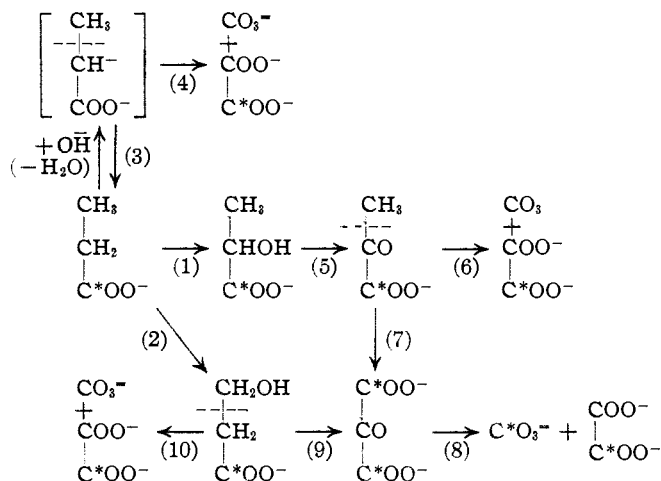


leads to further predictions and suggests future experiments.

TENTATIVE FORMULATION OF PROPIONATE OXIDATION BY ALKALINE PERMANGANATE



The mesoxalate formed from pyruvate by step (7) is "symmetrical" and therefore the C\* content of the carbonate and oxalate formed in (8) will be equal. It is evident from Tables II, III and IV that the rate of (6) is almost equal to the rate of (7), and (10) proceeds at approximately the same rate as (9). In other words *the α-β link is often ruptured before mesoxalate is produced*. While the ratios of (6)/(7) and (9)/(10) are independent of the hydroxide concentration, step (3) is favored over (1) and (2) by increasing alkalinity. The primary step in (3) is the reversible removal of hydrogen ion by OH<sup>-</sup> resulting in the forma-

tion of  $\text{H}_3\text{C}-\overset{\ominus}{\underset{\text{H}}{\text{C}}}-\text{COO}^-$  which due to the un-

shared electron pair may be more susceptible to oxidation.

### Summary

1. Methods for the rapid synthesis of  $\text{CH}_3\text{CH}_2\text{C}^*\text{OOH}$ ,  $\text{CH}_3\text{CHOHC}^*\text{OOH}$ , and  $\text{CH}_2\text{OHCH}_2\text{C}^*\text{OOH}$  using  $\text{C}^{11}\text{O}_2$  are described.

2. Oxidation of these acid anions by alkaline permanganate yields one mole of carbonate and oxalate each.

3. Oxalate is remarkably inert to alkaline permanganate (2 N in sodium hydroxide) even at 100°.

4. For propionate in hydroxide solutions of from 10<sup>-4</sup> to 2 N concentration ~71% of the carbonate is derived from the β-carbon. At higher hydroxyl ion concentration the α-β carbon bond is broken even

more preferentially.

5. No exchange between  $\text{C}^*\text{O}_3^-$  and  $\text{C}_2\text{O}_4^-$  could be detected.

6. With lactate and β-hydroxypropionate, ~70% of the carbonate originates from the β-carbon, and this value, within the experimental error, is unchanged by altering the hydroxide ion concentration from 2 to 12 N.

7. The results indicate that with propionate the α-β carbon bond is broken in strongly basic solutions before either α- or β-hydroxypropionate can be formed as an intermediate in the oxidation.

BERKELEY, CALIFORNIA

RECEIVED JULY 6, 1942

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

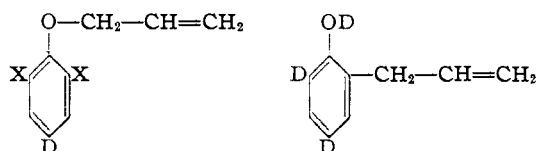
## Use of Deuterium as a Tracer in the Claisen Rearrangement

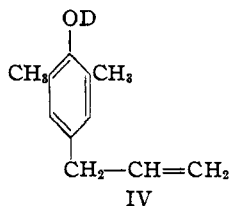
By G. B. KISTIAKOWSKY AND ROBERT L. TICHENOR

