sec^{-1}. Its value, 0.1055 sec^{-1}, at 50° is calculated from eq 5, as the activation energy for the mutarotation of glucose[10] is 23 kcal mol^{-1}.

Here k^1 and k^2 are the rate constants at absolute temperatures T_1 and T_2, respectively.

Oxidation Rate with Respect to Glucose. Since the reaction has a first-order dependence in vanadium(V) and glucose, the rate of disappearance of vanadium(V) is expressed by eq 6, where k_2 is the second-order rate constant.

$$\frac{-d[V(V)]}{dt} = k_2[V(V)][\text{glucose}] \qquad (6)$$

Since 1 mol of glucose reduces 2 mol of vanadium(V), one can write the relation shown in eq 7.

$$\frac{-d[V(V)]}{dt} = 2\frac{-d[\text{glucose}]}{dt} \qquad (7)$$

Table VI
The Percentage Concentrations of Free Aldehyde Sugars[a] and α and β Sugars[b] in Aqueous Solution

Sugar	[α-Pyranose sugar], %	[β-Pyranose sugar], %	[Free aldehyde sugar], %
D(+)-Glucose	36	64	0.024
D(+)-Mannose	64	36	0.064
D(+)-Galactose	35	65	0.082
D(+)-Xylose	29	71	0.17
D(+)-Arabinose	63	37	0.28

[a] Reference 11. [b] Reference 12

The value of the first-order rate constant with respect to glucose, k_g, at a given [vanadium(V)] can be calculated by proper substitutions in eq 8, which is derived from eq 6 and

$$k_g = \frac{k_1[\text{vanadium(V)}]}{2[\text{glucose}]} \qquad (8)$$

7. The values of k_g thus calculated are 0.376 × 10^{-5} and 0.32 × 10^{-5} sec^{-1} in solutions of 2 M sulfuric and perchloric acid, respectively.

Attainment of Mutarotation Equilibrium. Since in 2 M sulfuric acid solution the rate of mutarotation k' (0.1055 sec^{-1}) is about 28,000 times faster than the rate of oxidation of glucose with respect to glucose, k_g = 3.76 × 10^{-6} sec^{-1}, it is clear that the mutarotation equilibrium is immediately attained. The rate of oxidation of glucose is therefore not affected by the mutarotation of glucose. Thus the observed rate k_1 is the sum total of the rates contributed by each of the α and β anomers together with the contribution from the very small concentration of the sugar present as free aldehyde in the aqueous solution. The intermediate existence of the aldehyde sugar is well established in the mutarotation and its concentration has been determined on a percentage scale.[11] Therefore any experimental separation of the rates contributed by individual anomers is difficult, especially if the reaction is to be studied in a minimum 2 M acid solution and at 50° to have a measurable speed.

Correlation of Second-Order Rate k_2 and [Aldehyde Sugar]. It is interesting to note (Figure 4) that the plot of the second-order rate constant k_2, defined as $-d[V(V)]/(dt[\text{sugar}]\,[\text{vanadium(V)}])$ against [aldehyde sugar] is linear with an intercept on the rate axis. This plot is consistent with eq 9, which is based on the consideration of reac-

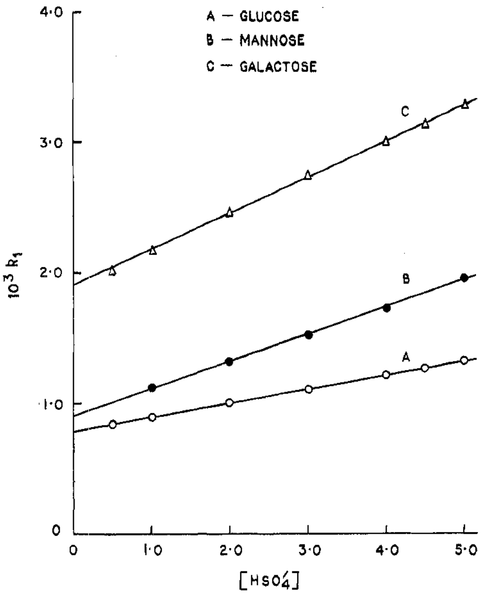

Figure 3. The linear plot between observed rate constant k_1 and $[HSO_4^-]$ at constant $[H^+]$: [vanadium(V)] = 0.02 *M;* [glucose] = 0.3 *M;* [mannose] = 0.3 *M;* [galactose] = 0.375 *M; T* = 50°.

