[CONTRIBUTION FROM NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Mechanism of the *para* Claisen Rearrangement. Evidence for a Dienone–phenyl Ether Rearrangement[1a]

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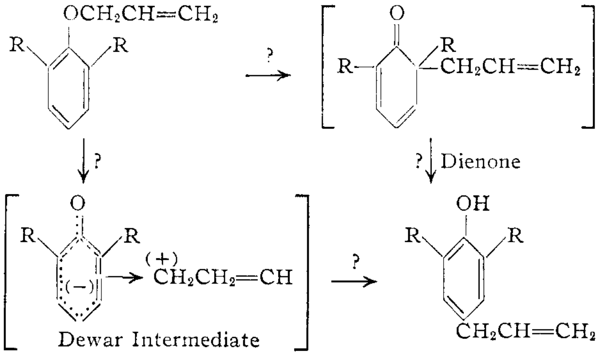
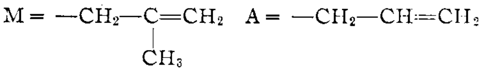
A study of the *para* Claisen rearrangement of allyl 2,6-dimethallylphenyl ether (I) and methallyl 2-allyl-6-methallylphenyl ether (II) has shown that in each case a mixture of 4-allyl-2,6-dimethallylphenol and 2-allyl-4,6-dimethallylphenol is obtained. When the reaction is stopped before completion, examination of the unreacted ether fraction shows that extensive rearrangement of the allyl ether I to the methallyl ether II has occurred. That the migration of allyl or methallyl groups from the *o*- to the *p*-positions during the *para* Claisen rearrangenent is not due primarily to a mixing of groups on oxygen with those in *ortho* positions prior to the *para* rearrangement is shown by the fact that nearly the same ratio of *p*-allyl to *p*-methallylphenol is obtained when the reaction is stopped before such mixing has occurred to an appreciable extent. These results are explained by the postulation of Hurd and Pollack of a double cycle mechanism and appear to exclude the Dewar mechanism. The ether interchange is of particular interest since it is apparently the first evidence for such an allylic rearrangement from carbon to oxygen.

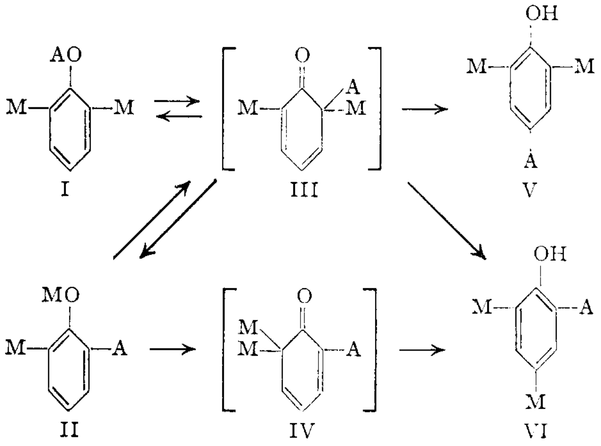
Since the publication of a preliminary report of this work[2] several papers have appeared[3b,4,5] which have reviewed the *para* Claisen rearrangement in some detail.[6] For this reason the present discussion will be confined largely to a more complete report of our work.

In an effort to decide between the mechanism involving the dienone intermediate first suggested by Hurd and Pollack[7a] and Mumm and Diederichsen[7b] and a modification[8] of the Dewar mechanism[9] it was decided to examine the rearrangement of allyl 2,6-dimethallylphenyl ether (I) and methallyl 2-allyl-6-methallylphenyl ether (II). It was anticipated that should the dienone intermediate be involved, rearrangement of the allyl ether I would lead by way of the dienone III not only to the phenol V in which the allyl group had migrated to a *para*-position of the benzene ring but also to the phenol VI in which a methallyl group appeared in the *para*-position and the allyl group remained in the *ortho*-position. Similarly, the ether II should give rise to a mixture of phenols (V and VI).

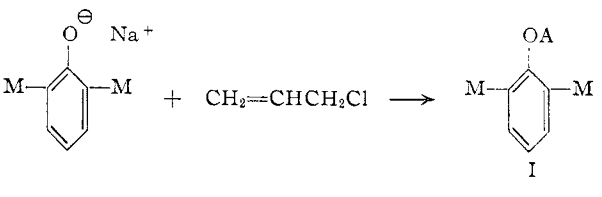




$$M = -CH_2-\underset{\underset{CH_3}{|}}{C}=CH_2 \quad A = -CH_2-CH=CH_2$$



The allyl ether I was synthesized from the sodium salt of 2,6-dimethylallylphenol[10] and the methallyl ether II from the salt of 2-methallylphenol as shown.



