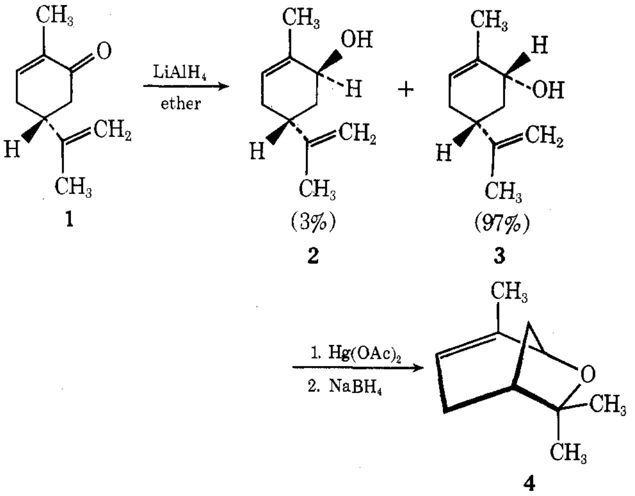
give (−)-*cis*-carveol (**3**). This is followed by internal oxymercuration with mercuric acetate and reduction with sodium borohydride to give the bicyclic ether in 83% overall yield.[4]



Reduction of (−)-carvone (**1**) with $LiAlH_4$ in ether at room temperature yields a mixture of *trans*- and *cis*-carveols.[5] Lowering the reaction temperature to −78 °C provides a near-quantitative yield of the alcohol containing 97% of the isomer with the desired cis stereochemistry. The alcohol isolated from the reduction was of adequate purity to be used directly in the next step.

Halpern and Tinker[6] have observed that the second-order rate constant for the intramolecular oxymercuration of 1-penten-5-ol to form the cyclic product is more than 10 times greater than the corresponding oxymercuration of 1-butene. This result is explained by the neighboring group participation of the terminal hydroxy group. Treatment of (−)-*cis*-carveol with an equimolar amount of mercuric acetate in a tetrahydrofuran–water mixture provided, after 9 days, greater than 85% conversion to the ring-closed mercurial, **5**, as shown by gas chromatography. The observation that only the (−)-*cis*-carveol undergoes internal oxymercuration and the (−)-*trans*-carveol fails to react provides direct and conclusive proof for the stereochemistry of the carveols.[5b]

Reduction of the mercurial was readily accomplished with sodium borohydride in an aqueous solution containing 0.4 M NaOH. Attempts to reduce the mercurial under less basic conditions or through the use of weaker reducing agents ($NaBH_3CN$) resulted in low yields of **4** with the major fraction of the mercurial reverting to the (−)-*cis*-carveol. This result is presumably due to the acid-promoted deoxymercuration of **5** to form **3** and Hg^{2+} followed by reduction of the Hg^{2+} by borohydride. Deoxymercuration is generally facile in the presence of coordinating anions such as acetate ion.[7] The results further suggest that the rate of reduction of Hg^{2+} is more rapid than the rate of reduction of **5**. Hence, by slowing down the deoxymercuration reaction that forms Hg^{2+} the pathway leading to the reduction of the alkyl mercurial will favorably compete with the pathway leading to the reduction of Hg^{2+}.

Experimental Section

Gas chromatographic analyses were carried out on a Varian Series 1200 gas chromatograph fitted with a 10-ft 3% Carbowax 20M column and temperature programmed from 120 to 170 °C at 10 °C/min. Optical rotations were measured on a Perkin-Elmer 114 polarimeter using 5-ml cells. Refractive indices were determined with a Bausch and Lomb refractometer.