$$k_2 = 2(k_{10}[G] + k_a[\text{aldehyde sugar}]) \qquad (9)$$

$$\text{vanadium(V)} + G \xrightarrow{k_{10}} \text{free radical} + V(IV) + H^+ \qquad (10)$$

$$\text{vanadium(V)} + \text{aldehyde sugar} \xrightarrow{k_a} \text{free radical} + V(IV) + H^+ \qquad (11)$$

$$\text{vanadium(V)} + \text{free radical} \xrightarrow{\text{fast}} \text{products} + V(IV) + H^+ \qquad (12)$$

tions 10–12, where G represents the sugar concentration present in pyranose form. It is to be further noted that no experimental support for vanadium(V)–glucose complex in 2 *M* sulfuric acid solution could be adduced from the spectrometric measurements. The spectrometric measurements were recorded on a Beckman DU spectrophotometer with cells of unit path length. There is a very small but definite increase in the optical density of vanadium(V)–glucose solution, but surprisingly enough, the optical density is not much affected by the increase in sugar concentration.

The oxidation products are formic acid and arabinose and the formation of a free radical during the reaction is confirmed by the induced polymerization of acrylonitrile, whereas neither vanadium(V) nor sugar solution alone induced the polymerization.

The ratio of the rates of oxidation of the free aldehyde sugar and pyranose sugar as calculated from the ratio of slope and intercept of the linear plot in Figure 4 is nearly 2900 in 2 *M* perchloric acid and 7900 in 2 *M* sulfuric acid at 50°. This would mean that most of the sugar is oxidized as aldehyde sugar.

This linear correlation helps to explain the observed reactivity of the different sugars (Table I), which is in the order xylose > arabinose > galactose > mannose > glucose. On the other hand, if sugars are oxidized in their pyranose form only, then the rates of oxidation of these sugars are expected to be of the same magnitude because of the almost identical percentage of the α and β forms (Table VI) of these sugars present at equilibrium,[12] which is not the case as is evident from the rate constants reported in Table I.

Acid Catalysis. The reaction has shown a dependence on the second power of hydrogen ion. The dependence of the rate on acidity has been further examined in accordance with the suggestions of Hammett and Bunnett. The plot between log k_1 and $-H_0$, the Hammett acidity function,[13] is linear but the slope values for glucose, mannose, and galactose are 0.5, 0.7, and 0.5, respectively, which are much less than the expected ideal slope of unity in the presence of perchloric acid of constant ionic strength. However, the slope values are much nearer to unity for the reaction in the presence of sulfuric or perchloric acid of varying ionic strength. These values are 0.8, 0.6, and 0.74 in sulfuric acid and 0.66, 0.75, and 0.6 in perchloric acid for glucose, mannose, and galactose, respectively. The H_0 values are those due to Paul and Long.[14]

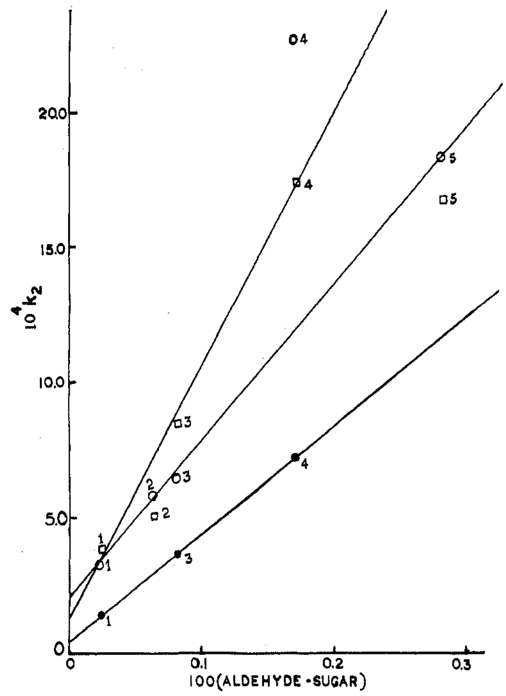

Figure 4. The linear plot between the second-order rate constant k_2 $((-d[V(V)]/dt)/[V(V)][\text{sugar}])$ and [aldehyde sugar]: 1, glucose; 2, mannose, 3, galactose; 4, xylose; 5, arabinose; ●, sulfuric acid, 40°; □, sulfuric acid, 50°; ○, perchloric acid, 50°.

The plot of (log $k_1 + H_0$) against log a_{H_2O}, suggested by Bunnett,[15] is linear with "w" values equal to 0.66, 2.4, and 1.0 in sulfuric acid and 2.7, 3.6, and 2.2 in perchloric acid for glucose, mannose, and galactose, respectively. It is felt desirable[6] not to attach any mechanistic significance to the "w" value as has been discussed by Bunnett[15] except that a water molecule participates in the mechanism.

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Registry No.—Vanadium(V), 7440-62-2.