Since it was anticipated that the trisubstituted phenolic products V and VI would be difficult to separate, their independent syntheses were attempted with the hope that a suitable analytical method might be devised. However, such attempts were unsuccessful. For this reason it was decided to hydrogenate catalytically the product mixtures

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[1] (a) Based upon a Ph.D. thesis submitted by H. W. Johnson, Jr., to the University of Illinois, 1954. (b) National Science Foundation Fellow, 1953–1954.

[2] D. Y. Curtin and H. W. Johnson, Jr., THIS JOURNAL, **76**, 2276 (1954).

[3] (a) K. Schmid, W. Haegele and H. Schmid, *Experientia*, **9**, 414 (1953); (b) K. Schmid, W. Haegele and H. Schmid, *Helv. Chim. Acta*, **37**, 1080 (1954); (c) P. Fahrni, W. Haegele, K. Schmid and H. Schmid, *ibid.*, **38**, 783 (1955).

[4] S. J. Rhoads, R. Raulins and R. D. Reynolds, THIS JOURNAL, **76**, 3436 (1954); S. J. Rhoads and R. L. Crecelius, *ibid.*, **77**, 5057, 5060 (1955).

[5] E. N. Marvell and R. Teranishi, *ibid.*, **76**, 6165 (1954).

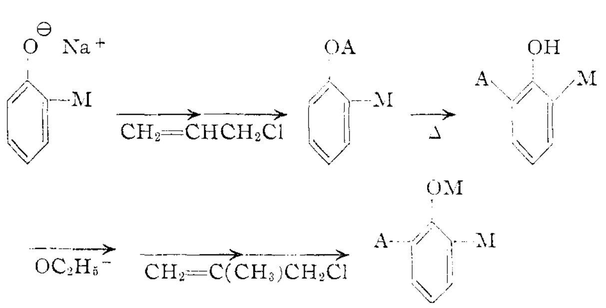
[6] See D. S. Tarbell, "Organic Reactions," Vol. 2, Edited by R. Adams, John Wiley and Sons, Inc., New York, N. Y., 1944, Chapter 2, for a more complete review of the older work.

[7] (a) C. D. Hurd and H. Pollack, *J. Org. Chem.*, **3**, 550 (1938); (b) O. Mumm and J. Diederichsen, *Ber.*, **72**, 1523 (1939).

[8] See J. P. Ryan and P. R. O'Conner, THIS JOURNAL, **74**, 5866 (1952). The intermediate could be formulated either as a π-complex with the aromatic ring bound preferentially to one end of the allyl group or as an unsymmetrical ion pair, or as a structure intermediate between these two extremes.

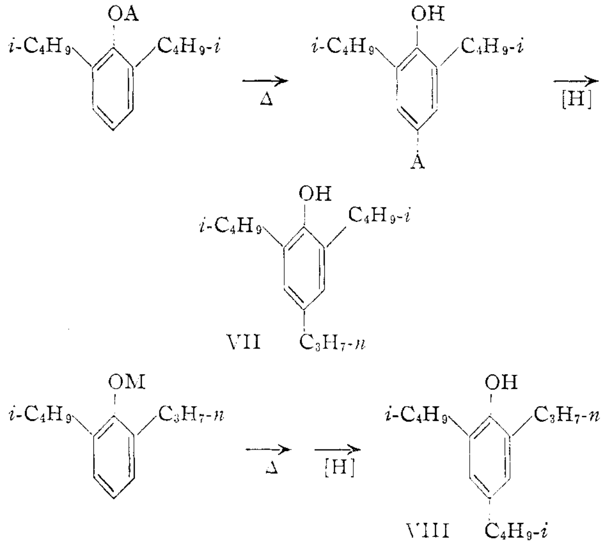
[9] M. J. S. Dewar, "Electronic Theory of Organic Chemistry," Oxford Press, London, England, 1949, p. 229.

[10] Q. R. Bartz, R. F. Miller and R. Adams, THIS JOURNAL, **57**, 371 (1935).



II

from the rearrangements of ethers I and II and to analyze the mixture of hydrogenated phenols VII and VIII. For comparison, the trialkylphenol VII was synthesized independently by rearrangement of allyl 2,6-diisobutylphenyl ether followed by reduction, as shown; VIII was synthesized by a similar series of reactions from 2-propyl-6-isobutylphenol.



