[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WYOMING]

The *para*-Claisen Rearrangement. IV. Demonstration of Intramolecularity[1]

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Rearrangement of a mixture of the γ-ethylallyl ether of 2,6-dimethylphenol and the γ-methylallyl ether of methyl *o*-cresotinate has failed to give any evidence of crossed products. It is concluded that the *para*-Claisen rearrangement of γ-substituted allylic ethers is strictly intramolecular.

The intramolecular nature of the *para*-Claisen rearrangement of unsubstituted allyl ethers has been demonstrated convincingly by Schmid and Schmid who rearranged C-14 labeled allyl 2,6-dimethylphenyl ether in the presence of allyl 2-carbomethoxy-6-methylphenyl ether and found no exchange.[3] At approximately the same time the work of Schmid and Schmid appeared, a similar experiment was in progress in our laboratories with substituted allylic ethers, the results of which accord with the findings of Schmid and Schmid and extend the generalization to allylic ethers with small γ-alkyl substituents.[4]

As a pair of ethers suitable for a "crossing" experiment, the γ-methylallyl ether of methyl *o*-cresotinate I and the γ-ethylallyl ether of 2,6-dimethylphenol II were chosen. Choice of this pair of ethers was dictated by the fact that their rates of rearrangement are nearly the same (*cf.* Fig. 1) and thus a "mixed" rearrangement of these two should provide the best opportunity for the observation of crossed products (V and VI). With respect to the ease of isolation of crossed products, an alternative pair, the γ-ethylallyl ether of methyl *o*-cresotinate VII and the γ-methylallyl ether of 2,6-dimethylphenol VIII would have been more desirable, but as shown in Fig. 1, the relative rates of this pair were not so favorable.

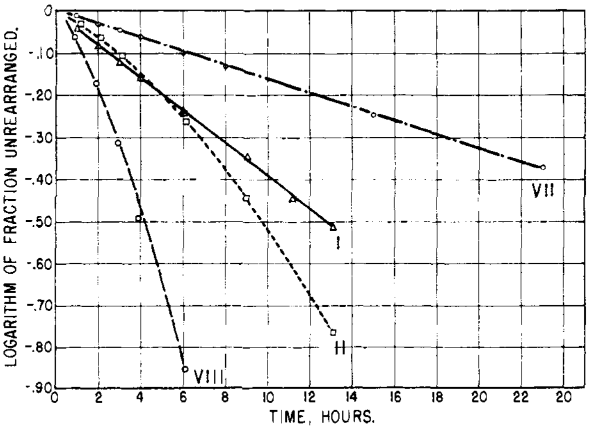
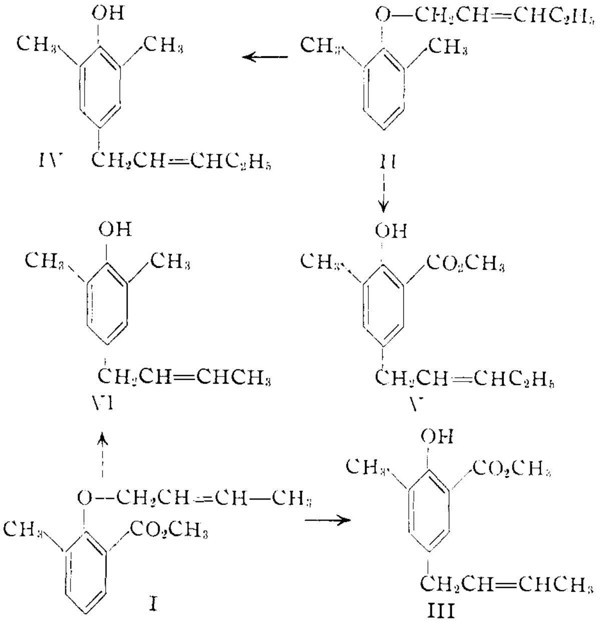


Fig. 1.—Rates of rearrangement of allylic ethers I, II, VII and VIII at 158.4°.



