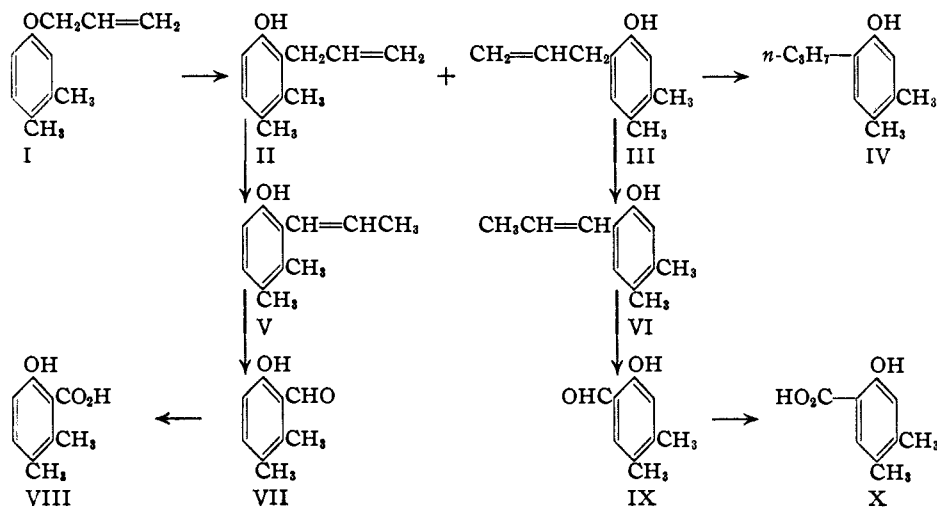


[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Claisen Rearrangement of Allyl 3,4-Dimethylphenyl Ether¹BY C. S. MARVEL AND N. A. HIGGINS²

In connection with an investigation of inhibitors we had need for a sample of 3,4-dimethyl-6-propylphenol (IV) and prepared it by the Claisen rearrangement of allyl 3,4-dimethylphenyl ether (I) followed by hydrogenation



We found that the rearrangement of the allyl ether (I) gave rise to a mixture of phenols (II and III) as might be expected from the report of Claisen and Eisleb³ on the behavior of allyl 3-methylphenyl ether. Reduction of this mixture gave a mixture of the two propyl phenols from which a single isomer separated as a crystalline solid, m. p. 59°, in 52% yield.

Since it appears that no one has carefully examined the isomers that may be formed in an allyl rearrangement of this type,⁴ we have established the structure of the two isomers and determined their ratio in our rearrangement mixture.

The mixed phenols (II and III) were isomerized with alkali to give the mixed propenyl phenols (V and VI), which were then ozonized to give the mixed aldehydes (VII and IX). These aldehydes are known compounds⁵ and have different crystalline forms so the mixture obtained by ozonization could be separated mechanically into the two pure aldehydes. The identities of these aldehydes were confirmed by oxidation to the known acids (VIII and X).⁶

By the quantities of the two aldehydes obtained, it was established that in the original rearrange-

ment 70 ± 5% of the 6 isomer (III) and 30 ± 5% of the 2 isomer (II) was produced. Hence the pure *n*-propylphenol which was obtained by hydrogenation must have been the desired 3,4-dimethyl-6-*n*-propylphenol (IV).

