(4-bromophenyl)-aniline (XII),[7] and the amine converted to 4-(4-bromophenyl)-phenol (VIII).[7] The crude product so obtained was refluxed with an excess of acetic anhydride and 0.25 mole of anhydrous sodium acetate for two hours, and the product (IX) was recovered in the usual manner. A mixture of ligroin and benzene was used for recrystallizations. The product was obtained as colorless irregular plates; m. p. 128–129°. On the basis of the amount of compound X used, the yield was low.

Anal. Calcd. for $C_{14}H_{11}O_2Br$: Br, 27.5. Found: Br, 27.2.

A sample of 4-(4-bromophenyl)-phenol (VIII) obtained by the hydrolysis of 4-(4-bromophenyl)-phenyl benzenesulfonate (VII)[1] was also used for the preparation of this compound (IX). The yield of the crude acetate (IX) corresponded to 92% on the basis of the benzenesulfonate used. The m. p. 128–129° was the same as for the product described above, the crystals were similar, and a mixture of samples of the two preparations melted between 128 and 129°.

(7) Bell and Robinson, *J. Chem. Soc.*, 1127 (1927).

Summary

1. Although the bromination of 4-phenylphenyl benzenesulfonate or 4-phenylphenyl benzoate yields the 4-(4-bromophenyl)-phenyl ester, the introduction of bromine into 4-phenylphenyl acetate results in substitution in the ortho position (or positions) with respect to the acetyloxy group. The behavior of the acetate, therefore, is analogous to that of 4-phenylphenol.

2. These results are in keeping with a previous suggestion that steric effects may determine the positions taken by substituents entering an ester molecule.

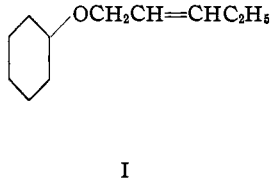
PULLMAN, WASHINGTON RECEIVED AUGUST 21, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

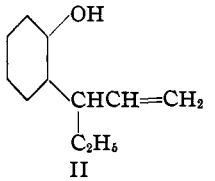
The Rearrangement of Phenyl Allyl Ethers. III. The Synthesis of α-(ortho-Methoxyphenyl)-propionic Acid

BY WALTER M. LAUER AND LOUIS I. HANSEN[1]

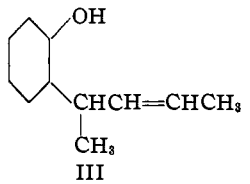
The rearrangement of γ-ethylallyl phenyl ether (I) yields both o-(α-ethylallyl)-phenol (II), and o-(α,γ-dimethylallyl)-phenol (III).[2]



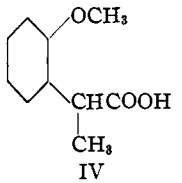
I



II



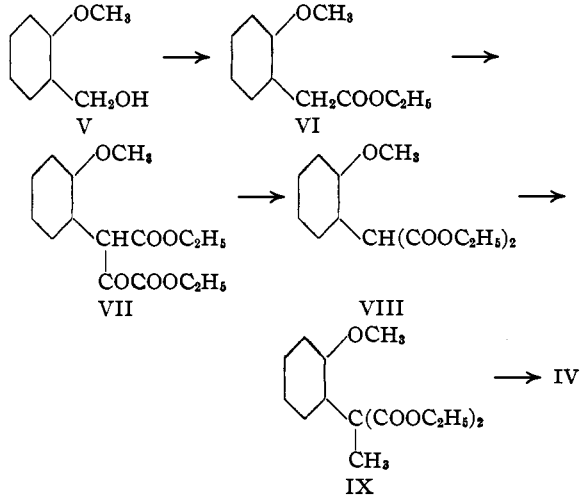
III



IV

The structure of the abnormal rearrangement product (III) is based upon several lines of evidence which need not be considered here. However, one method of approach which was used involves the conversion of this abnormal rearrangement product into α-(o-methoxyphenyl)-propionic acid (IV). This acid has not been described previously. Therefore, it was the purpose of the present study to synthesize this acid and to compare it with the product obtained by the degradation of the abnormal rearrangement product (III).

A number of promising syntheses were studied and the desired acid was prepared in two independent ways. The synthetic product proved to be identical with that obtained from the abnormal rearrangement product. An outline of the most satisfactory synthesis follows



The corresponding compounds in the para series were also prepared.