In the mechanisms proposed for the Claisen rearrangement<sup>1</sup> the assumption is made that the hydrogen atom displaced by the migrating allyl group moves to the oxygen atom of the resulting phenol. It was thought that definite evidence of the movement of the displaced hydrogen atom could be obtained by using deuterium as a tracer. We have, therefore, carried out the rearrangement of the allyl ethers of 2,4,6-trideutero-phenol (I)

(1) D. Stanley Tarbell, *Chem. Rev.*, **27**, 495 (1940).

and 4-deutero-2,6-dimethyl-phenol (III). Our results are summarized in Table I.





The acetate of IV formed during the analysis for phenolic deuterium showed no detectable deuterium content (analysis by combustion and infrared absorption, estimated  $\ll 0.25\%$  deuterium in the resulting water).

TABLE I

Expt. No.	Compound	% D in indicated positions		% D on oxygen after rearrangement	
		Calcd. <sup>a</sup>	Found <sup>b</sup>	Calcd.	Found
1	Allyl 2,4,6-tri-deuterophenyl ether	51	51	51	15 <sup>e</sup>
2		77	70	70	52
3		77	70	70	52
4	2-Allyl-4,6-di-deuterophenol	50			2.5 <sup>e</sup>
5	Allyl 4-deutero-2,6-dimethylphenyl ether	72.3	< 20 <sup>d</sup>	< 20	15
6		72	< 20 <sup>d</sup>	< 20	13

<sup>a</sup> Assuming equilibrium between the indicated positions, the phenolic hydrogen (the phenol was deuterated before the ether was made) and the heavy water. Losses in alkylation were neglected. <sup>b</sup> Calcd. from total analyses (combustion) and assumption all the deuterium was on the indicated positions. <sup>c</sup> After heating the phenol, not after a rearrangement; see text. <sup>d</sup> These are upper limits assuming all the deuterium in the 4-position. If the methyl groups had been deuterated a far higher value (factor of 21) should have been found. <sup>e</sup> This low value can be attributed to poor technique in this first experiment.

This result together with 5 and 6 of Table I allow us to conclude that in the rearrangement of III all the displaced hydrogen goes to the oxygen; none is to be found elsewhere in the molecule. We may also conclude that the structure of III is correct, *i. e.*, that deuteration of the methyl groups and the meta positions was negligible.

From results 2 and 3 of Table I we see that 74% of the displaced hydrogen of I moves to the oxygen, but some 26% is unaccounted for. The low figure may be due to (1) loss of deuterium by exchange during evolution of hydrogen chloride (see analysis) or (2) to some exchange with other hydrogen of the molecule subsequent to rearrangement. Reason (2) is partly excluded by result 4 of Table I. (1) is reasonable in view of the known exchanges of esters.<sup>2</sup>

(2) Hsü, Ingold and Wilson, *J. Chem. Soc.*, 79 (1938).

Kincaid and Tarbell<sup>3</sup> have found that the rate of ortho rearrangement is first order. It is unlikely that a unimolecular reaction proceeds by two paths of nearly equal free energies of activation. Our results with III indicate that its rearrangement proceeds by a single path. In view of these two facts we are rather inclined to say that the rearrangement of I goes by a single path and that our low results can be attributed to experimental errors.

Result 4 of Table I shows that negligible exchange occurs between the phenolic hydrogen and deuterium in the ortho and para positions of 2-allyl phenol when the phenol is subjected to a heat treatment equal to that employed in the rearrangement of I.

Our picture of the movement of the hydrogen atom in the para rearrangement is not that of a directed jump, but rather that the proton is displaced by the migrating allyl group and subsequently finds its way to some oxygen anion.