(−)-*cis*-Carveol (3). To 12.0 g (0.316 mol) of $LiAlH_4$ (Alpha Inorganics) in 700 ml of anhydrous diethyl ether cooled to −78 °C was added dropwise 46.6 g (0.310 mol) of (−)-carvone (Aldrich) in 75 ml of anhydrous diethyl ether over a 1-h period. Aliquots were removed, quenched with aqueous H_2SO_4, and the ether layer analyzed directly with gas chromatography. After an additional 30 min, the reduction was complete and the excess $LiAlH_4$ was quenched with a solution of wet ether. This mixture was then poured onto crushed ice; 200 ml of 10% H_2SO_4 was added, and the ether and aqueous layers were separated. The aqueous layer was extracted with two additional 100-ml portions of ether. All the ether layers were combined and dried over anhydrous sodium sulfate, and the solvent was removed in vacuo to yield 46.1 g (97.7%) of a clear liquid containing 97% (−)-*cis*-carveol and 3% (−)-*trans*-carveol. The (−)-carveol mixture obtained was used in the next step without further purification: bp 110 °C (13 mm); $[\alpha]^{25}{}_D$ −25.8° (neat); $n^{25}{}_D$ 1.4960 [lit.[5] bp 101 °C (10 mm); $[\alpha]^{25}{}_D$ −23.9° (neat); $n^{25}{}_D$ 1.4959]. Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.57; H, 10.60.

(+)-Pinol (4). To a solution of 15.25 g (0.100 mol) of (−)-carveol mixture in 100 ml of THF was added dropwise a solution consisting of 30.60 g (0.096 mol) of mercuric acetate in 50 ml of water. The progress of the reaction was monitored by gas chromatography. Reaction aliquots were removed periodically and quenched with base and reduced by the addition of 0.5 M $NaBH_4$ in 3 M NaOH; the aqueous phase was saturated with sodium chloride, and the THF phase analyzed directly with gas chromatography. The results indicated that more than 85% of the (−)-carveol mixture was converted to the oxymercurated product after 9 days.

The solution containing the oxymercurated product was cooled to 15 °C and made basic with the dropwise addition of 25 ml of 3 M NaOH. A cooled solution consisting of 5.7 g (0.15 mol) of sodium borohydride (Alpha Inorganics) and 100 ml of 3 M NaOH was then added dropwise to the basic solution of the mercurial. After a 3-h reaction period the aqueous phase was saturated with NaCl and 25 ml of ether was added to aid in the separation of phases. The organic phase was removed and dried over anhydrous sodium sulfate. The THF–ether in the organic phase was removed by distillation at atmospheric pressure. Two distillations of the crude product under reduced pressure provided **4** in greater than 99% purity: bp 65 °C (11 mm); $[\alpha]^{25}{}_D$ 81.1° (neat); $n^{25}{}_D$ 1.4670 [lit.[2] bp 64–65 °C (11 mm); $[\alpha]^{25}{}_D$ 87.5°; $n^{20}{}_D$ 1.4698]; NMR (neat) δ 4.98 (m, 1), 3.75 (d, 1, J = 3.5 Hz), 1.50–2.28 (m, 8), 1.19 (s, 3), 1.08 (s, 3). Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.57; H, 10.47.

Registry No.—**1**, 6485-40-1; **2**, 2102-58-1; **3**, 2102-59-2; **4**, 55822-06-5.

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Non-Saytzeff Alumina-Catalyzed Dehydration of 2-Ferrocenyl-3-methyl-2-butanol

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In the last 10 years a wide investigation on the heterogeneous dehydration of alcohols catalyzed by metal oxides gave some explanations on how the metal oxide works as a catalyst. The results are reviewed in the literature.[1–4]

As to orientation, alumina,[5,6] hydroxyapatite,[7] and thoria[8] have been found to be very selective with respect to elimination from secondary alcohols. Alumina and hydroxyapatite give predominant Saytzeff orientation, while with thorium oxide Hofmann orientation is found. The sole exception is that reported by Vojtko et al.,[9] who obtained 97% of $Me_2CHCH_2CH{=}CH_2$ from the dehydration of 4-methyl-2-pentanol over alumina at 250 °C.

More recently, other Lewis acids, such as nickel sulfate, aluminum sulfate, zinc sulfide, and silica, have been used as catalyst in the dehydration of secondary alcohols,[10] the resulting orientation being analogous to that observed with alumina.

Fewer studies regard tertiary alcohols, but no selectivity is found with both alumina and thoria, as the Saytzeff/Hofmann ratio is a statistical one, depending on the number of hydrogens.

Also, the recent result reported by Peeters[11] about a non-Saytzeff dehydration of 2-methyl-2-pentanol over Al_2O_3 falls actually within the general behavior. This author obtains 65.3 as the highest percentage of 1-alkene, with a value of 70% after extrapolating to zero contact time, in order to neglect isomerization. With this alcohol the statistical orientation would give 75% of the terminal olefin.