The γ-methylallyl and γ-ethylallyl ethers of methyl *o*-cresotinate, their rearrangement products and rate data were available to us from other studies.[5]

The γ-methylallyl and γ-ethylallyl ethers of 2,6-dimethylphenol (VIII and II) were synthesized by standard methods and their rates of rearrangement in the pure liquid measured at 158.4°. Rearrangement gave the corresponding 4-(γ-methylallyl)- and 4-(γ-ethylallyl)-2,6-dimethylphenols (VI and IV), characterized by the 3,5-dinitrobenzoates of their dihydro derivatives. Infrared spectra also were obtained for these compounds and confirmed their structural assignment.

The "mixed" rearrangement was carried out by heating equimolar portions of the two ethers I and II in a sealed, evacuated tube for 33 hours at 158°. Separation of the rearrangement products into 2,6-dimethylphenol derivatives and *o*-cresotinic acid derivatives was accomplished by sodium bicarbonate extraction of the saponified reaction mixture.

Examination of the sodium bicarbonate-soluble fraction failed to reveal any evidence of the "crossed" product V. This fraction consisted of a quantity of crude acid equivalent to 84% of the theoretical yield (assuming 100% rearrangement). Recrystallization from hexane permitted an 89.4% recovery of the acid corresponding to III. The

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[1] Taken from the Ph.D. dissertation of R. L. Crecelius, University of Wyoming, June, 1954.

[2] Research Corporation Fellow, 1952–1953.

[3] H. Schmid and K. Schmid, *Helv. Chim. Acta*, **36**, 489 (1953).

[4] To what extent the rule of strict intramolecularity will hold is not known with certainty. D. S. Tarbell in "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, pp. 14–15, cites examples which appear to involve concurrent dissociation. These compounds are characterized by a high degree of substitution in the allylic system.

[5] (a) S. J. Rhoads, R. Raulins and R. D. Reynolds, THIS JOURNAL, **76**, 3456 (1954); (b) S. J. Rhoads and R. L. Crecelius, *ibid.*, **77**, 5057 (1955).

amount of pure acid recovered corresponds to at least a 75.2% yield of the product expected from an intramolecular rearrangement of I.

The fraction containing the 2,6-dimethylphenol derivatives was vacuum distilled to yield a light yellow oil amounting to 87% of the theoretical yield (assuming 100% rearrangement). Subsequent fractionation gave four fractions, corresponding to 74.1% of the theoretical yield. The last three fractions, which represented 86% of the total distillate, proved to be pure IV as judged by refractive index, infrared analysis and characterization by known derivatives. Hydrogenation of a portion of the first fraction followed by preparation of the 3,5-dinitrobenzoate of the dihydro derivative gave solid material of a wide melting range which did not improve on recrystallization. Since pure derivatives could not be isolated from this first fraction, infrared analysis was used to establish the absence of the crossed product VI.

Figure 2 shows the 9.0–13.2 μ region of the infrared spectra for the intramolecularly produced phenol IV, the phenol expected by an intermolecular rearrangement VI, a synthetic mixture of 15 mole % of VI and 85 mole % IV, and the unknown sample from fraction 1 of the 2,6-dimethylphenol derivatives.

The usable differences observed in the spectra of IV and VI are the strong absorption peak at 9.41 μ in the spectrum of VI which is present only as a very faint peak in the spectrum of IV, and a rather strong absorption at 12.73 μ in VI which is completely absent from the spectrum of IV.

A comparison of the curves in Fig. 2 reveals that the spectrum of the unknown sample shows little resemblance to that of the 4-(γ-methylallyl) substituted phenol VI, but is practically superimposable on that of IV, the intramolecular product. Similar to the synthetic mixture containing 15% of VI, the unknown sample appears to have the beginning of a faint peak at 9.41 μ; however, the unknown shows none of the absorption in the 12.7–13.0 μ region which is beginning to appear in the synthetic mixture. It may safely be concluded that the amount of intermolecularly produced VI in fraction 1 of the 2,6-dimethylphenol derivatives is less than 15 mole %. Since this fraction, because of boiling point differences, should be enriched in VI (if it were, in fact, formed) and since this fraction represents only 14% of the total phenolic product, it may be deduced that the reaction mixture from the "mixed" rearrangement contained less than 3 mole % of crossed products. The *para*-rearrangement of γ-methyl and γ-ethyl substituted allylic ethers is, apparently, a strictly intramolecular process.

