The compound could likewise be prepared in the following manner. A solution of the anilide (195°) (I) (1.0 g.) in methanol (100 ml.) treated with concentrated hydrochloric acid (2 ml.), was allowed to stand at room temperature for seven hours and then refluxed for eleven hours. The resulting solution was neutralized with a sodium carbonate solution, treated with water until precipitation occurred and then concentrated with an air stream. The white solid (1.0 g.) obtained melted at 128–129° and was identical with the compound from the thionyl chloride method.

The anil (221°) (VIII) when treated in a similar fashion to the above gave the normal methyl ester of 2-benzoylbenzoic acid.

Hydrolysis of 1-Keto-2,3-diphenyl-3-methoxyisoindole (III).—A solution of 1-keto-2,3-diphenyl-3-methoxyisoindole (III) (1.0 g.) in acetic acid (20 ml.) and concentrated hydrochloric acid (2 ml.) was allowed to stand for seventeen hours at room temperature. During this time white crystals (0.60 g.) melting at 195–197° separated. An additional amount (0.25 g.) was obtained by addition of water to the filtrate. A mixture with the anilide (195°) (I) gave no lowering when melted together.

1-Keto-2-ethyl-3-methoxy-3-phenylisoindole (VII).—A solution of the N-ethylamide (VI) (1.0 g.) in thionyl chloride (10 ml.) was allowed to stand at room temperature for twenty minutes. The excess thionyl chloride was removed under reduced pressure, methanol (50 ml.) added and the resulting solution allowed to stand at room temperature for eleven hours. Addition of water gave an oil which was taken up in ether and washed with a sodium carbonate solution. Removal of the ether gave an oil which gave white crystals (0.72 g.) upon the addition of 30–60° petroleum ether. After two crystallizations from the same solvent the compound melted at 73–75°.

Anal. Calcd. for $C_{17}H_{17}O_2N$: C, 76.40; H, 6.36. Found: C, 76.33; H, 6.68.

The compound (VII) could likewise be prepared in the following way. A solution of the N-ethylamide (VI) (1.0 g.) in methanol (40 ml.) and concentrated hydrochloric acid (1 ml.) was allowed to stand at room temperature for fourteen hours and then refluxed for ten hours. Neutralization with sodium carbonate followed by concentration in an air stream gave an oil which formed white crystals (0.45 g.) melting at 75–78° which were identical with the above (VII).

Hydrolysis of 1-Keto-2-ethyl-3-methoxy-3-phenylisoindole (VII).—A solution of 1-keto-2 ethyl-3-methoxy-3-phenylisoindole (VII) (0.5 g.) in a mixture of glacial acetic acid (10 ml.) and concentrated hydrochloric acid (1 ml.) was allowed to stand for twelve hours and poured into water. The N-ethyl amide (VI) (0.4 g.) thus obtained melted at 170–173° and gave no lowering when mixed with an authentic sample.

Normal N-Methyl Anilide (XI).—To a cold solution of the acid chloride of 2-benzoylbenzoic acid, prepared from the acid (7.5 g.) and thionyl chloride, in benzene (20 ml.), methylaniline (10 ml.) in dry benzene (10 ml.) was added and the resulting solution allowed to stand for twenty-four hours at room temperature and then poured into water. Extraction with ether followed by washing with dilute acid and sodium bicarbonate gave an oil upon removal of the solvent. The oil upon being taken up in a mixture of benzene and (80–90°) petroleum ether gave, after treatment with norite and aluminum oxide, upon cooling, white crystals (1.5 g.) (XI) which melted at 125–140°. Two crystallizations from the same mixture gave white crystals melting at 144–146°.

Anal. Calcd. for $C_{21}H_{17}O_2N$: C, 80.00; H, 5.39. Found: C, 80.23; H, 5.49.

Summary

The polarographic method offers a suitable means of ascertaining the type and the approximate amount of ring-chain tautomerism present with amides of 2-benzoylbenzoic acid.