The rearrangements of ethers I and II were carried out both by heating the ether without a solvent and by heating the ether mixed with one-half of its weight of diethylaniline in a nitrogen atmosphere at temperatures of from 220 to 245°. The phenolic fraction of the product was extracted with Claisen alkali and distilled through a Holtzmann column. The product from each rearrangement boiled over the same narrow range and it is believed that no separation of the phenolic products was effected in this distillation. In each case the product mixture was hydrogenated over platinum oxide in ethanol solution. The uptake of hydrogen varied from 85 to 105% of the theoretical amount. These products were again distilled and found to boil over a narrow range. In this case it is assumed that no separation of the products VII and VIII occurred and this assumption is confirmed by the observation that the boiling points of the two independently prepared phenols VII and VIII were identical. The composition of the mixture of the reduced phenols VII and VIII was determined by infrared analysis and considered to be a measure of the relative amounts of phenols V and VI. The results are recorded in Table I.

TABLE I

PRODUCTS FORMED IN THE REARRANGEMENT OF THE ETHERS I AND II

Ether	Reacn. time, min.	Bath temp., °C.	Total yield of phenols, %, V and VI	Recovd. ethers, %	Composition of phenols,[a] % V	VI	Composition of ethers, % I	II
I[c]	2.0	230	25	52	56[c]	44	99.5	0.6
I[c]	3.5	230	61	30	55[c]	45	83	16
I[b]	4.0	242	30	0	49[b]	51	..	..
I[b]	3.5	220	26	45	53[b]	47	89	12
I[b]	5.0	220	51	11	52[b]	48	51	49
I[b]	30.0	220	51	2	53[b]	47	56.	44
II[c]	40.0	240	63	0	41[c]	59	..	..
II[c]	4.0	220	6	69	40[c,d]	60[c,d]	7	93
II[b]	40.0	220	40	11	34[b]	66	8	92
II[b]	90.0	220	32	1	34[b]	66	..	..

[a] From the infrared analysis of the mixture of reduced phenols (VII and VIII). [b] Carried out with no solvent. [c] Reaction in 50% by weight of diethylaniline. [d] Estimated from curves recorded with normal rather than expanded scale.

It is seen that in both the rearrangement of I and the rearrangement of II, mixtures of V and VI were formed which consisted of 34 to 56% of the *p*-allyl product V and 44 to 66% of the *p*-methallyl product VI. It was thus established that during the *para* Claisen rearrangement there was mixing of the allylic groups in the *ortho* positions of the benzene ring with the allylic group on the oxygen atom.

While such results are consistent with a dienone intermediate, as indicated previously, neither these results nor those of the other investigators cited,[3,5] exclude the possibility that the dienones III and IV might not be in the direct path of the rearrangement of an allyl group from the oxygen to the *p*-position. That is, the dienone could be formed reversibly and go to the *p*-allylphenols by a rearrangement to the ethers I and II which could then rearrange directly to the *p*-substituted phenols V and VI by the modified Dewar mechanism.

In order to exclude such a possibility, then, it was necessary to show that under the conditions of the rearrangement there was no rearrangement of allyl ether I to the methallyl ether II. The rearrangement reaction of the allyl ether I was stopped, therefore, before completion and both the phenolic fraction and the ether fraction were subjected to infrared analysis. After about 50% completion of the reaction in the absence of any solvent it was found that, under the conditions previously described, extensive rearrangement of the allyl ether I into the methallyl ether II had occurred during the Claisen rearrangement. This was shown by an examination of the recovered starting material which consisted of approximately 51% of the ether I and 49% of the ether II. In diethylaniline the rearrangement of one ether to the other was slower relative to the *para* Claisen rearrangement and the amount of the methallyl ether II in the reaction mixture from the allyl ether I was only about 16%.

