pected on the basis of the $pK_a$-activity curve reported by Bell and Roblin.[5]

### Experimental

**Methoxyamine.**[6]—This compound (b. p. 49–50°, hydrochloride m. p. 149°) was prepared by the methylation of hydroxylaminedisulfonic acid[7] with methyl sulfate. It was found necessary to use freshly prepared hydroxylamine disulfonic acid to obtain maximum yields.

**Benzyloxyamine.**[8]—This compound (b. p. 118° at 30 mm.) was prepared by the hydrolysis of O-benzyl acetoxime.

**$N^4$-Acetyl-$N^1$-methoxysulfanilamide.**—To a solution of 6.1 g. of methoxyamine hydrochloride in 40 ml. of pyridine was added 17.1 g. of acetylsulfanilyl chloride, in portions with stirring and cooling. The mixture was stirred overnight at room temperature, poured into water, filtered and dried at 100°. The yield of crude is quantitative. One crystallization from a benzene–, alcohol mixture gave colorless waxy crystals, m. p. 205–206°.

*Anal.* Calcd. for $C_9H_{12}O_4N_2S$: N, 11.5. Found: N, 11.4.

**$N^1$-Methoxysulfanilamide.**—Fifteen grams of the acetyl derivative was refluxed in 150 ml. of 2 *N* hydrochloric acid for one hour. On cooling and neutralization with excess sodium acetate a white solid was obtained which on crystallization from water gave 66% of a product, m. p. 134.5–135.0°.

*Anal.* Calcd. for $C_7H_{10}O_3N_2S$: N, 13.9. Found: N, 14.0.

**$N^4$-Acetyl-$N^1$-benzyloxysulfanilamide.**—The acetyl derivative was prepared in a manner similar to that given for the $N^1$-methoxy derivative. On crystallization from aqueous alcohol a 50% yield of a product, m. p. 181–182°, was obtained.

*Anal.* Calcd. for $C_{15}H_{16}O_4N_2S$: N, 8.76. Found: N, 8.65.

**$N^1$-Benzyloxysulfanilamide.**—Nine and four-tenths grams of the acetyl derivative was hydrolyzed by refluxing for one hour in 100 ml. of 6 *N* hydrochloric acid. The mixture was placed in a refrigerator overnight and filtered. The crystalline precipitate was triturated with excess aqueous sodium acetate, filtered and finally crystallized from alcohol. Eighty-three per cent. of a white crystalline product was obtained, m. p. 130°.

*Anal.* Calcd. for $C_{13}H_{14}O_3N_2S$: N, 10.1. Found: N, 10.1.

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[5] Bell and Roblin, This Journal, **64**, 2908 (1942).

[6] Traube, Ollendorf and Zander, *Ber.*, **53**, 1477 (1920).

[7] Raschig, *Ber.*, **40**, 4581 (1907); Traube, *ibid.*, **53**, 1477 (1920).

[8] Behrend and Leuchs, *Ann.*, **257**, 206 (1890).

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Received July 30, 1945

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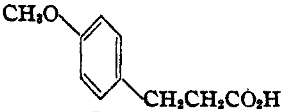
## The Cyclization of β-*p*-Methoxyphenylpropionic Acid

By William S. Johnson and Wesley E. Shelberg

In connection with some studies on the formation of cyclic ketones by intramolecular acylation,[1] we have found that the cyclization of β-*p*-methoxyphenylpropionic acid, I, affords a particularly interesting case. Chakravarti and Swaminathan[2] have noted that this acid is especially resistant to cyclization. Using the Friedel–Crafts reaction of the acid chloride with aluminum chloride in nitrobenzene they found conditions whereby 6-methoxyhydrindone-1, II, could be obtained in about 20% yield.



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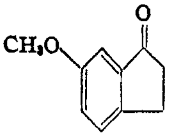

II

Since hydrogen fluoride has been shown to have a unique cyclizing power in the case of γ-(4-methoxy-3-biphenyl)-butyric acid[3] (which resists cyclization by the Friedel–Crafts method[4]), it seemed worthwhile to investigate the action of this reagent in the present case. When the acid I was treated by the customary procedure,[3] only a 3% yield of the cyclic ketone was realized, 94% of unchanged acid being recovered. When the reaction was conducted in a closed bomb a 36% yield of the ketone was obtained after five days at room temperature. The low susceptibility of the acid to cyclization is attributable largely to the deactivating influence of the *p*-methoxyl group toward the meta position involved in the acylation. This effect has been noted before. For example, while γ-phenylbutyric acid is cyclized to tetralone-1 in 92% yield by hydrogen fluoride,[3] the *p*-methoxy derivative is converted by the same treatment to 7-methoxytetralone-1 in only 61.5% yield.[5] The even greater resistance of the lower homolog I to cyclization observed in the present work would, therefore, seem to be due to the size of the ring formed, and is consistent with the premise that six-membered rings are formed more readily than five-membered ones.[1]

