[CONTRIBUTION NO. 283 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

# Friedel-Crafts Type Reactions on Biphenyl[1]

BY SAMUEL L. SILVER AND ALEXANDER LOWY

The purpose of this investigation has been to study various types of Friedel-Crafts reactions on biphenyl and to determine the structure of the products.

The only detailed investigation of Friedel-Crafts reactions on biphenyl is that of Adam,[2] who studied the reactions of several halogenated hydrocarbons and acid derivatives. Several ketones have been prepared by various workers.[3]

The present investigation has shown that the diacetyl and bis-(chloroacetyl) biphenyls are of the *p,p'*-type. These positions may be considered the points of attack within the biphenyl nucleus in ketone syntheses by means of the Friedel-Crafts reaction. Diacetylation of biphenyl does not take place under the usual conditions with acetic anhydride, while the use of acetyl chloride results in the formation of *p,p'*-diacetylbiphenyl.

Liebermann and Zsuffa[4] obtained *p*-xenoic acid by heating a mixture of biphenyl, oxalyl chloride, aluminum chloride and carbon disulfide, followed by the usual treatment. In this investigation di-*p*-xenyl ketone and *p*-xenil were obtained, no *p*-xenoic acid being isolated.

Biphenyl, in reactions with benzenesulfonyl chloride and thionyl chloride, gave *p*-xenylsulfonylbenzene and *p*-xenyl-*p*-sulfinylbiphenyl, respectively.

## Experimental Part

The apparatus described by Riddell and Noller,[5] and powdered aluminum chloride, 99.5% pure, were used throughout the investigation. In the reactions with chloroacetic anhydride, chloroacetyl chloride (monomolecular), oxalyl chloride, benzenesulfonyl chloride and thionyl chloride, the theoretical proportions of the reagent and of biphenyl were used, and a 10% excess over the theoretical quantity of aluminum chloride was employed. In the dimolecular reactions with acetyl and chloroacetyl chlorides large excesses of the acyl halides and of aluminum chloride were used. The weight of acetyl chloride was two and a half times that of biphenyl (or of the monoacetyl compound), and a proportionate amount of chloroacetyl chloride was used; a six-fold quantity of aluminum chloride was employed.

In general the procedure was as follows. The aluminum chloride was suspended in a solution of biphenyl (or suspension of the monoacyl compound) in a suitable volume of carbon disulfide, and the reagent was added slowly from the dropping funnel. The mixture was refluxed on a water-bath, with the exception of Expt. H, until hydrogen chloride evolution had practically ceased. The reaction product was hydrolyzed in the usual manner, the carbon disulfide being removed either prior to or after hydrolysis. Purification was obtained by repeated crystallization from a suitable solvent, in the presence of bone black.

TABLE I

FRIEDEL-CRAFTS REACTIONS

| Expt. | Reactants with aluminum chloride | Product |
|---|---|---|
| A | Biphenyl and acetyl chloride | *p,p'*-Diacetylbiphenyl |
| B | Methyl *p*-xenyl ketone and acetyl chloride | *p,p'*-Diacetylbiphenyl |
| C | Biphenyl and chloroacetic anhydride | Chloromethyl *p*-xenyl ketone |
| D | Biphenyl and chloroacetyl chloride | Chloromethyl *p*-xenyl ketone |
| E | Biphenyl and chloroacetyl chloride | *p,p'*-Bis-(chloroacetyl)-biphenyl |
| F | Chloromethyl *p*-xenyl ketone and chloroacetyl chloride | *p,p'*-Bis-(chloroacetyl)-biphenyl |
| G | Biphenyl and oxalyl chloride | Di-*p*-xenyl ketone |
| H | Biphenyl and oxalyl chloride | *p*-Xenil |
| I | Biphenyl and benzenesulfonyl chloride | *p*-Xenylsulfonylbenzene |
| J | Biphenyl and thionyl chloride | *p*-Xenyl-*p*-sulfinylbiphenyl |

The reactions studied and characteristics of the products are given in Table I; the derivatives prepared to substantiate the structure of the products and the reagents employed are listed in Table II.