In order to decide whether the *p*-methallylphenol VI was, in fact, being formed from the O-allyl ether I by way of the dienone III or was coming from I by way of the O-methallyl ether II (by the Dewar mechanism) the rearrangement of the O-allyl ether

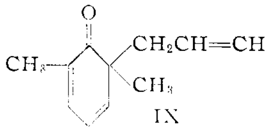
I was carried to only about 25% completion, at which point there had been essentially no rearrangement of the allyl ether I to the methallyl ether II. Under these conditions when no appreciable concentration of the rearranged ether II had accumulated it would seem reasonable to conclude that the products which had been formed at that time had come almost entirely from the ether I. It is seen from the results in Table I that the phenol fraction again consisted of about 56% of the *p*-allylphenol V and 44% of the *p*-methallylphenol VI. Such an argument would be invalid, however, if the methallyl ether II, although present in very small concentration, rearranged very much faster than the allyl ether (I). A qualitative comparison of the relative rates of rearrangements of I and II as indicated by the times required for partial completion of the two reactions indicated that II was actually somewhat slower. Examination of the products of rearrangement of the ether II after some 6% reaction showed that the composition of the phenolic fraction was 40% of *p*-allylphenol V and 60% of *p*-methallylphenol VI. Under such conditions the recovered ether consisted of 93% of the methallyl ether II with only 7% of the allyl ether I. The results with the methallyl ether II thus confirm in a qualitative sense the results obtained with the allyl ether I.

Although the data presented here are not sufficiently accurate for a careful quantitative analysis of the relative rates of the various reactions concerned, it is of interest to compare them with each other insofar as this is possible. It is seen that ratio of the amounts of the phenolic products from the rearrangement of the allyl ether I gives an indication of the relative rates of conversion of the dienone III to phenols V and VI, respectively. This ratio of allyl to methallyl migration is thus approximately 60/40 or 1.5.

The rearrangement of the methallyl ether II is complicated by the fact that both dienones III and IV might be expected to be formed at comparable rates. Dienone III should then rearrange to give the *p*-allylphenol V and the *p*-methallylphenol VI in the same ratio of 60/40 that was observed in the reaction of the allyl ether I. The dienone IV, however, can only rearrange with allyl migration to the *p*-allylphenol V. It is not surprising, therefore, that the major product from the allyl ether I is the *p*-allylphenol V but that from the methallyl ether II is the *p*-methallylphenol VI.

The results reported here are consistent, thus, with a mechanism of rearrangement by way of a dienone intermediate and appear to exclude the modified Dewar mechanism for the major part of the reaction.

The isolation by Conroy and Firestone[11] of 2-allyl-2,6-dimethylcyclohexa-3,5-dienone (IX) (as the Diels-Alder adduct with maleic anhydride)



IX

from the partial rearrangement of allyl 2,6-dimethylphenyl ether suggested that it might be possible to detect the dienone IV as a reaction intermediate. For this reason the carbonyl region of the spectrum of the total reaction mixture recovered from an incomplete rearrangement of the allyl ether I was examined carefully. No trace of carbonyl absorption could be found, however. It appears, therefore, that our system differs from that of Conroy and Firestone and that no appreciable concentration of dienone accumulates during the reaction.

It should, perhaps, be stated here that the demonstration of the migration of an allyl group (tagged either with a substituent or with carbon-14) from an *ortho* to a *para* position, has been made by two other groups[3,5] at the same time as the present work was carried out. In these other studies, the possibility of interchange of allyl groups between oxygen and an *ortho* position was not examined, however. Recently Schmid[12] has made a preliminary report of such an exchange.

Experimental[13]

Allyl 2,6-Dimethallylphenyl Ether (I).—To a solution of 0.25 mole of sodium ethoxide (prepared from 5.7 g. of sodium) in 200 ml. of absolute ethanol was added slowly, with stirring, 50.5 g. (0.25 mole) of 2,6-dimethallylphenol[10] (b.p. 109–110° (2 mm.), $n^{20}\text{D}$ 1.5315). The solution was heated to reflux and 21 g. (0.28 mole) of allyl chloride was added dropwise with stirring. After 12 hours under reflux the solution was diluted with 250 ml. of water and the mixture was extracted with petroleum ether. The petroleum ether extracts were washed with Claisen alkali and water, the solution dried over magnesium sulfate, and the solvent removed. Distillation gave 42 g. (69%) of the ether I, b.p. 105–107° (0.7 mm.), $n^{20}\text{D}$ 1.5199.

Anal. Calcd. for $C_{17}H_{22}O$: C, 84.3; H, 9.1. Found: C, 84.3; H, 9.4.