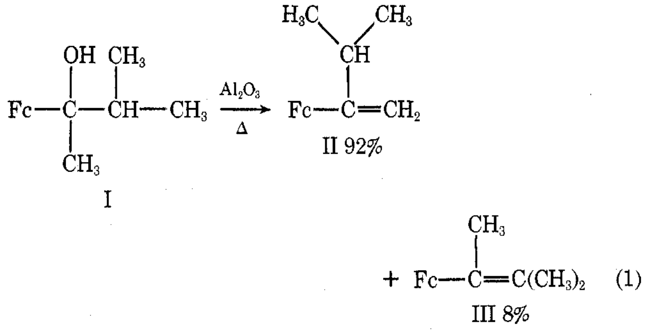
We now wish to report a truly non-Saytzeff result as obtained by the dehydration of 2-ferrocenyl-3-methyl-2-butanol (I) over Al_2O_3.

Ferrocenyl alcohols are known to undergo dehydration when treated with alumina.[12–14]

In the course of our studies on the methoxymercuration of vinylferrocene and related compounds,[15] the alkenes have been prepared by heating a mixture of alumina and the appropriate alcohol without solvent by a modification of the methods reported in the literature.[12–14]

After 2-ferrocenyl-3-methyl-2-butanol (I) was heated with Al_2O_3, the reaction mixture was taken up on a column and eluted with 40–70 °C petroleum ether to yield a red oil. On VPC examination this product was shown to consist of two species in the ratio 9:1. The NMR spectrum of the mixture in CCl_4 solution, Me_4Si being the internal standard, shows a group of signals which can be attributed to α-isopropylvinylferrocene (II) as follows: δ 1.17, doublet, $J = 7$ Hz, and δ 2.67, septet, $J = 7$ Hz (area ratio 6:1), due to the isopropyl group; δ 3.95, singlet, and δ 4.00–4.57, multiplet, due to the ferrocenyl system; δ 5.12 and 4.82, doublets, $J = 2$ Hz, due to the vinylic β protons.

Two more signals, i.e., at δ 1.72 and 2.02, with relative intensities 2:1, can be attributed to α,β,β-trimethylvinylferrocene (III). By comparing the areas of these signals with those due to the isopropyl protons, the more alkylated olefin turns out to form in 8% yield of the total product (eq 1):



(1)

This result is reproducible and independent of temperature in the tested range (105–180 °C). Contact times were between 10 min and 1 h, the percentage of α,β,β-trimethylvinylferrocene increasing with time up to 15%.

A run at 110 °C was quenched after 1 min to yield isopropylvinylferrocene exclusively.

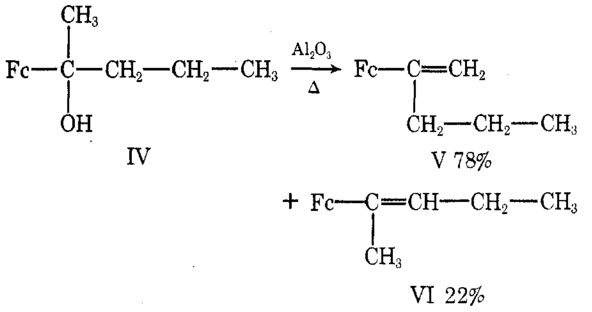
Ca. 1% of III appears when isopropylvinylferrocene is heated for 30 min at 140 °C, thus indicating that isomerization is negligible under the conditions used.

Dehydration experiments were made also with 2-ferrocenyl-2-pentanol (IV) and 2-ferrocenyl-2-butanol (VII), by heating these alcohols with Al_2O_3 for 20 min at 150 °C.

The reaction mixtures, treated as described above and examined on VPC, showed two peaks in both cases, their ratios being 9:1 and 8:1, respectively.

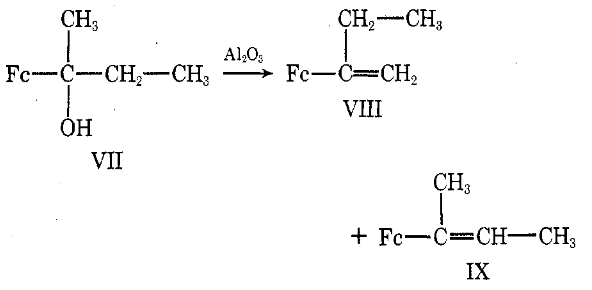
The NMR spectra of these mixtures in CCl_4 solutions are quite complicated in the alkyl protons region. However, it is possible to attribute the signals in the vinyl protons region to the different isomers.