*Anal.* Expt. E. Calcd. for $C_{16}H_{12}O_2Cl_2$: Cl, 23.10. Found: Cl, 22.82, 23.27. Expt. I. Calcd. for $C_{18}H_{14}O_2S$: S, 10.88. Found: S, 10.95, 11.05. Expt. J. Calcd. for $C_{24}H_{18}OS$: S, 9.05. Found: S, 9.18, 9.26.

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(1) Abstracted from a thesis presented by Samuel L. Silver to the Graduate School in partial fulfilment of the requirements for the Ph.D. degree.

(2) Adam, *Ann. chim.*, [6] **15**, 224 (1888).

(3) (a) Willgerodt and Scholtz, *J. prakt. Chem.*, [2] **81**, 394 (1910); (b) Collet, *Bull. soc. chim.*, [3] **17**, 510 (1897); (c) Delaville, *Compt. rend.*, **184**, 463 (1927); (d) Dilthey, *J. prakt. Chem.*, [2] **101**, 195 (1920); (e) Wolfe, *Ber.*, **14**, 2031 (1881); (f) Scholl and Seer, *Ann.*, **394**, 149 (1912); (g) Schlenk and Bergmann, *ibid.*, **464**, 32 (1928); (h) Gomberg and Bailar, THIS JOURNAL, **51**, 2233 (1929); (i) Drake and Bronitsky, *ibid.*, **52**, 3718 (1930); (j) Scholl and Neovius, *Ber.*, **44**, 1078 (1911).

(4) Liebermann and Zsuffa, *ibid.*, **44**, 857 (1911).

(5) Riddell and Noller, THIS JOURNAL, **52**, 4368 (1930).

TABLE I (*Concluded*)

| Expt. | Solvent | Crystalline form | Yield, % | M. p., °C. | Ref. |
|---|---|---|---|---|---|
| A | EtOH | Gleaming colorless leaflets | 43 | 191 | 3d |
| B | EtOH | Gleaming colorless leaflets | 51 | 191 | 3d |
| C | Dil. EtOH, 3:1 | Pale yellow needles | 41 | 122–123 | 3b |
| D | Dil. EtOH, 3:1 | Pale yellow needles | 77 | 122–123 | 3b |
| E | Dipropyl ketone | Long brittle pale yellow needles | 35 | 228–229 | . . |
| F | Dipropyl ketone | Long brittle pale yellow needles | 52 | 228–229 | . . |
| G | Benzene | Gleaming white leaflets | 40 | 236 | 6 |
|  | AcOH | Yellow needles | 25 | 140–141 | 7a, b, c |
| H | Expt. G | Expt. G | 8.6<br>52 | G<br>G | 6<br>7a, b, c |
| I | EtOH | Gleaming colorless platelets | 43 | 148.5 | . . |
| J | EtOH, pptd. by EtOAc | . . . | . . | 207–208 | . . |

**Notes on Table I.**—Methyl *p*-xenyl ketone, used in Expt. B, was prepared by a method similar to that of Drake and Bronitsky.[31] In Expts. E and F the hydrolysis product was first extracted with boiling alcohol to remove chloromethyl *p*-xenyl ketone. The products in experiments G and H were separated by extraction of the hydrolysis product with cold benzene, in which *p*-xenil is very soluble. Experiment H was conducted at a temperature of 0–5°. The hydrolysis product in experiment I was a pasty mass. The pasty nature disappeared on boiling several times with water. No suitable solvent could be found for the product of Expt. J. The method used gave a pale cream, flocculent precipitate.