Allyl 2-Methallylphenyl Ether.—To a solution of 0.60 mole of sodium ethoxide in 300 ml. of absolute ethanol was added slowly, with stirring, 80 g. (0.54 mole) of 2-methallylphenol.[10] The solution was heated to reflux and 66.6 g. of allyl bromide was added slowly with stirring. After 3 hours under reflux, two-thirds of the solvent was removed at reduced pressure. To the suspension which resulted was added 300 ml. of water and the solution extracted with petroleum ether until the extract became colorless and the aqueous solution did not change color on further extraction. The petroleum ether extracts were washed with Claisen alkali and the petroleum ether removed. Fractionation of the product yielded 76 g. (75%) of allyl 2-methallylphenyl ether, b.p. 64–65° (0.05 mm.), $n^{20}\text{D}$ 1.5220.

Anal. Calcd. for $C_{13}H_{16}O$: C, 83.0; H, 8.5. Found: C, 82.6; H, 8.7.

2-Allyl-6-methallylphenol.—Allyl 2-methallylphenyl ether (72 g.) was heated under nitrogen with 36 g. of diethylaniline at 240–245° for 30 minutes. After the reaction mixture had cooled in a nitrogen atmosphere, 100 ml. of petroleum ether was added, and the solution was extracted with 6 *N* sulfuric acid, washed with water, and extracted with Claisen alkali. The alkaline solution was acidified with 6 *N* sulfuric acid, after washing with petroleum ether. The suspension was extracted with petroleum ether, the extracts washed with

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(11) H. Conroy and R. A. Firestone, THIS JOURNAL, **75**, 2530 (1953).

(12) H. Schmid, "Congress Handbook," XIVth International Congress of Pure and Applied Chemistry, Zurich, July, 1955, p. 65. NOTE ADDED IN PROOF (May 1, 1956).—This work has now been published in full [F. Kalberer, K. Schmid and H. Schmid, *Helv. Chim. Acta*, **39**, 555 (1956)].

(13) All melting points are corrected. Analyses were performed by Mr. Joseph Nemeth, Mrs. Ester Fett, Mrs. Katherine Pih and Mrs. Lucy Chang. Infrared spectra were determined on a Perkin-Elmer spectrophotometer, model 21, by Miss Helen Miklas, Mrs. Rosemary Hill, Mrs. Beverly Thomas and Mr. James Brader. The infrared spectra of the compounds employed in this investigation are recorded in the Ph.D. Dissertation by Harry W. Johnson, Jr., at the University of Illinois and reproduced by Univ. Microfilms, Ann Arbor, Michigan.

water, and after removal of the petroleum ether the residue was fractionated to yield 51 g. (71%) of colorless liquid, b.p. 69–71° (0.2 mm.), n^{20}_{D} 1.5335.

Anal. Calcd. for $C_{13}H_{16}O$: C, 83.0; H, 8.5. Found: C, 82.9; H, 8.6.

2-Allyl-6-methallylphenyl 3,5-dinitrobenzoate was prepared from 2-allyl-6-methallylphenol by treatment with 3,5-dinitrobenzoyl chloride in pyridine. After recrystallization from ethanol it had m.p. 112–113°.

Anal. Calcd. for $C_{20}H_{12}O_6N_2$: C, 62.8; H, 4.7; N, 7.3. Found: C, 62.9; H, 4.7; N, 7.3.

Methallyl 2-Allyl-6-methallylphenyl Ether (II).—To a solution of sodium ethoxide (prepared from 1.1 g. of sodium) and 70 ml. of absolute ethanol was added slowly with stirring 7.97 g. of 2-allyl-6-methallylphenol (0.043 mole) and 5.0 g. (0.05 mole) of methallyl chloride. After 1 hour of refluxing the solution was allowed to cool, and 100 ml. of water was added. After extraction of the mixture with petroleum ether and extraction of the petroleum ether extracts with Claisen alkali, the removal of the petroleum ether and distillation of the neutral product gave 6.5 g. (63%) of the ether II, b.p. 74–75° (0.09 mm.), n^{20}_{D} 1.5198.

Anal. Calcd. for $C_{17}H_{22}O$: C, 84.3; H, 9.1. Found: C, 84.4; H, 9.2.

2,6-Diisobutylphenol.[10]—2,6-Dimethallylphenol (31.5 g.) was hydrogenated in absolute ethanol over platinum oxide catalyst. The theoretical amount of hydrogen was taken up. Filtration of the solution, removal of the ethanol and distillation yielded 28.3 g. of 2,6-diisobutylphenol, b.p. 66–67° (0.08 mm.), n^{20}_{D} 1.5016.

Allyl 2,6-Diisobutylphenyl Ether.—This ether was prepared from 2,6-diisobutylphenol,[10] n^{20}_{D} 1.5016, b.p. 66–67° (0.08 mm.), and allyl bromide by a procedure similar to the preparation of the allyl ether I above. The product, purified by distillation, was obtained in 55% yield, b.p. 68–69° (0.1 mm.), n^{20}_{D} 1.4915.