Supplementary Material Available. The kinetic data involving the variation in the concentrations of vanadium(V), aldo sugars, dependence of the rate on glucose concentration in 4 *M* sulfuric and perchloric acid, effect of ionic strength on the rate, and the mechanism of oxidation as effected by the various vanadium(V) species in sulfuric acid will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.00 for photocopy or $2.50 for microfiche, referring to code number JOC-75-1248.

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Rapid Separation of Organic Mixtures by Formation of Metal Complexes

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A convenient and efficient technique for resolving alcohol mixtures by preferential complexation by calcium chloride or manganese chloride with one alcohol of the mixture is reported. Isolation of the complex formed and regeneration of the alcohol allows purification of certain alcohols. Catalytic amounts of ethanol enhance the complexing ability of the metal halides. The separation of commercial mixtures of *cis-* and *trans-*4-*tert*-butylcyclohexanol, technical geraniol, and contrived mixtures of cyclododecanol–cyclododecanone were investigated and optimum conditions for these systems were determined.

Often the most difficult and time-consuming aspect of a synthetic procedure is the process of separating the desired compound from a crude product mixture containing similar compounds. The rapid pace at which modern synthetic chemistry is advancing is in large measure due to the development of powerful chromatographic methods for resolving mixtures. However, chromatographic procedures work best on a small scale and become exceedingly difficult to perform as the quantity of materials to be separated increases.

By contrast, the classical chemical methods for separation are not as limited by scale; these methods usually involve making a derivative of a functional group which can be separated from impurities by nonchromatographic means (e.g., recrystallization). Derivative formation requires an extra step and once purified the derivative is often difficult to decompose.

We have for several years been purifying mixtures of organic alcohols by complex formation with calcium chloride and other anhydrous metal halides. The literature contains only isolated reports on the use of such complexes to purify mixtures.[1] The original procedure of Jones and Woods for purification of commercial geraniol exemplifies the simplicity of the general method.

The geraniol–citronellol[2] mixture (~60:40) is dissolved in hexane and stirred with finely ground anhydrous calcium chloride. Although calcium chloride is completely insoluble in hexane, it is quickly digested by the alcohol to form a solid complex. The complex is filtered, washed with hexane, and dissolved in water, whereupon essentially pure geraniol is liberated. The whole procedure is easily carried out in several hours on a kilogram scale if necessary. Although only 35% of the geraniol is recovered in this way, it is difficult to imagine a more convenient means of isolating it from this mixture.

We have now established that this separation technique is applicable to many alcohol mixtures. A large number of mixtures containing other coordinating functional groups (e.g., amines, amides, esters, epoxide, ketones, aldehydes, acids, and nitriles) were also examined. However, for unknown reasons, the various metal complexing agents were generally less effective in separating mixtures containing functional groups other than alcohols. Before elaborating on specific applications, it will be helpful to discuss the properties of the complexes which are formed with alcohols.

Chart I

Salt	Alcohol	Alcohol/salt
$CaCl_2$	Geraniol	1.9
$CaCl_2$	α-Phenethyl alcohol	1.3
$CaBr_2$	Menthol	2.2
$MnCl_2$	Menthol	1.0
$MnCl_2$	α-Phenethyl alcohol	1.4

Nature of Alcoholates. The formation of alcoholates of anhydrous metal halides is well precedented and the stoichiometry $MX_2(ROH)_2$ is common for divalent metal ions (e.g., Mn, Ni, Ca, Zn, and Mg).[3] Since these complexes were of only small alcohols (i.e., MeOH, EtOH), we prepared and analyzed several larger complexes. As shown in Chart I, the stoichiometry of the complexes varies between one and two alcohols. These complexes were formed in the presence of a large excess of the alcohol.

An early clue about the course of complex formation and the reason for its specificity was provided by the observation that the hexane filtrate obtained during isolation of the solid complexes contained dissolved calcium chloride. In fact, alcohols such as oleoyl alcohol and citronellol, which did not form solid complexes with $CaCl_2$, dissolved large quantities of the salt in hexane. Similarly, complex mixtures of alcohols which, when pure, formed solid complexes in the standard procedure (i.e., stirred in hexane with the anhydrous salt) resulted in complete dissolution of the anhydrous salt in the hexane. Thus, although most alcohols form complexes, some crystallize more readily than others from the nonpolar solvents employed.

Another important aspect of complex formation is that the alcohols in the solid complexes stirring in hexane exchange rapidly with the alcohols in solution. This exchange process was demonstrated by isolating the $CaCl_2$ complex of 1-decanol and then stirring it in a hexane solution containing cyclohexanol (ca. 1.5 equiv). After stirring for 0.5 hr