TABLE II

IDENTIFICATION OF PRODUCTS

| Compound | Reagent | Derivative | M. p., °C. DME = dimethyl ester | Ref. |
|---|---|---|---|---|
| *p*,*p*′-Diacetylbiphenyl | $CrO_3$–AcOH | Biphenyl-4,4′-dicarboxylic acid | DME 212–213 | 8 |
| *p*,*p*′-Bis-(chloroacetyl)-biphenyl | $KMnO_4$, sl. alkaline | Biphenyl-4,4′-dicarboxylic acid<br>Terephthalic acid | DME 212–213<br>DME 140 | 8<br>9 |
| Di-*p*-xenyl ketone | $PCl_5$ | Di-*p*-xenyl ketone chloride | 135–136 | 10 |
|  | $CrO_3$–AcOH | Benzophenone-4,4′-dicarboxylic acid | DME 224 | 11 |
|  | KOH fusion | *p*-Xenoic acid<br>Biphenyl | 224<br>70 | 4<br>. . |
| *p*-Xenil | *o*-Phenylenediamine | Di-*p*-xenylquinoxaline | 210 | 7b |
|  | $CrO_3$–AcOH | Terephthalic acid | DME 140 | 9 |
|  | Pyridine, perhydrol, NaOH | *p*-Xenoic acid | 224 | 4 |
|  | Bz, EtOH, KOH | *p*-Xenilic acid | 185–188 | 7b |
| *p*-Xenylsulfonylbenzene | $CrO_3$–AcOH | Phenylsulfonyl benzene-4-carboxylic acid | 267 | 12 |
| *p*-Xenyl-*p*-sulfinyl-biphenyl | 10% $KMnO_4$ | *p*-Xenyl-*p*-sulfonylbiphenyl | 215–216 | 13 |

**Notes on Table II.**—The splitting of *p*-xenil to *p*-xenoic acid was accomplished by the general method of Schapiro.[14]

The rearrangement of *p*-xenil to *p*-xenilic acid was performed as follows. To a solution of 0.5 g. of *p*-xenil in 15 cc. of benzene and 5 cc. of alcohol were added 0.5 g. of potassium hydroxide and 1 cc. of water. The mixture was refluxed for ten minutes, extracted with 100 cc. of water, and the acid precipitated by acidification of the aqueous solution. The acid was recrystallized from benzene–heptane mixture (1:1).

The oxidation product of *p*-xenyl-*p*-sulfinylbiphenyl was extracted from the precipitated manganese dioxide with boiling alcohol.

All esters were prepared by the method given by Mulliken.[9]

**Reaction of Vinyl Chloride.**—Dry vinyl chloride was passed into a mixture of 77 g. of biphenyl, 73 g. of aluminum chloride and 400 cc. of olefin-free ligroin, for two hours at a temperature of −5 to 5°. Hydrolysis with cracked ice and hydrochloric acid gave a fluorescent green ligroin layer, which was washed free of acid and steam distilled until only small amounts of biphenyl passed over. The viscous residue was dried with calcium chloride, and then distilled *in vacuo*. Between 125 and 210° at 3 mm. a yellow oil was collected, which could not be separated by repeated fractionation. The experiment was repeated at the temperature of molten biphenyl, in the absence of a solvent. Similar products were obtained as in the low temperature experiment.

## Summary

1. Various acyl halides and acid anhydrides

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(6) Schilow, *Chem. Zentr.*, **101**, II, 2524 (1930).

(7) (a) Gomberg and Bachmann, THIS JOURNAL, **50**, 2767 (1928); (b) Gomberg and Van Natta, *ibid.*, **51**, 2243 (1929); (c) Wittig and Leo, *Ber.*, **63**, 948 (1930).

(8) Weiler, *ibid.*, **23**, 1061 (1899).

(9) Mulliken, "Identification of Pure Organic Compounds," Vol. I, p. 85.

(10) Straus and Dützmann, *J. prakt. Chem.*, [2] **103**, 43 (1921).

(11) Limpricht, *Ann.*, **312**, 96 (1900).

(12) Weeden and Doughty, *Am. Chem. J.*, **33**, 426 (1905).

(13) Gabriel and Deutsch, *Ber.*, **13**, 387 (1880).

(14) Schapiro, *ibid.*, **66**, 1371 (1933).

have been shown to react with biphenyl in Friedel–Crafts reactions to give *p*-substitution products. The structure of the products has been proved by the preparation of derivatives.

2. Vinyl chloride, under variable temperature conditions, forms complex products which cannot be separated by fractional vacuum distillation.