Anal. Calcd. for $C_{17}H_{26}O$: C, 82.9; H, 10.6. Found: C, 82.8; H, 10.5.

4-Allyl-2,6-diisobutylphenol.—Allyl 2,6-diisobutylphenyl ether (9.5 g.) was rearranged in 4.7 g. of diethylaniline at 230–260° for 45 minutes. After cooling under nitrogen and isolation of the product as in the case of 2-allyl-6-methallylphenol above, a yield of 5.7 g. (61%) of 4-allyl-2,6-diisobutylphenol, b.p. 84–86° (0.06 mm.), n^{20}_{D} 1.5077, was obtained.

Anal. Calcd. for $C_{17}H_{26}O$: C, 82.9; H, 10.6. Found: C, 82.7; H, 10.7.

2,6-Diisobutyl-4-propylphenol (VII) was prepared by hydrogenation of 3.51 g. of 4-allyl-2,6-diisobutylphenol in 45 ml. of absolute ethanol over platinum oxide at atmospheric pressure. Distillation of the product gave 3.9 g. (90%) of 2,6-diisobutyl-4-propylphenol, b.p. 88–89° (0.1 mm.), n^{20}_{D} 1.4980.

Anal. Calcd. for $C_{17}H_{28}O$: C, 82.3; H, 11.3. Found: C, 82.6; H, 11.3.

2,6-Diisobutyl-4-propylphenyl 3,5-Dinitrobenzoate.—This ester was prepared in 70% yield by treatment of the phenol VII with 3,5-dinitrobenzoyl chloride in pyridine. After crystallization from 95% ethanol it had m.p. 102–103°.

Anal. Calcd. for $C_{24}H_{20}O_6N_2$: C, 65.2; H, 6.7; N, 6.3. Found: C, 65.4; H, 6.7; N, 6.4.

2-Isobutyl-6-propylphenol.—2-Allyl-6-methallylphenol (7.97 g.) was reduced at room pressure in absolute ethanol over platinum oxide to give 6.5 g. (81.7%) of the saturated phenol, b.p. 60–62° (0.1 mm.), n^{20}_{D} 1.5101. Redistillation gave 6.3 g. of product, b.p. 56–57° (0.03 mm.), n^{20}_{D} 1.5098.

Anal. Calcd. for $C_{13}H_{16}O$: C, 81.2; H, 10.0. Found: C, 80.7; H, 9.7.

2-Isobutyl-6-propylphenyl Methallyl Ether.—2-Isobutyl-6-propylphenol (5.87 g., 0.031 mole) was converted to the methallyl ether by a procedure similar to that used for the preparation of II above. The product isolated by distillation amounted to 4.9 g. (65%) of ether, b.p. 62–65° (0.02 mm.), $n^{22.5}_{\mathrm{D}}$ 1.4946. Another reaction produced product, b.p. 66–68° (0.05 mm.), n^{20}_{D} 1.4915.

Anal. Calcd. for $C_{17}H_{26}O$: C, 82.9; H, 10.6. Found: C, 82.7; H, 10.7.

2-Isobutyl-6-propyl-4-methallylphenol.—2-Isobutyl-6-propylphenyl methallyl ether (12.8 g.) was rearranged in 6.0 g. of diethylaniline at 250° for 30 minutes. Isolation of the phenolic product as in the rearrangements above gave, on distillation, 8.0 g. (62.5%) of phenol, b.p. 86–88° (0.05 mm.), n^{22}_{D} 1.5085.

Anal. Calcd. for $C_{17}H_{26}O$: C, 82.9; H, 10.6. Found: C, 82.7; H, 10.8.

2,4-Diisobutyl-6-propylphenol (VIII).—The hydrogenation of 4.01 g. of 4-methallylphenol above was carried out in absolute ethanol over platinum oxide at room temperature as in the hydrogenation described above. Distillation of the product gave 3.7 g. (91%) of phenol, b.p. 84–85° (0.07 mm.), n^{20}_{D} 1.4968.

Anal. Calcd. for $C_{17}H_{28}O$: C, 82.3; H, 11.3. Found: C, 82.1; H, 11.2.

2,4-Diisobutyl-6-propylphenyl 3,5-dinitrobenzoate (m.p. 110.5–111.5°) was obtained from the phenol VIII by treatment with 3,5-dinitrobenzoyl chloride in pyridine and recrystallization of the product from ethanol.