Experimental

Allyl 3,4-Dimethylphenyl Ether.—To 175 ml. of absolute alcohol in a 500-ml., three-necked flask, fitted with stirrer, dropping funnel, and condenser were added 11.5 g. (0.5 mole) of sodium chips. When solution was effected, 61.0 g. (0.5 mole) of 4-hydroxy-1,2-dimethylbenzene was added and the flask heated in an oil-bath to 85–90°. The mixture was stirred, and 41.8 g. (0.55 mole) of distilled allyl chloride was added slowly. The reaction mixture was heated for fifteen hours, stirring being discontinued after seven hours. The cooled reaction mixture was poured into 1 liter of water in a separatory funnel and the layers separated. The aqueous layer was extracted with two 100-ml. portions of petroleum ether (b. p. 35–45°) and the extract was combined with the previous organic layer. This solution was washed with 10% sodium hydroxide solution to remove unreacted starting material, dried over anhydrous magnesium sulfate, and distilled in a modified Claisen flask. The allyl 3,4-dimethylphenyl ether, 66.1 g., b. p. 75–79° (3 mm.), n_D^{20} 1.5200, d_4^{20} 0.9543, was obtained in 82% yield.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.45; H, 8.70; MR, 49.87. Found: C, 81.40; H, 8.70; MR, 51.28.

Mixed 2- and 6-Allyl-3,4-dimethylphenols.—Allyl 3,4-dimethylphenyl ether, 66.1 g. (0.41 mole), was rearranged by heating with one-half its weight of freshly distilled diethylaniline in a 245° bath for one-half hour. The boiling point of the mixture rose gradually during this time from 218 to 231°. The cooled mixture was dissolved in petroleum ether (b. p. 35–45°) and the diethylaniline removed by several washes with dilute sulfuric acid. The product was then removed as the potassium salt by extraction with aqueous-alcoholic potassium hydroxide (35 g. of potassium hydroxide, 25 g. of water, 90 g. of methanol) in four equal portions. The alkaline solution was washed with petroleum ether, acidified, and extracted exhaustively with petroleum ether. The petroleum ether solution was dried over anhydrous magnesium sulfate and distilled in a modified Claisen flask. The mixed 2- and 6-allyl-3,4-dimethylphenols distilled at 82–85°

(1) This investigation was carried out under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program.

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(3) Claisen and Eisleb, *Ann.*, **401**, 21 (1913).

(4) Tarbell, "The Claisen Rearrangement" ("Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944).

(5) Clayton, *J. Chem. Soc.*, **97**, 1404 (1910).

(1 mm.), n_D^{20} 1.5434, d_4^{20} 0.9671. The yield was 46.8 g. or 71% of the theoretical amount.

Mixed 3,4-Dimethyl-2-propylphenol and 3,4-Dimethyl-6-propylphenol.—Hydrogenation of 46.8 g. of the mixed 2- and 6-allyl-3,4-dimethylphenols in ethanol solution at 25° with a Raney nickel catalyst proceeded smoothly and the theoretical amount of hydrogen was absorbed in twenty minutes. The catalyst was removed by filtration and the mixture distilled in a modified Claisen flask to yield 30.6 g. (65%) of mixed 3,4-dimethyl-2-propylphenol and 3,4-dimethyl-6-propylphenol, b. p. 77–77.5° (<1 mm.).

3,4-Dimethyl-6-propylphenol.—The mixture of 3,4-dimethyl-2-propylphenol and 3,4-dimethyl-6-propylphenol was a very viscous oil. When this material had stood for two weeks, crystals began to form; crystal growth proceeded, but the whole of the material did not crystallize. The crystals were removed by filtration through a sintered glass filter; thus 16.0 g. (52%) of the material was obtained as a white crystalline solid. This was recrystallized four times from petroleum ether (b. p. 35–45°) to a constant melting point of 59°.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.45; H, 9.75. Found: C, 80.49; H, 9.83.

Mixed 3,4-Dimethyl-2-propenylphenol and 3,4-Dimethyl-6-propenylphenol.—To a 500-ml. round-bottomed flask containing 152 g. of *n*-amyl alcohol was added 105 g. of potassium hydroxide flakes. The mixture was refluxed for a short time, the clear supernatant liquid decanted, and to it was added 40 g. (0.247 mole) of the rearrangement product from allyl 3,4-dimethylphenyl ether (2- and 6-allyl-3,4-dimethylphenols). The solution was heated at the boiling point for twenty-four hours, the amyl alcohol removed by steam distillation, and the remaining solution acidified with phosphoric acid. The acidified solution was extracted with four 100-ml. portions of ether and the ether solution dried over anhydrous magnesium sulfate and distilled without fractionation. A yield of 24.6 g. (61.6%) of mixed 3,4-dimethyl-2-propenylphenol and 3,4-dimethyl-6-propenylphenol was obtained.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.45; H, 8.70. Found: C, 81.90; H, 8.59.