(1) Abstract of Ph.D. thesis, submitted to the University of Minnesota, March, 1938. Paper III, THIS JOURNAL, **58**, 1392 (1936).

(2) Lauer and Filbert, THIS JOURNAL, **58**, 1388 (1936); Hurd and Puterbaugh, *J. Org. Chem.*, **2**, 381 (1938).

In addition, α-(*o*-methoxyphenyl)-butyric acid was synthesized, since this acid is related to the normal rearrangement product (II), in the same way that α-(*o*-methoxyphenyl)-propionic acid is related to the abnormal rearrangement product (III).

Experimental

***o*-Methoxybenzyl alcohol** (V) (b. p. 130–131° at 15 mm.) was prepared from *o*-methoxybenzaldehyde according to the excellent procedure of Davidson and Bogert[3] using a crossed Cannizzaro reaction.

The α-naphthylurethan (m. p. 135–136°) was prepared.[4]

***o*-Methoxybenzyl chloride** was prepared by saturating a solution of 112 g. of *o*-methoxybenzyl alcohol in 500 ml. of benzene with dry gaseous hydrogen chloride according to the directions of Pschorr[5]: yield, 112 g. (88%); b. p. 104–105° at 10 mm.

***o*-Methoxybenzyl cyanide** was obtained by refluxing the chloride (85 g.) in acetone (900 ml.) with a concentrated aqueous solution containing potassium cyanide (80 g.).

Ethyl *o*-methoxyphenylacetate (VI), (b. p. 137–138° at 13 mm.).—A mixture of *o*-methoxybenzyl cyanide (104 g.), alcohol (104 ml.) and a solution of potassium hydroxide (46 g.) in water (50 ml.) was refluxed for ten hours. The reaction mixture was then poured into water, cooled and filtered, and extracted with ether. The aqueous alkaline solution was warmed on the steam-bath to remove the ether and some of the alcohol. Acidification with 10% sulfuric acid produced an oil (100 g.) which solidified on standing. Crystallization from a petroleum ether–ether mixture yielded the pure acid, m. p. 123–124°. The *o*-methoxyphenylacetic acid was esterified.

Diethyl *o*-Methoxyphenylmalonate (VIII).—Absolute alcohol (172 ml.), in a three-necked flask fitted with a mercury-sealed stirrer, reflux condenser and dropping funnel, was treated with sodium (5.64 g.). After the reaction mixture had cooled to 60°, freshly distilled ethyl oxalate (35.8 g.) was added rapidly with vigorous stirring. The addition of the ethyl ester of *o*-methoxyphenylacetic acid (47.5 g.) followed. Stirring was discontinued and the reaction mixture was then poured into a beaker. The sodium salt crystallized out after standing at room temperature for several hours. The thick paste was stirred thoroughly with dry ether (200 ml.) and then filtered. The *o*-methoxyphenyl oxalacetic ester was liberated from its sodium salt with dilute sulfuric acid and then extracted from the aqueous solution with ether. The combined ether extracts were dried over sodium sulfate. After the ether had been removed by distillation, the residual oil was heated by means of a metal or oil-bath. The pressure was reduced to approx. 15 mm. and the temperature was raised gradually to 125°, at which temperature the evolution of carbon monoxide began. The temperature was then increased slowly to 175° and maintained approximately four hours until the evolution of carbon monoxide was complete. The distillate combined with the residue in the distilling flask yielded diethyl *o*-methoxyphenyl malonate (36 g., b. p. 162–164° at 4.5 mm.) upon distillation under reduced pressure.

Anal. Calcd. for $C_{14}H_{18}O_5$: C, 63.2; H, 6.8. Found: C, 63.8; H, 7.2.

Diethyl Ester of *o*-Methoxyphenylmethylmalonic Acid (IX).—Sodium (1.3 g.) was dissolved in absolute alcohol (15.5 g.) contained in a three-necked flask fitted with a mercury-sealed stirrer, reflux condenser and dropping funnel. Diethyl *o*-methoxyphenylmalonate (15 g.) was then added slowly with cooling. The reaction mixture was allowed to remain in an ice-bath for two hours after the addition of the ester. At the end of this period the reaction mixture was heated in a steam-bath and methyl iodide (8.4 g.) was added dropwise. The reaction mixture was heated under reflux until it became neutral to litmus, and then poured into water. The oily layer was separated and the aqueous layer extracted with ether. The combined ether extracts were then dried over sodium sulfate. Distillation yielded a product (12.5 g.) boiling at 152–153° under a pressure of 2.8 mm.