### Experimental

**Deuteration of Phenols.**—Ordinary phenol was deuterated by exchange with heavy water in the presence of hydrogen chloride for the time (two hours) and temperature (100°) shown by Koizumi<sup>4</sup> to be necessary for attaining equilibrium. Best and Wilson<sup>5</sup> have shown that only the ortho and para positions of phenol are deuterated under these conditions. 2,6-Dimethylphenol was deuterated by allowing it to exchange with heavy water for thirty hours at 100° in the presence of hydrogen chloride. No previous work has been done on its deuteration and we made no direct determination of the amount of substitution, but subsequent analyses of the ethers showed that the methyl groups and the meta positions did not exchange. We can explain the very low amount of deuterium in the 4 position (< 20% instead of a calculated 72%) by an increased rate of loss during the formation of the ether or by a failure to attain equilibrium in the initial exchange. These analyses of III (Table I) are an upper limit and thus prove that the methyl groups and the meta positions are not deuterated.

**Preparation of Ethers.**—13.5 g. (0.34 mole) of sodium hydroxide, 25 cc. of water, 15 cc. of freshly distilled allyl bromide, 25 cc. of acetone and 10 g. (0.106 mole) of 2,4,6-deuterophenol (or 13 g. of 2,6-dimethyl-4-deuterophenol)<sup>6</sup> were added quickly in this order to a 3-neck, 250-cc. flask equipped with a wire stirrer, reflux condenser and dropping funnel. The mixture was stirred and refluxed for two hours, cooled, extracted with petroleum ether, and the extract washed with sodium hydroxide, then with water and finally dried over magnesium sulfate (neutral drying

(3) Kincaid and Tarbell, *THIS JOURNAL*, 61, 3085 (1939).

(4) Masao Koizumi, *Bull. Chem. Soc., Japan*, 14, 353 (1939).

(5) A. P. Best and C. L. Wilson, *J. Chem. Soc.*, 28 (1938).

(6) We wish to thank Dr. W. E. Vaughan and the Shell Development Co. for the gift of 2,6-dimethylphenol.

agent to slow exchange). After concentration on the steam-bath the allyl phenyl ether was distilled at a pressure of 10 mm. (2 mm. for allyl 2,6-dimethylphenyl ether) through a small Podbielniak column. A faint yellow color persisted in all our preparations of allyl 2,6-dimethylphenyl ether. All the other compounds were colorless and all of them had boiling points and refractive indices in agreement with those in the literature.

**Rearrangement.**—The purified ether was placed in a clean Pyrex tube, cooled, evacuated, frozen and melted under vacuum to remove dissolved gases and then sealed off. The tube was heated in a Wood's metal bath until samples of the non-deuterated phenyl ether, rearranging simultaneously, were found to be almost entirely soluble in 20% sodium hydroxide solution. Bath temperatures and times: allyl phenyl ether, 230–240°, five to six hours; allyl 2,6-dimethylphenyl ether, 190–200°, four to five hours.

**Analysis of Phenolic Hydrogen.**—Three to four grams of the product of rearrangement, 3 cc. of acetyl chloride and a boiling chip were placed in the reaction bulb of a gas train, and the hydrogen chloride which evolved was swept through a dry ice-acetone-cooled trap to remove acetyl chloride, and was collected in a liquid air trap. The liquid air trap was then cut off from the gas train, evacuated and the gas allowed to evaporate into the evacuated infrared absorption cell. A reservoir of ordinary hydrogen chloride was connected to the filling system so that the pressure in the cell could be increased if insufficient gas was obtained from the phenol. When hydrogen chloride was added from the reservoir, the gases were mixed by freezing down in a liquid-air trap.

The infrared absorption of the resulting mixture of hydrogen and deuterium chlorides was measured over the absorption region for both components (3.46 and 4.8  $\mu$ ).<sup>7</sup> The measurements were made at a total pressure of 368 mm. with a cell 20 cm. long. From the infrared absorption plates a curve of absorption percentage vs. wave length was obtained, and by measuring the area of the bands we can estimate the concentration of deuterium by comparing the area with the areas observed when known concentrations of deuterium were present. In determining the area of an absorption band there is considerable uncertainty in determining the base line (the blank). It was found that this base line apparently varied as the cell was used, and, therefore, in all measurements the edges of the absorption curve on either side of the absorption region were used as a base line. This was probably the greatest source of error in the analyses. The accuracy of analysis of a deuterium chloride-hydrogen chloride mixture was not better than  $\pm 5\%$  but was sufficient for the present purpose.