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[CONTRIBUTION FROM THE INSECTICIDE DIVISION, BUREAU OF CHEMISTRY AND SOILS, UNITED STATES DEPARTMENT OF AGRICULTURE]

# Rotenone. XXXI. The Synthesis of 2-Hydroxy-4,5-dimethoxyphenylacetic Acid

BY L. E. SMITH AND F. B. LAFORGE

By the action of chloromethyl ether on the sodium compound of 2-hydroxy-4,5-dimethoxybenzaldehyde, the corresponding methoxymethyl ether was obtained; by condensation with hippuric acid this compound readily yielded an azlactone from which the 2-hydroxy-4,5-dimethoxyphenylacetic acid was obtained by saponification and oxidation in the usual manner.

## Experimental Part

**Sodium Compound of 2-Hydroxy-4,5-dimethoxybenzaldehyde.**—Six grams of 2-hydroxy-4,5-dimethoxybenzaldehyde was added to a hot solution of sodium ethylate prepared by dissolving 0.8 g. of sodium in 50 cc. of absolute alcohol. The difficultly soluble sodium compound separated on cooling; it was removed by filtration, washed with alcohol and ether, and dried in a vacuum desiccator. The yield was 5.8 g. The alcohol–ether filtrate was evaporated to dryness; the residue was dissolved in a little dilute aqueous alkali, filtered, and the solution was acidified. The recovery was 0.8 g. of unchanged aldehyde.

**Methoxymethyl Ether of 2-Hydroxy-4,5-dimethoxybenzaldehyde.**—Six and two-tenths grams of the sodium compound was suspended in 30 cc. of dry toluene, and 2.4 g. of chloromethyl ether was added. The suspension was shaken from time to time at room temperature and after two hours 20 cc. of 5% aqueous sodium hydroxide solution was added, together with the same volume of ether. After separation from the aqueous portion, the ether–toluene solution was washed with water, dried, and evaporated. An oily product, which crystallized to a solid mass, remained. The yield was 3.4 g. After recrystallization from petroleum ether it melted at 61°.

*Anal.* Calcd. for $C_{11}H_{14}O_5$: C, 58.40; H, 6.19. Found: C, 58.33; H, 6.05.

One and a half grams of unchanged 2-hydroxy-4,5-dimethoxybenzaldehyde was recovered by acidification of the aqueous alkaline solution.

**Azlactone of Methoxymethyl Ether of 2-Hydroxy-4,5-dimethoxybenzaldehyde.**—Two grams of the substituted benzaldehyde, 1.75 g. of hippuric acid, 1 g. of anhydrous sodium acetate and 6 cc. of acetic anhydride were mixed together and heated on the steam-bath for two hours. After cooling, the acetic anhydride was decomposed with water, and the solid products were separated by filtration and washed with water and alcohol. The material was then recrystallized from ethyl alcohol. It separated from concentrated solutions in this solvent as red cubes and from dilute solutions as yellow needles. Both forms melted at 168°, the yellow form turning red at about 150°. The yield was 2.6 g.

*Anal.* Calcd. for $C_{20}H_{19}O_6N$: $OCH_3$ (3), 25.2. Found: $OCH_3$, 24.81.

**2-Hydroxy-4,5-dimethoxyphenylacetic Acid.**—A suspension of 2 g. of the azlactone in 20 cc. of 10% potassium hydroxide was boiled under reflux for five hours. The solution was then cooled, treated with 10 cc. of 10% hydrogen peroxide added in small portions and allowed to stand overnight. Dilute hydrochloric acid was added carefully until the solution gave a slightly acid reaction to congo paper. The solution was then extracted with five portions of ether, and the ethereal solution was dried over sodium sulfate. The solvent was removed, and the residue was subjected to steam distillation to remove the benzoic acid. At the same time hydrolysis of the methoxymethyl group occurred. The aqueous solution remaining after steam distillation was boiled with decolorizing carbon and filtered. The filtrate was saturated with sodium chloride and extracted repeatedly with ether. The ethereal extract yielded 0.8 g. of substance. It was recrystallized from water. The product obtained melted at 102° but contained water of crystallization, which can be removed by drying to constant weight at about 100°. The anhydrous material melted at 138°.

*Anal.* Calcd. for $C_{10}H_{12}O_5$: C, 56.6; H, 5.66; $OCH_3$ (2), 29.24; mol. wt., 212. Found: C, 56.36; H, 6.04; $CH_3O$, 28.9; mol. wt. (by titration), 217.

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