The unmethylated malonic ester was separated from the methylated ester by means of fractional hydrolysis at room temperature with a dilute solution (4.5%) of potassium hydroxide. After the ether solution of the mixture of esters had been shaken with the alkali for a period of six hours, the aqueous layer was acidified with dilute hydrochloric acid. Extraction with ether yielded a solid which, upon crystallization from a mixture of ether and petroleum ether, melted at 137.5–138° with decomposition. Decarboxylation gave *o*-methoxyphenylacetic acid (m. p. 123–124°).

A second treatment of the ether solution with dilute potassium hydroxide at room temperature for a four-hour period did not yield any isolable acid. The ether solution upon distillation gave an oil (b. p. 150–151° at 2.6 mm.) which solidified (m. p. 42–43°).

Anal. Calcd. for $C_{15}H_{20}O_5$: C, 64.29; H, 7.14. Found: C, 64.14; H, 7.15.

Hydrolysis and Decarboxylation of the Diethyl Ester of *o*-Methoxyphenylmethylmalonic Acid.—A solution of the pure ester (2 g.) in alcohol (15 ml.) was refluxed for one hour with a slight excess of potassium hydroxide solution (10%). The reaction mixture was then poured into water and acidified with dilute hydrochloric acid. Extraction with ether gave a solid which, upon crystallization from a mixture of ether and petroleum ether, melted at 148.5–149° with decomposition.

Anal. Calcd. for $C_{11}H_{12}O_5$: C, 58.9; H, 5.4. Found: C, 58.6; H, 5.8.

Decarboxylation was accomplished by refluxing the dibasic acid in xylene for two hours. After the xylene was removed by distillation under reduced pressure, an oil which solidified remained. Crystallization from a mixture of ether and petroleum ether yielded the desired monobasic acid of m. p. 101–102°.

A mixed melting point taken with the acid prepared by the degradation of the abnormal rearrangement product (III) showed no depression.

α-(*o*-Methoxyphenyl)-butyric acid was prepared by the ethylation of diethyl *o*-methoxyphenylmalonate using ethyl iodide. The procedure was similar to that used for

(3) Davidson and Bogert, THIS JOURNAL, **57**, 905 (1935).
(4) Bickel and French, *ibid.*, **48**, 747–751 (1926).
(5) Pschorr, *Ann.*, **373**, 76 (1910).

methylation. Diethyl *o*-methoxyphenylethylmalonate is a solid of m. p. 66–67°.

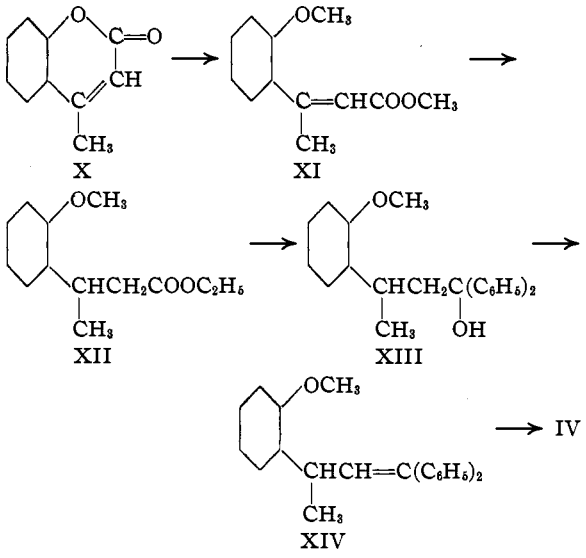
Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.3; H, 7.5. Found: C, 65.0; H, 7.5.

Hydrolysis and decarboxylation yielded the solid α-(*o*-methoxyphenyl)-butyric acid (m. p. 56–57°; b. p. 165–166° at 10 mm.).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.0; H, 7.2. Found: C, 67.5; H, 6.9.