The Friedel–Crafts method of cyclization has also been investigated. Using a modified procedure of Newman[6] we have been able to obtain yields of II as high as 85%. The acid chloride of I was prepared with phosphorus pentachloride, the phosphorus oxychloride being removed under reduced pressure, and the cyclization was conducted in benzene with aluminum chloride at room temperature for three and one-half hours. Three interesting observations result from this work: (1) In spite of the intrinsic resistance of I to cyclization it is unnecessary to heat the reaction mixture as advocated in previous general procedures.[1,6] (2) As observed by Newman, it is important to remove the phosphorus oxychloride. When this was not done the yield of II dropped to 69%. (3) Even though the reaction was carried out in benzene solution, little, if any, intermolecular acylation occurred. Thus, in spite of the low cyclization susceptibility of I, the intramolecular reaction is preferred.

### Experimental[7]

β-*p*-Methoxyphenylpropionic acid, I, has been prepared in excellent yield by Howard J. Glenn from anisaldehyde.

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[1] Adams, "Organic Reactions," Vol. II, 1944, p. 114.

[2] Chakravarti and Swaminathan, *J. Ind. Chem. Soc.*, **11**, 101 (1934).

[3] Fieser and Hershberg, This Journal, **61**, 1272 (1939).

[4] Fieser and Bradsher, *ibid.*, **58**, 1738 (1936).

[5] Campbell and Todd, *ibid.*, **64**, 928 (1942).

[6] Newman, *ibid.*, **60**, 2947 (1938); **62**, 870 (1940).

[7] All melting points are corrected.

From 55 g. of the aldehyde and 65 g. of malonic acid in 75 cc. of pyridine and 1 cc. of piperidine there was obtained after sixteen hours of heating on the steam-bath and acidification with 20% hydrochloric acid, 71.3 g. (99% yield) of *p*-methoxycinnamic acid, m. p. 171.6–173.2°, clearing at 188–189.5°. This substance is known to form liquid crystals on melting; reported m. p. 170[8] and 186°.[9] Hydrogenation of this acid (35.6 g.) in glacial acetic acid (200 cc.) over Adams catalyst (0.1 g.) gave a quantitative yield (36.0 g.) of crude *β*-*p*-methoxyphenylpropionic acid, m. p. 100–104°. For the cyclizations it was found desirable to recrystallize this product three times from alcohol, giving material melting at 103.5–104° (reported m. p. 104°[10]).

**Cyclization with Hydrogen Fluoride.**—A solution of 3.04 g. of *β*-*p*-methoxyphenylpropionic acid in about 100 cc. of anhydrous hydrogen fluoride was allowed to stand in a platinum vessel overnight. The material which remained was dissolved in ether, washed with water and then with 5% sodium bicarbonate solution. Acidification of the bicarbonate washings afforded 2.86 g. (94% recovery) of unchanged acid I, m. p. 103–104°. The neutral material amounted to 81 mg. (3% yield) of colorless 6-methoxyhydrindone-1, m. p. 105–108°. The ketone crystallized from alcohol in the form of long needles, m. p. 108–109° (reported, 109°[2,11]).

When 4.01 g. of the acid I was treated as described above except that the reaction mixture was allowed to remain in a closed copper bomb for five days, the yield of ketone II was 1.31 g. (36%), m. p. 106–107.5°. The uncyclized acid amounted to 2.30 g. (57% recovery), m. p. 102–103°

**Cyclization by the Friedel–Crafts Method.**—Three grams of *β*-*p*-methoxyphenylpropionic acid and 3.64 g. of phosphorus pentachloride were mixed with shaking in a 50-cc. Claisen flask. The mixture melted and hydrogen chloride was evolved. After the initial reaction, the volatile phosphorus compounds were removed at the water pump by heating the flask in an oil-bath at 80–90°. The almost colorless acid chloride was then transferred with the aid of 70 cc. of dry, thiophene free benzene into a flame-dried, three-necked 500-cc. flask fitted with a calcium chloride tube, a Hershberg stirrer and a rubber-tubed addition flask[12] containing 2.33 g. of fresh aluminum chloride. The solution was chilled (ice-bath) just to the solidification point and the aluminum chloride was added in portions over a period of ten to fifteen minutes. After stirring for three and one-half hours at room temperature the dark-red addition complex was decomposed with a mixture of ice and concentrated hydrochloric acid, and the mixture was worked up by extraction with ether and washing thoroughly with 2% potassium hydroxide solution containing salt to minimize emulsion formation. Evaporation of the dried (over anhydrous sodium sulfate) organic layer afforded 2.29 g. (85% yield) of colorless needles of 6-methoxyhydrindone-1, m. p. 103–105°. After recrystallization from alcohol the m. p. was 108–109°. The best recovery (about 94%) of pure material, m. p. 108–109°, was obtained by reduced pressure evaporative distillation of the crude ketone.