Thus, the dehydration product of 2-ferrocenyl-2-pentanol (IV) (eq 2) shows two doublets at δ 5.48 and 5.08 ($J = 2$ Hz), due to the β vinylic protons of V, and a broad singlet at δ 4.72, due to the β vinylic proton of VI. By comparing the areas of these signals, V and VI turn out to be 78 and 22% of the total amount.



(2)

The dehydration product of 2-ferrocenyl-2-butanol (VII) (eq 3) shows two doublets, at δ 5.52 and 5.12 ($J = 2$ Hz), due to the β vinylic protons of VIII, and a broad singlet at δ 4.78, due to the β vinylic proton of IX. By comparing the areas of these signals, VIII and IX turn out to be 85 and 15% of the total amount.



(3)

It may be worth noting that the observed orientation does not appear to result from a stability difference due to hindrance to coplanarity in compound III, as compared to II. Judging from Dreiding models, coplanarity of the vinylic double bond with the cyclopentadienyl ring seems equally well attained in both cases. Further work is needed for an assessment of the orientation factors involved under the investigated conditions.

Experimental Section

VPC experiments have been carried out with a Fractovap C Erba instrument equipped with 1-m column of 5% methylsilicone SE-30 on Chromosorb W 60–80 with 0.5% ATPET.

NMR spectra were recorded with a JEOL C60-HL spectrometer, using CCl_4 as solvent and Me_4Si as internal standard.

Alumina (Merck, neutral, Brockmann) sieved to 80–140 mesh was calcined in air at 500 °C[10] and immediately used for the dehydration runs, after cooling under dry nitrogen atmosphere. The same results of dehydration isomer distribution were obtained by using neutral alumina (Merck, Brockmann I) sieved to 140–230 mesh, basic alumina (Merck, Brockmann I) sieved to 140–230 mesh, basic alumina (Merck, Brockmann I) sieved to 80–140 mesh, and commercial neutral alumina (Merck, Brockmann II–III).

2-Ferrocenyl-3-methyl-2-butanol (I) was obtained in a 100% yield by treating 2.6 g (0.01 mol) of isobutyrylferrocene with the equivalent amount of methyllithium in anhydrous diethyl ether. The reaction layer, hydrolyzed with aqueous 10% NH_4Cl, extracted with diethyl ether, and dried over anhydrous Na_2SO_4, gave an orange-yellow solid (mp 43–44 °C), the structure of which was confirmed by NMR spectroscopy.

Isobutyrylferrocene has been prepared in a 69% yield by Friedel–Crafts acylation of ferrocene with isobutyryl chloride and aluminum chloride in CH_2Cl_2.[16]

2-Ferrocenyl-2-pentanol and 2-ferrocenyl-2-butanol were prepared by the same way, starting from butyrylferrocene and propionylferrocene, respectively. These ketones were synthesized according to the literature.[17,18]

Several runs of alumina-catalyzed dehydration have been performed by heating 1 g of 2-ferrocenyl-3-methyl-2-butanol with 50 g of Al_2O_3 without solvent, at a temperature ranging between 105 and 180 °C and reaction times from 10 min to 1 h. The brown reaction mixture was eluted with 40–60 °C petroleum ether on an alumina column. The red oil obtained after evaporation of the solvent was examined by VPC and NMR. Like other vinylferrocenes, the reaction products decompose on standing, both in solution and without solvent, to give a brown residue, which is insoluble in organic solvents.

Acknowledgment. The author wishes to thank Professor G. Illuminati for helpful discussions.

Registry No.—I, 36928-96-8; isobutyrylferrocene, 41406-84-2.

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Carbonyl Oxygen Exchange of Phenyl Acetate during Acid-Catalyzed Hydrolysis

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The hydrolysis reactions of carboxylic acid derivatives usually proceed through tetrahedral addition intermediates, whose presence has generally been inferred from the observation of carbonyl oxygen exchange concurrent with the hydrolysis.[1] We report here an investigation into the extent of such exchange during the acid-catalyzed hydrolysis of phenyl acetate. No such study appears to have been reported, although phenyl esters have been found to undergo *no* exchange during base hydrolysis,[2] an observation which can be explained in terms of expulsion of the better leaving group, phenoxide, from the tetrahedral intermediate.