Anal. Calcd. for $C_{24}H_{30}N_2O_6$: C, 65.2; H, 6.7; N, 6.3. Found: C, 65.3; H, 6.6; N, 6.4.

Rearrangement of Allyl 2,6-Dimethallylphenyl Ether.—The ether was rearranged in quantities of 10 to 20 g., either without solvent or with one-half of its weight of diethylaniline in a nitrogen atmosphere in a flask heated for the time and temperature indicated in Table I. After the reaction mixture was allowed to cool, 100 ml. of petroleum ether was added and the solution was extracted with 6 *N* hydrochloric acid and then with Claisen alkali (4 × 50 ml.). The petroleum ether solution after being washed with water and dried over magnesium sulfate was distilled to yield the recovered starting material, b.p. 74–77° (0.1 mm.), in those experiments which were carried out to incomplete reaction. The Claisen alkali solution was washed with petroleum ether, diluted with an equal volume of water, and acidified with 6 *N* hydrochloric acid. The phenolic product was extracted with petroleum ether; the extracts were washed with water, dried, and distilled to yield the phenol mixture. Almost the entire phenolic product had b.p. 91–92° (0.1 mm.).

The phenolic product was hydrogenated in 15 ml. of absolute ethanol (4.151 g. over 15 mg. of pre-reduced platinum oxide in 45 ml. of absolute ethanol). The hydrogen uptake amounted to 85–105% of theoretical and required approximately 3 hours. After removal of the platinum catalyst and the solvent, the reduced phenol was distilled to yield 3.8 g. of product, b.p. 84–85° (0.05 mm.), n^{22}_{D} 1.5033. Redistillation gave 3.5 g. of product, b.p. 84–85° (0.05 mm.), n^{20}_{D} 1.4970.

Anal. Calcd. for $C_{17}H_{22}O$: C, 82.3; H, 11.3. Found: C, 82.0; H, 11.3.

The results of the infrared analyses are shown in Table I. The method employed is described below.

Rearrangement of Methallyl 2-Allyl-6-methallylphenyl Ether (II).—The rearrangement was carried out in the same general way as that used for the allyl ether I described above. However, the relative slowness of the reaction necessitated considerably longer reaction times. As before, the crude product was reduced with hydrogen over platinum and the hydrogen uptake amounted to over 90% of the theoretical amount. A typical analysis of the reduced phenolic product is given below.

Anal. Calcd. for $C_{17}H_{28}O$: C, 82.3; H, 11.3. Found: C, 82.0; H, 11.0.

The results of the infrared analyses of both the phenolic fraction and the recovered ether are given in Table I. The method employed is described below.

Computation of the Compositions of the Phenolic Fractions from the Infrared Spectra.—Compositions of phenolic fractions were calculated from infrared spectra of 30% solutions of the unknowns and the two pure phenols (VII and VIII) in carbon tetrachloride measured with the Perkin-Elmer model 21 spectrophotometer in 0.1 mm. balanced cells with an expanded scale. The frequencies 812 and 820 cm.$^{-1}$ were used. With the assumption that Beer's law holds and the percentage transmissions at each of these frequencies, from each curve two simultaneous equations were obtained which on solution gave values of the concentrations of the phenols VII and VIII. When the assumption was made that no other product was present (*i.e.*, by assuming that the sum of the mole fractions equals 1) a second value for each concentration could be obtained, and these values were then averaged.

TABLE II

INFRARED ANALYSES OF MIXTURES OF PHENOLS V, II AND VIII OBTAINED FROM THE REARRANGEMENT OF ETHERS I AND II[a]

	Transmission, %					
Ether	812 cm.$^{-1}$	820 cm.$^{-1}$	% of VII	Av. % VII	% VIII	Av. % VIII
I	67.6	59.2	58.5 54.4	55.9 ± 3	45.6 42.5	44.0
I	66.9	59.9	56.3 53.3	54.8 ± 2	46.7 43.7	45.2
I	61.7	63.2	48.3 49.3	48.8 ± 3	50.7 51.7	51.2
I	60.5	55.9	53.7 52.6	53.1 ± 2	47.4 46.3	46.9
I	70.7	67.5	51.0 52.3	51.7 ± 2	47.7 48.0	48.4
I	66.4	60.8	54.5 51.2	52.8 ± 3	48.8 45.5	47.2
II	53.9	60.0	41.7 40.6	41.0 ± 2	59.4 58.3	58.9
II	..	..	Estimated visually			
II	52.5	66.2	35.2 32.8	33.6 ± 2	67.1 64.8	66.1
II	54.9	69.4	35.5 32.3	33.9 ± 2	67.7 64.5	66.1
	34.8	77.5	Pure phenol VII			
	91.2	38.8	Pure phenol VIII			

[a] On each line are data for the reaction described on the corresponding line of Table I.