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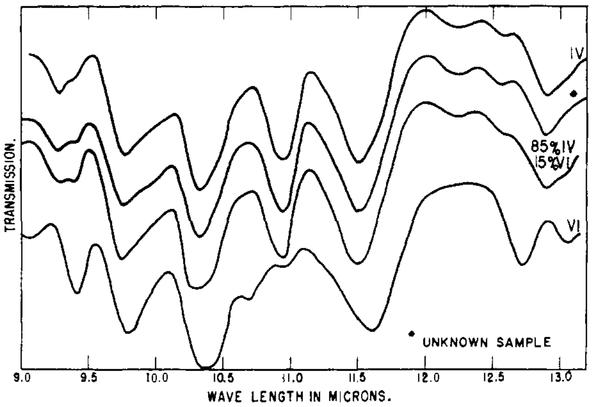

Fig. 2.—Infrared absorption spectra for the pure phenols IV and VI, a synthetic mixture of 85 mole % IV and 15 mole % VI, and the unknown sample from fraction 1 of the 2,6-dimethylphenol derivatives from the "mixed" rearrangement. Spectra were obtained with a Perkin-Elmer model 12C spectrophotometer with liquid samples 0.025 mm. thick.

Experimental[6]

Materials.—The preparation and properties of the γ-methylallyl and γ-ethylallyl ethers of methyl *o*-cresotinate (I and VII), their corresponding phenols (III and V) and derivatives thereof have been described in detail in earlier papers.[5] Pertinent rate data for these compounds will be found in the preceding paper of this series.[5b] Eastman Kodak Co. "White Label" 2,6-dimethylphenol was purified by sublimation before use, m.p. 45.2–45.7°.

Preparation and Rearrangement of the γ-Alkyl Allyl Ethers of 2,6-Dimethylphenol.—A typical procedure for the preparation of the allylic ethers of 2,6-dimethylphenol is recorded here. Properties of the individual compounds are given below.

A. **Preparation.**—To a freshly prepared solution of sodium methoxide in absolute methanol was added one equivalent of 2,6-dimethylphenol. The appropriate allylic chloride (1 mole equivalent) was added to the refluxing methanolic solution of sodium phenoxide over a period of *ca.* 20 minutes. Separation of sodium chloride began immediately and the reaction mixture tested neutral after 1-2 hours at reflux. The reaction mixture was worked up in the usual manner,[5] Claisen alkali being employed to separate the phenolic and ethereal fractions. The ethers, purified by distillation *in vacuo*, distilled as colorless oils and gave negative phosphomolybdic acid spot tests.[7] In both cases, small quantities (5–10%) of higher boiling diallylated products were found and were identified as such by hydrogenolysis to the corresponding hydrogenated rearrangement products (*cf.* ref. 5).

The yields and physical properties of the ethers prepared by this method follow: γ-methylallyl 2,6-dimethylphenyl ether (VIII): 43%, b.p. 55–56° at 0.3 mm., $n^{20}\text{D}$ 1.5075 (reported[8] b.p. 84–88° at 1 mm., $n^{20}\text{D}$ 1.5082); **γ-ethylallyl 2,6-dimethylphenyl ether** (II): 47%, b.p. 75–77.5° at 0.6 mm., $n^{20}\text{D}$ 1.5044.

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.1; H, 9.5. Found: C, 82.4; H, 9.7.

B. **Rearrangement.**—Rearrangement of II and VIII was accomplished by refluxing 3 hours in diethylaniline. Worked up in the usual way[5] the rearrangement products were purified by distillation. Both rearrangement products (IV and VI) distilled as colorless oils, gave positive phosphomolybdic acid tests (deep blue), and solidified to waxy solids on standing in the refrigerator. Yields and properties of phenols are: 2,6-dimethyl-4-(γ-methylallyl)-phenol (VI): 67%, b.p. 89–90° at 0.5 mm., $n^{20}\text{D}$ 1.5370 (reported[8] b.p. 107–109.5° at 1 mm., $n^{20}\text{D}$ 1.5376), solid at room temperature; **2,6-dimethyl-4-(γ-ethylallyl)-phenol** (IV): 78.5%, b.p. 115–118° at 1.5 mm., $n^{20}\text{D}$ 1.5312, m.p. (after sublimation) 46.1–46.6°.

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[6] All melting points are corrected. Microanalyses were performed by the Clark Microanalytical Laboratory, Urbana, Ill.