Acidification of the alkaline washings gave 130 mg. (4% recovery) of crude starting acid I.

When the reaction time was extended to twenty hours the yield of ketone, m. p. 104–106°, was 86%. When only one-half hour was allowed for the reaction the yield of neutral material dropped to 60%.

In one experiment the volatile phosphorus compounds were not removed. The neutral fraction obtained from 3.00 g. of I amounted to 1.86 g. (69% yield) of very crude dark semi-solid ketone, m. p. after drying on a porous plate, 105–106°. The recovered acid I amounted to 0.650 g. (22%), m. p. 99–101°.

An attempt to cyclize the acid chloride of I with stannic chloride gave a poor (about 10%) yield of crude ketone II.

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RECEIVED JULY 2, 1945

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[8] Knoevenagel, *Ber.*, **31**, 2596 (1898).

[9] Bowden, "The Phase Rule and Phase Reactions," Macmillan and Co., London, 1938, p. 277.

[10] Barger and Walpole, *J. Chem. Soc.*, 1720 (1909).

[11] Ingold and Piggott, *ibid.*, 1469 (1923).

[12] Fieser, "Experiments in Organic Chemistry," 2nd. ed., D. C. Heath and Co., Boston, Mass., 1941, p. 311.

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## Reaction of Furfural Derivatives with Maleic Anhydride

By WERNER HERZ

During an investigation of the behavior of some substituted furans toward maleic anhydride, products have been obtained in several instances which indicate that a series of reactions previously observed by La Parola[1] can be extended to derivatives of furfural. The latter isolated N-substituted maleamic acids from reaction mixtures containing maleic anhydride and certain Schiff bases. Corresponding substances, N-methylmaleamic acid, previously reported by Piutti and Giustiniani,[2] and N-*o*-chlorophenylmaleamic acid, were obtained by the author when furfurylidenemethylamine and furfurylidene-*o*-chloroaniline were treated with maleic anhydride. Addition of the anhydride to furfural phenylhydrazone, resulting in furfural 1-maleylphenylhydrazone and paralleling the addition to benzaldehyde phenylhydrazone reported by La Parola, was also noted.

### Experimental[3]

**N-Methylmaleamic Acid.**—A solution of 20 g. of furfurylidenemethylamine in 150 ml. of ether was shaken with 25 g. of maleic anhydride, added in small portions. A heavy yellow precipitate was formed almost immediately with evolution of much heat. Two recrystallizations from a mixture of alcohol and ether gave 27 g. of white plates, m. p. 154°, five degrees higher than reported by Piutti and Giustiniani.[2] From hot glacial acetic acid, the product separates in the form of white needles. The crystals are soluble in water, dilute acid, acetic acid and hot ligroin, very soluble in dilute base and alcohol and only slightly soluble in ether, cold ligroin and carbon tetrachloride. Upon boiling with concd. sodium hydroxide, the odor of methylamine becomes noticeable.

*Anal.* Calcd. for $C_5H_7O_3N$: C, 46.51; H, 5.43; neut. equiv., 129. Found: C, 46.59; H, 5.42; neut. equiv., 128.

**N-*o*-Chlorophenylmaleamic Acid.**—To a solution of 6 g. of furfurylidene-*o*-chloroaniline in 25 ml. of ether was added 4 g. of maleic anhydride, with boiling until dissolved. Needles began to separate soon; after standing overnight, the crystal mass was separated by filtration and recrystallized twice from ether. Four grams of product, light-green needles, m. p. 132°, was obtained. The long needles are soluble in alcohol, hot water and dilute base, and partially soluble in ether. Upon boiling with strong sodium hydroxide, *o*-chloroaniline separates.

For purposes of comparison, the acid was also prepared by the method of Hurd, Roe and Williams.[4] One and eight-tenths grams of the product, m. p. 132°, was obtained from 1.5 g. of *o*-chloroaniline and 1.2 g. of maleic anhydride. A mixed melting point determination established the identity of the two substances.[5]

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[1] La Parola, *Gazz. chim. ital.*, **64**, 919 (1934); **65**, 624 (1935).

[2] Piutti and Giustiniani, *ibid.*, **26** I, 431 (1896).

[3] All melting points are uncorrected.

[4] Hurd, Roe and Williams, *J. Org. Chem.*, **2**, 314 (1937).

[5] Also prepared by the same method were the following unlisted compounds: N-*m*-chlorophenylmaleamic acid, light-green needles from alcohol, m. p. 187–188°; N-*p*-chlorophenylmaleamic acid, light-green needles from alcohol, m. p. 199°.