**Hydrogen Chloride and Deuterium Chloride.**—Hydrogen chloride was obtained by dropping hydrochloric acid onto sulfuric acid. Deuterium chloride was made by the method of Langseth and Klit.<sup>8</sup> The resulting gas probably contained traces of sulfur dioxide. The thionyl chloride which we used was purified as recommended by Fieser.<sup>9</sup>

(7) We used the instrument described by Gershinowitz and Wilson, *J. Chem. Phys.*, **6**, 197 (1938). We wish to thank Professor E. Bright Wilson, Jr., for advice and help in operation of the spectrograph.

(8) A. Langseth and A. Klit, *Kgl. Danske Videnskab. Selskab. Math.-fys. Medd.*, **15**, No. 13, 22 (1937); *Chem. Abs.*, **32**, 2515 (1938).

(9) Fieser, "Experiments in Organic Chemistry." D. C. Heath and Co., Boston, 1935, p. 339.

**Analysis for Deuterium on Carbon.**—Nuclear deuterium was determined by combustion and the density of the resulting water found by the falling drop method or by use of the interferometer.<sup>10</sup>

**Acetate of 4-Allyl-2,6-dimethylphenol.**—As a check on the course of the reactions used to produce hydrogen chloride, the resulting acetates were purified and identified by their physical constants or by analysis. The acetate of 4-allyl-2,6-dimethylphenol is a new compound, a colorless oil, b. p. (2 mm.) 105–110°, bath temperature 146–160°,  $n_D^{25}$  1.5050. *Anal.* Calcd. for  $C_{13}H_{16}O_2$ : C, 76.42; H, 7.90. Found: C, 76.81; H, 8.33. The phenol from which this acetate was prepared was carefully purified and found to melt at 26–27°,  $n_D^{25}$  1.5356. The phenylurethan of this phenol melted at 137–139° (uncor.) after two recrystallizations from ligroin.

**Polymerization During Rearrangement.**—We were troubled at first by a polymerization of allyl phenyl ether similar to that described by Hurd.<sup>11</sup> Occasionally, some would polymerize during the rearrangement, whereas much of our material gave 95% yields of the expected phenol. It was found that the addition of one drop of allyl bromide to 2 g. of the ether (which was known to rearrange normally) produced polymerization. None of the other reactants or products acted in this manner. Careful removal of allyl bromide during distillation (prevention of diffusion of allyl bromide from first fraction into later fractions in the multiple receiver of the still by removal of first fraction before completing the distillation) gave, in all cases, an ether which rearranged without darkening or polymerization.

### Summary

1. The deuterium atom displaced by the migrating allyl group in the Claisen rearrangement of allyl 4-deutero-2,6-dimethylphenyl ether becomes the phenolic deuterium of the product.
2. It has been shown that the bulk of the deuterium displaced by the migrating allyl group in the rearrangement of allyl 2,4,6-trideuterophenyl ether becomes the phenolic deuterium of the product. It is likely that all the displaced deuterium becomes phenolic deuterium.
3. Phenolic tautomerism of 2-allylphenol was not observed to occur to an appreciable extent on heating for the time and temperature necessary to rearrange allyl phenyl ether (six hours at 210–230°).
4. A new method for estimating the deuterium content of hydrogen chloride-deuterium chloride mixtures has been outlined. It has been used in estimating the deuterium content of phenolic hydrogen.

CAMBRIDGE, MASS.

RECEIVED JUNE 6, 1942

(10) We thank Edward S. Lewis for the use of his apparatus and for the analysis of several samples. The apparatus is described by Keston, Rittenberg and Schoenheimer, *J. Biol. Chem.*, **122**, 227 (1937).

(11) Charles D. Hurd and Louis Schmerling, *THIS JOURNAL*, **59**, 107 (1937).