TABLE III

INFRARED ANALYSES OF THE RECOVERED ETHERS FROM THE CLAISEN REARRANGEMENT OF ETHERS I AND II[a]

Starting ether	925 cm.$^{-1}$	1050 cm.$^{-1}$	2920 cm.$^{-1}$	% of I	Av. % of I	% of II	Av. % of II
I	47.5	93.4	43.6	99.5	..	0.6	..
I	41.3	85.5	42.4	84.8 82.7	83.2	17.3 15.2	16.5
I	..	..	..	..	..	..	..
I	40.4	88.7	42.6	89.2 87.9	88.5	12.1 10.8	11.5
I	49.4	72.7	41.2	52.9 49.8	51.3	50.2 47.1	48.7
I	47.2	74.5	42.1	56.7 54.8	55.8	45.2 43.3	44.2
II	..	..	..	..	..	..	..
II	62.3	46.4	43.4	7.1 6.0	6.5	94.0 92.9	93.5
II	66.1	58.4	43.3	10.4 6.2	8.3	93.8 89.6	91.7
	37.5	85.0	42.4	Pure ether I			
	64.1	50.0	47.1	Pure ether II			

[a] On each line are data for the reactions described on the corresponding lines of Tables I and II.

Application of this method to a known mixture containing 48.5% of the phenol IV and 51.5% of phenol VII gave values of 49 ± 2% of IV and 52 ± 2% of VII. Probable errors were calculated from the usual equation.[14] The data are recorded in Table II.

Computation of the Compositions of the Recovered Ether Fractions.—The spectra for this purpose were obtained in a 10% solution in carbon tetrachloride with the Perkin-Elmer model 21 spectrophotometer. Again simultaneous equations were solved using the log per cent. transmissions at the frequencies 925 and 1050 cm.$^{-1}$. Analysis of a known mixture containing 19.5% of the ether II and 80.5% of the ether I gave by this method the calculated values of 23 ± 3% of II and 77 ± 3% of I. Data are recorded in Table III.

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(14) L. P. Hammett, "Introduction to the Study of Physical Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1952, p. 404.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE SCHOOL OF PHARMACY, UNIVERSITY OF CALIFORNIA]

Synthesis of Some 1-Phenyl-2-amino-3-substituted-amino-1-propanols from α-Oximino Mannich Bases

BY MANFRED E. WOLFF[1] AND J. F. ONETO

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The synthesis of ten new 1-phenyl-2,3-diamino-1-propanol derivatives together with some previously unreported intermediates is described. The treatment of β-substituted-aminopropiophenone derivatives with isobutyl nitrite in anhydrous methanol saturated with hydrogen chloride has furnished the corresponding α-oximino ketones in good yield. A method for the reduction of α-oximino ketones to the corresponding amino alcohols utilizing lithium aluminum hydride has been developed.

In order to study the pharmacological effects of structural changes in 1-phenyl-2-amino-1-propanol, the preparation of a series of 1-phenyl-2,3-diamino-1-propanol salts having a primary 2-amino group and a tertiary 3-amino function was required. Such molecules are of interest since they are structurally related to compounds possessing sympathomimetic, antihistaminic and antispasmodic activities.

Williams and Day[2] have previously reported the preparation of 1-phenyl-2-amino-3-(4-morpholinyl)-1-propanol *via* the interaction of dibenzylamine with α-bromo-β-(4-morpholinyl)-propiophenone hydrobromide followed by catalytic debenzylation and reduction. An alternate synthesis of this type of compound, involving the reduction of α-oximino Mannich base hydrochlorides to the corresponding amino alcohols was undertaken.

The intermediate Mannich base hydrochlorides employed in the investigation were prepared according to published procedures. The melting

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(1) This paper represents part of a dissertation submitted by M. E. Wolff in partial fulfillment of the requirements for the Ph.D. degree in pharmaceutical chemistry, 1955.

(2) A. L. Williams and A. R. Day, THIS JOURNAL, **74**, 3875 (1952).