[7] V. M. Platovskaya and S. G. Vatkina, *J. App. Chem.* (*U. S. S. R.*), **10**, 202 (1937); *C. A.*, **31**, 4232 (1937). This is an extremely delicate test for hindered phenols which do not exhibit the usual ferric chloride test.

[8] E. N. Marvell, A. V. Logan, L. Friedman and R. W. Ledeen, THIS JOURNAL, **76**, 1922 (1954).

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.1; H, 9.5. Found: C, 81.7; H, 9.3.

3,5-Dinitrobenzoates of VI and IV.—The phenols VI and IV were best characterized[9] as the 3,5-dinitrobenzoates prepared by heating the phenol dissolved in pyridine with a slight excess of 3,5-dinitrobenzoyl chloride for 20-30 minutes in a water-bath. The oily precipitate which formed was taken up in ether and washed with 2% sodium carbonate. The esters were recrystallized from 95% ethanol. **The 3,5-dinitrobenzoate of VI** formed shiny, pinkish platelets, m.p. 117.9-118.6°. **The 3,5-dinitrobenzoate of IV** crystallized as colorless fine needles, m.p. 148.2-149.4°.

Anal. Calcd. for $C_{20}H_{20}N_2O_6$: C, 62.5; H, 5.2; N, 7.3. Found: C, 62.3; H, 5.6; N, 6.9.

Hydrogenation of VI and IV.—Hydrogenation of VI and of IV proceeded with the uptake of 1 mole equivalent of hydrogen. **The 2,6-dimethyl-4-pentylphenol** was a waxy solid, m.p., after sublimation, 46.2-47.2°. The 4-butyl- and 4-pentylphenols were converted directly to their 3,5-dinitrobenzoates in the manner described above.

3,5-Dinitrobenzoate of 2,6-dimethyl-4-butylphenol, colorless needles, m.p. 118.4-119.3° from hexane, strongly depresses the m.p. of the 3,5-dinitrobenzoate of VI.

The 3,5-dinitrobenzoate of 2,6-dimethyl-4-pentylphenol formed as light yellow feathery needles from 95% ethanol, m.p. 129.0-129.4°.

Anal. Calcd. for $C_{20}H_{22}N_2O_6$: C, 62.2; H, 5.7; N, 7.3. Found: C, 62.5; H, 5.5; N, 7.3.

Rate Measurements.—Rates of rearrangement of IV and VI in the pure liquid were measured at 158.4° by the method described in the preceding paper.[5b] The data, together with that of the rates of rearrangement of ethers I and VII at the same temperature, are plotted in Fig. 1. It will be noted that the data for IV and VI do not give straight lines when plotted by the first-order rate equation. Both compounds show an upward trend in rate as the reaction proceeds. Such results accord with the earlier findings of Tarbell and Kincaid[10] who noticed the same effect with the allyl ethers of 2,6-dimethylphenol and *p*-cresol and also observed that this upward trend disappeared when the rearrangement was carried out in more dilute solution. First-order rate constants for IV and VI calculated by the integrated equation for successive points are given in Table I.

TABLE I

t, sec.	Rearranged, %	$k \times 10^5$ sec.$^{-1}$	t, sec.	Rearranged, %	$k \times 10^5$ sec.$^{-1}$
γ-Methylallyl 2,6-dimethylphenyl ether (VI), T = 158.4°			γ-Ethylallyl 2,6-dimethylphenyl ether (IV), T = 158.4°		
3000	12.9	4.64	4260	7.12	1.70
6600	32.5	5.93	7920	14.2	1.94
10200	51.5	7.07	11700	22.1	2.14
13800	67.1	8.12	15920	30.7	2.38
21840	86.1	10.13	22560	45.3	2.68
			30000	60.6	3.10
			44400	79.0	3.82

