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.

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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

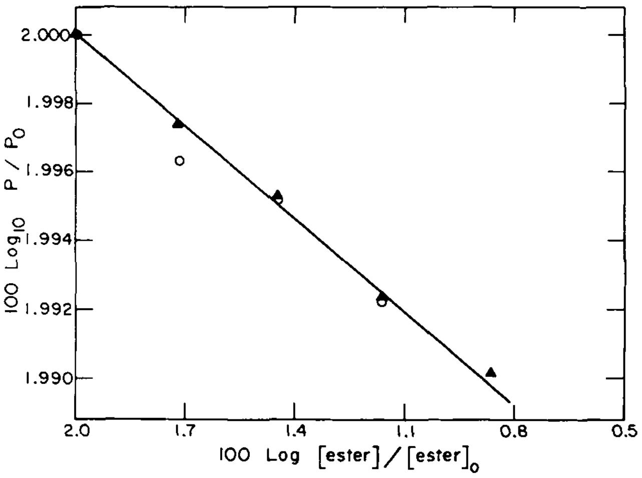
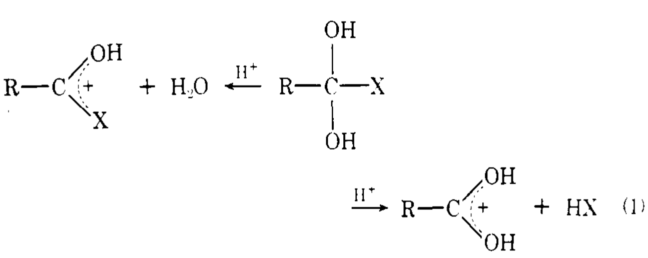


Figure 1. Concurrent hydrolysis and exchange of phenyl acetate; P, P_0 = % ^{18}O (excess) at times t and 0, (○,▲) = duplicate experiments.

intermediate is probably acid catalyzed with expulsion of a neutral leaving group and formation of a resonance stabilized cation, eq 1 (where the proton transfer may occur simultaneously with leaving group departure or in a prior equilibrium).



$$R{-}\overset{+}{C}(OH)(X) + H_2O \xleftarrow{H^+} R{-}C(OH)_2{-}X \xrightarrow{H^+} R{-}\overset{+}{C}(OH)(OH) + HX \quad (1)$$

Three factors are then important in determining k_H/k_E: (1) the intrinsic leaving group abilities of HX vs. H_2O, (2) the basicities of X vs. OH, and (3) the relative stabilities of the cationic products (i.e., the driving force for expulsion[11]). For phenyl acetate 1 and 3 favor the forward process (expulsion of PhOH) while 2 favors the reverse (expulsion of H_2O), the observed k_H/k_E ratio then suggesting that the former are more important.

This is the opposite situation to that found in considering amide hydrolysis and exchange, where again hydrolysis dominates (e.g., for benzamide, k_H/k_E = 320[12]). Here, however, one must argue that factor 2, the much greater basicity of nitrogen, is the more important, since 1 and 3 must favor expulsion of OH over NH_2.

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Registry No.—*o*-Phenyl-*N*-methylacetimidate, 22084-79-3; acetonitrile, 75-05-8; phenyl acetate, 122-79-2; phenol, 108-95-2.

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Carbon-13 Nuclear Magnetic Resonance Spectra of Kojic Acid and Other 4-Pyrone Derivatives

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4-Pyrone derivatives are common flavoring agents and food preservatives which have been investigated with regard to bactericidal activity.[1] Considerable uncertainty remains as to the degree of aromaticity of kojic acid and of its parent structure, 4-pyrone, despite the application of a large number of chemical and spectroscopic criteria.[2,3] Thus, 4-pyrones are reported to give substitution products upon bromination.[4] The lack of reactivity of 4-pyrones in Diels–Alder reactions is remarkable.[5] The dipole moment of 4-pyrone (ca. 4 D) is substantially larger than that calculated for a non-resonance-stabilized molecule (ca. 2 D).[3,6,7]

The ^1H NMR spectra have been interpreted in terms of ring current effects, which were considered to reflect a high degree of aromaticity.[6] Abraham has questioned deductions regarding the degree of aromaticity based on ring current effects,[8] and these observations remain controversial. The vicinal ^1H coupling constant between H-2 and H-3 (5.9 or 6.2 Hz)[3,9] is similar both to aromatic compounds and to 2-cyclohexenone.

The most damaging evidence against aromaticity is the very low magnetic susceptibility, which is regarded by Beak et al. as indicative of essentially no aromatic character.[10]

To the best of our knowledge, no ^{13}C NMR studies of kojic acid or pyrone derivatives have appeared,[11] although Goldstein and co-workers were able to obtain some significant data from the study of ^{13}C satellites in ^1H spectra.[9] The ^{13}C chemical shifts determined in this study are recorded in Table I, and the various ^{13}C–H coupling constants are listed in Table II. In general, the ^{13}C data, like the observations mentioned above, are similar to α,β-unsaturated ketones in some respects and to aromatic heterocycles in other respects. In toto, we feel that these data and the data cited above support the postulate that a degree of aromaticity is present in the 4-pyrone system.

Scheme I illustrates the chemical shifts of kojic acid in relation to various model compounds. In the nonaromatic

Scheme I