4,5- and 5,6-Dimethylsalicylaldehydes.—A solution of 8.4 g. (0.052 mole) of mixed 3,4-dimethyl-2-propenylphenol and 3,4-dimethyl-6-propenylphenol in 400 ml. of chloroform was ozonized for six hours at 0° with approximately 4% ozone. The chloroform solution of the ozonide was treated with 120 ml. of water, and the chloroform was distilled from the mixture under reduced pressure. After the chloroform had been completely removed, the flask was heated vigorously and the contents distilled. A yield of 4.95 g. (63.8%) of aldehyde was obtained from the steam-distillate by ether extraction, while 1.4 g. of material remained in the pot.

The aldehyde thus obtained was converted to the bisulfite addition product by shaking vigorously with nearly saturated sodium bisulfite solution at about 40°. The white crystalline addition product was removed by suction filtration, washed repeatedly with ether, and finally decomposed with 150 ml. of warm 3% hydrochloric acid. The purified aldehyde was recovered by ether extraction, drying of the extract, and removal of the solvent by distillation. The solid, light-yellow aldehyde thus obtained was recrystallized from petroleum ether (b. p. 35–45°), the solution being allowed to cool very slowly so that large crystals formed. Two types of crystals were formed, long spike-like needles of 5,6-dimethylsalicylaldehyde and lustrous plates of the 4,5-isomer; a quantity of the material was separated into its component crystals mechanically. Thus it was determined that 70 = 5% of the material crystallized as plates and 30 = 5% as needles. The two crops of crystals were separately recrystallized first from dilute alcohol and then from petroleum ether (b. p. 35–45°). The plates of 4,5-dimethylsalicylaldehyde melted at 69° and the needles of 5,6-dimethylsalicylaldehyde at 70°.

Anal. Calcd. for $C_9H_{10}O_2$: C, 72.00; H, 6.72. Found: Plates—C, 72.04; H, 6.65; Needles—C, 72.10; H, 6.60.

Clayton⁴ who prepared a similar mixture of aldehydes from a Reimer-Tiemann reaction on 3,4-dimethylphenol found that 4,5-dimethylsalicylaldehyde crystallized in plates, m. p. 71°, and the 5,6-isomer in needles, m. p. 72°.

4,5-Dimethylsalicylic Acid.—About 0.1 g. of 4,5-dimethylsalicylaldehyde was sprinkled into 0.6 g. of fused sodium-potassium hydroxide (50–50 containing a little water) at 210° in a nickel crucible. As soon as gas evolution had ceased the mixture was cooled, dissolved in water, filtered, and acidified. The 4,5-dimethylsalicylic acid which precipitated was collected on a filter, dried, and recrystallized from aqueous methanol. The purified product melted at 197.6°. The literature⁵ reports a melting point of 198–199°.

5,6-Dimethylsalicylic Acid.—This material was prepared from 5,6-dimethylsalicylaldehyde exactly as described above for 4,5-dimethylsalicylic acid. The 5,6-dimethylsalicylic acid melted at 140°. Clayton⁵ describes this acid as melting at 142–143°.

Summary

The rearrangement of allyl 3,4-dimethylphenyl ether gives 70 = 5% of 6-allyl-3,4-dimethylphenol and 30 = 5% of 2-allyl-3,4-dimethylphenol.

Reduction of this mixture of allyl phenols gives a 50% yield of crystalline 3,4-dimethyl-6-*n*-propylphenol.

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RECEIVED FEBRUARY 26, 1948