Mixed Rearrangement.—Equimolar portions of I (8.10 g.) and II (7.00 g.) were placed in a previously cleaned and flamed reaction tube reduced at one end to facilitate sealing. The reaction tube contents were chilled in a Dry Ice-acetone-bath and the tube evacuated to less than 1 mm. pressure and sealed. The tube was held at 158.4° for 33 hours in a constant temperature bath. At the end of the heating period the tube contents were diluted with 100 ml. of petroleum ether and extracted with several portions of Claisen alkali in order to separate phenolic from any unrearranged ethereal material. Acidification of the alkali extracts with 6 *N* sulfuric acid and ice freed the phenolic rearrangement products which were taken up in ether. The ether-freed phenolic material was heated for one-half hour with four times its weight of 30% methanolic potassium hydroxide to saponify the methyl cresotinate derivatives. At the end of this time, the reaction mixture again was acidified and taken up in ether. The ether solution so obtained was extracted 11 times with 25-ml. portions of 5% sodium bicarbonate solution to remove the cresotinic acid derivatives. The combined sodium bicarbonate extracts were washed once with ether to remove any 2,6-dimethylphenol derivatives entrained in the extracts and then acidified to precipitate the cresotinic acid derivatives. The latter precipitate was taken up with ether, dried over anhydrous magnesium sulfate and filtered through a layer of sodium sulfate.

Treatment of the Bicarbonate-soluble Fraction.—Removal of the solvent from the bicarbonate-soluble fraction left 6.37 g. (84%) of crude acid, m.p. 127-129°. Recrystallized from hexane, the acid melted at 132.6-134.4° and proved identical with authentic 2-carboxy-4-(γ-methylallyl)-6-methylphenol, m.p. 133.5-134.5°.[5b] Careful recrystallization of the crude acid permitted the recovery of 89.4% with a melting point higher than 130° (*cf.* the m.p. of the "crossed" product, 2-carboxy-4-(γ-ethylallyl)-6-methylphenol which is 115-116°[5a]). This amount of acid corresponds to a 75.2% yield of the product resulting from an intramolecular rearrangement. Some contamination by 2,6-dimethylphenol derivatives was detected in the concentrates of the mother liquors during this recrystallization procedure, indicating that the m.p. of the crude acid was lowered by this material rather than by the presence of the crossed product.

Treatment of the Bicarbonate-insoluble Fraction.—Removal of the ether from the dried 2,6-dimethylphenol derivatives left a light yellow oil which after a simple vacuum distillation weighed 6.2 g. (87% of theory). This material then was fractionated in a micro Podbielniak-type column and the following fractions cut: fraction 1, b.p. 92-151° at 3.5 mm., $n^{20}\text{D}$ 1.5288-1.5294, 0.72 g., 13.9% of total distillate; fraction 2, b.p. 151° at 3.5 mm., $n^{20}\text{D}$ 1.5308, 0.90 g.; fraction 3, b.p. 151° at 3.5 mm., $n^{20}\text{D}$ 1.5308, 2.11 g.; fraction 4 (forced), $n^{20}\text{D}$ 1.5305, 1.46 g. Fractions 2, 3 and 4 account for 86% of the total distillate.

Samples of fractions 2, 3 and 4 were hydrogenated separately and the dihydro derivatives (m.p. 45-46°, 48-49°, 44-45.6°, respectively) were converted to the 3,5-dinitrobenzoates. In each case, good yields of 3,5-dinitrobenzoate of 2,6-dimethyl-4-pentylphenol were obtained, m.p. 126.6-129.0°, no depression on admixture with an authentic sample. Infrared analysis also confirmed these fractions as essentially pure 2,6-dimethyl-4-(γ-ethylallyl)-phenol (IV).

Hydrogenation of a sample of fraction 1 consumed 99% of the theoretical amount of hydrogen; however, preparation of the 3,5-dinitrobenzoate gave a light yellow solid which did not lend itself to purification. The best m.p. obtained for this material was 111.6-121.4°. A marked m.p. depression was observed when the material was mixed with the 3,5-dinitrobenzoate of authentic 2,6-dimethyl-4-butylphenol and essentially no depression when mixed with authentic 3,5-dinitrobenzoate of 2,6-dimethyl-4-pentylphenol.

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[9] Marvell[8] reports a phenylurethan derivative for VI. We found this and the α-naphthylurethan less satisfactory derivatives than the benzoates, although none of them appears to be completely stable or easily purified.

[10] D. S. Tarbell and J. F. Kincaid, THIS JOURNAL, **62**, 728 (1940). It is interesting to note that this acceleration of rate is not observed with the ethers of methyl *o*-cresotinate, a phenol of much lower acidity.