The physical properties of a few of the para compounds are: (a) ethyl *p*-methoxyphenylacetate, b. p. 148–150° at 14.5 mm.; (b) diethyl *p*-methoxyphenylmalonate, b. p. 161–162° at 3 mm., $n^{20}D$ 1.4988; (c) diethyl *p*-methoxyphenylmethylmalonate, b. p. 160–161° at 3.5 mm., $n^{20}D$ 1.4990. (*Anal.* Calcd. for $C_{15}H_{20}O_5$: C, 64.3; H, 7.1. Found: C, 63.9; H, 7.0); (d) *p*-methoxyphenylmethylmalonic acid, m. p. 149.5–150°. (*Anal.* Calcd. for $C_{11}H_{12}O_5$: C, 59.0; H, 5.4. Found: C, 59.1; H, 5.4); (e) α-(*p*-methoxyphenyl)-propionic acid, m. p. 56–57°.

A second but less satisfactory synthesis of α-(*o*-methoxyphenyl)-propionic acid made use of the following series of reactions



4-Methylcoumarin (X), prepared according to the directions of Stoermer and Sandow,[6] was converted to the **methyl ester of *o*-methoxy-β-methylcinnamic acid (XI)** using the procedure of these same investigators. Difficulty was experienced in the catalytic reduction of XI, consequently the ester was hydrolyzed to the acid by means of alcoholic potassium hydroxide.

Reduction of *o*-methoxy-β-methylcinnamic acid to the corresponding saturated acid was accomplished by the use of sodium amalgam. The unsaturated acid (18 g., 0.09 mole) was dissolved in 100 cc. of water containing sodium hydroxide (3.68 g., 0.09 mole). To this solution 4% sodium amalgam (150 g.) was added over a period of six hours, maintaining a temperature of 50° throughout. After twelve hours, reduction was complete. The filtered aqueous solution was then acidified with 10% sulfuric acid and extracted with ether. The combined ether extracts, after drying with sodium sulfate, yielded an oil which was distilled under reduced pressure (b. p. 172° at 9 mm.). After standing at room temperature for approximately one month, the product finally solidified (m. p. 49–50°).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.14; H, 7.23. Found: C, 68.26; H, 7.25.

Ethyl *o*-methoxy-β-methylhydrocinnamate (XII) (b. p. 153–154° at 9 mm.) was prepared by refluxing the saturated acid with absolute ethyl alcohol in the presence of a small amount of concd. sulfuric acid.

The conversion of the ester to the **carbinol XIII** was brought about in the following manner. To a solution of the Grignard reagent prepared from phenyl bromide (54.2 g.) and magnesium (8.3 g.) and ether (1500 cc.) was added an ether solution of the hydrocinnamate (29 g.). The rate of addition of the ester was regulated so that the reaction mixture refluxed slowly. After the addition of the ester, the mixture was refluxed for an additional two hours. The ether was then removed by distillation and the residue was heated on the steam-bath for one hour. The reaction mixture was decomposed with ice and sulfuric acid, and then extracted with ether. The combined ether extracts were washed with water and after the ether was removed, the residue was steam distilled to remove the diphenyl. The residual oil in the distilling flask was then taken up in ether and dried. The product (35 g.), which was obtained after the removal of the ether, did not crystallize.

The carbinol XIII was dehydrated in accordance with the procedure of Schlenk and Bergmann[7] by refluxing with acetic anhydride. The yellow oil which resulted from this dehydration could not be crystallized but was oxidized directly.

Oxidation of XIV.—A solution of XIV (2 g.) in acetic acid (15 ml.) was placed in a bath at 50–60°. To this solution was added dropwise chromic acid (1.5 g.) dissolved in water (3 ml.) and acetic acid (6 ml.). After oxidation was complete, the reaction mixture was steam distilled. Benzophenone was isolated from the steam distillate. The contents of the distilling flask were then subjected to extraction with ether, and the ether extract was shaken with a 5% solution of sodium carbonate. The alkaline aqueous extract, after acidification with sulfuric acid (10%), produced an oil, which upon distillation at reduced pressure yielded a crystalline solid (m. p. 101–102°). This solid proved to be the desired acid IV.

Summary

α-(*o*-Methoxyphenyl)-propionic acid has been synthesized in two different ways. It is identical with the product previously obtained by the degradation of the abnormal rearrangement product of γ-ethylallyl phenyl ether. This synthesis therefore supplies evidence of the correctness of the structures which have already been assigned to the abnormal rearrangement product of γ-ethylallyl phenyl ether and to its degradation product.

MINNEAPOLIS, MINN. RECEIVED MAY 29, 1939

(6) Stoermer and Sandow, *Ber.*, **53**, 1285 (1920).

(7) Schlenk and Bergmann, *Ann.*, **463** 50 (1928).