In general the A-2 hydrolysis of phenyl esters is found to be very similar to that of simple alkyl esters, for example in comparisons of absolute rates,[3] entropies of activation,[4] rate–acidity dependencies,[5] and substituent effects.[4–6] Some difference might, however, be anticipated in the exchange process with the quite different leaving group tendencies of *O*-phenyl vs. *O*-alkyl.

Experimental Section

Phenyl Acetate-*carbonyl*-^{18}*O*. The hydrochloride salt of *O*-phenyl-*N*-methylacetimidate[7] (15 g) was mixed with 30 ml of dry acetonitrile and 2 g of ^{18}O water (12.3% ^{18}O, Miles Laboratories) was added. After refluxing for 1 h, the cooled solution was added to water and extracted with ether. Quantitative GC analysis of the ether extract revealed that the imidate salt had been completely hydrolyzed, but to a mixture of 65% phenyl acetate and 35% phenol. The latter was removed by washing briefly with cold 1 N NaOH. Washing with water, drying ($MgSO_4$), and distillation yielded pure ester, isolated yield 6.4 g (58%). Mass spectrometric analysis indicated an ^{18}O content of ca. 12.2%.

A variety of experimental conditions were employed in an attempt to improve the yield of ester, but in every case lower yields in fact resulted, the remainder of the product being phenol. Hydrolysis in 0.1 N HCl was found to produce 66% phenyl acetate and 34% phenol. (Under the hydrolysis conditions the ester product is stable.)

Hydrolysis. The hydrolysis rate in 1.5 N HCl in 40:60 (v/v) dioxane–water was determined as previously described.[5]

Exchange. The labeled ester (2 g) was dissolved in 500 ml of 1.5 N HCl in 40:60 dioxane–H_2O and the solution thermostated at 25.0 °C. At appropriate intervals samples were withdrawn and extracted with methylene chloride. This was washed with cold 1 N NaOH and water and dried ($MgSO_4$) and the solvent was removed. GC analysis showed that the small amount of remaining liquid was pure ester.

The ^{18}O content of this ester was determined by direct mass spectrometric analysis on an AEI MS902 equipped with a vacuumetrics ratiometer. With each sample approximately 40 values of the (P + 2)/P ratio were obtained by repeat scanning, and the average value then was compensated for natural abundance of isotopes in other positions.[8] The reproducibility was about 0.03 atom % for samples run during the same day. In a control experiment a sample of labeled ester was mixed with ca. tenfold of its hydrolysis products, dissolved in the hydrolysis medium, and immediately subjected to the workup and analysis procedure. No change was observed in the amount of label present.

Results and Discussion

The ^{18}O content of unreacted phenyl acetate is listed for varying amounts of hydrolysis in Table I, and plotted as a function of hydrolysis in Figure 1. These reveal a small, but significant amount of exchange concurrent with hydrolysis, and yield a value of 120 for k_H/k_E, the ratio of the hydrolysis and exchange rates.

Table I. Excess Oxygen-18 in Phenyl Acetate Samples after Partial Hydrolysis in Acidic Solution[a]

Completion of hydrolysis,[b] %	% ^{18}O (excess)	
	Run A	Run B
0	11.98	12.07
48.0	11.88	12.00
73.0	11.85	11.94
86.0	11.77	11.87
92.7		11.82
k_H/k_E[c]	118	124

[a] 40:60 dioxane–water containing 1.5 N HCl. [b] Rate constant for hydrolysis = 0.000218 s^{-1}. [c] Reciprocal of slope of plot of log (P/P_0) vs. log $([ester]/[ester]_0)$; see Figure 1.

In comparison to simple alkyl esters this value is considerably larger, e.g., with ethyl acetate[9] and *n*-propyl acetate,[4] $k_H/k_E = 5$, and with methyl formate,[10] $k_h/k_E = 11$. These k_H/k_E ratios are determined by the partitioning of the tetrahedral intermediate to reagents (exchange) or products (hydrolysis), recognizing that in acid solution the breakup of this