KNOXVILLE, TENN. RECEIVED JANUARY 31, 1944

[CONTRIBUTION FROM THE RESEARCH DIVISION OF THE GENERAL PRINTING INK CORPORATION]

Orientation in the Biphenyl System.[1] Derivatives of 2-Aminobiphenyl[2]

BY A. H. POPKIN, G. M. PERRETTA AND R. SELIG

As a continuation of the studies of orientation in the biphenyl system, it was decided to prepare 2-dimethylaminobiphenyl and to observe its behavior in various reactions. This compound should prove more versatile than the 4-isomer[3] because of the possible existence of an activated hydrogen in the 5 position in competition with the known activity of the 4′ hydroxygen.[1,4]

Evans and Williams[5] reported the preparation of 2-dimethylaminobiphenyl in 94% yield from the reaction of dimethyl sulfate on 2-aminobiphenyl. In duplicating this reaction, a 92% yield of methylated product was obtained. On treatment with acetic anhydride followed by distillation, 2-dimethylaminobiphenyl and 2-(N-methyl)-acetamidobiphenyl were obtained in 66:34 ratio. This indicates that the yield previously reported is for a mixture of dimethyl and monomethyl compounds rather than pure dimethyl compound.

The action of methyl alcohol and sulfuric acid on 2-aminobiphenyl at elevated temperature and pressure gave 82–85% yields of a methylated mixture. This when acetylated was found to consist of 2-dimethylaminobiphenyl and 2-(N-methyl)-acetamidobiphenyl in the ratio of 87:13. The identity of the latter was established by analysis and synthesis in 84% yield by the reaction of sodium and methyl iodide on a solution of 2-acetamidobiphenyl in dry xylene.

2-(N-Methyl)-acetamidobiphenyl showed a greater stability toward hydrolysis than 2-acetamidobiphenyl and its derivatives[6] which is in agreement with the observation of Schoorl[7] on the stability of N-methylacetanilide.

---

(1) Previous paper, Popkin and McVea, THIS JOURNAL, **66**, 796 (1944).

(2) Presented before the Division of Organic Chemistry, Cleveland meeting of the American Chemical Society, April, 1944.

(3) Banus and Tomas, *Anal. Fis. Quim.*, **19**, 293 (1921); Vorländer, *Ber.*, **58**, 1913 (1925); Bell and Kenyon, *J. Chem. Soc.*, 2705 (1926); Kenyon and Robinson, *ibid.*, 3050 (1926).

(4) Popkin, THIS JOURNAL, **65**, 2043 (1943).

(5) Evans and Williams, *J. Chem. Soc.*, 1199 (1939).

(6) Popkin and Perretta, THIS JOURNAL, **65**, 2046 (1943).

(7) Schoorl, *Pharm. Weekblad*, **78**, 433 (1941).

A preliminary study of the behavior of 2-dimethylaminobiphenyl indicated the existence of a para-bond activation similar to that in dimethylaniline. When dimethylaniline is oxidized with cupric chloride[8] Methyl Violet is formed. Oxidation of 2-dimethylaminobiphenyl under the same conditions resulted in a dyestuff having color and lake-forming properties characteristic of triphenylmethane dyes of the Methyl Violet type.

Experimental

Preparation of 2-Dimethylaminobiphenyl: Method 1.—Into a 2-liter beaker was placed 254 g. of 2-aminobiphenyl (Monsanto Chemical Company). To this was added slowly and with stirring 675 g. of dimethyl sulfate and 270 g. of 30% aqueous sodium hydroxide solution, the addition requiring four hours. The dimethyl sulfate was added in approximately 15-g. portions, each followed by a portion of sodium hydroxide solution until neutrality was obtained. The temperature was maintained below 30°. An additional 130 cc. of the sodium hydroxide solution then was required to bring about complete neutrality. The product was present as two layers. The upper layer, after separation and washing with two portions of 150 cc. of water, weighed 270 g., 92% yield. This was treated with 57 g. of acetic anhydride. A temperature rise of ten degrees was obtained indicating a substantial quantity of *n*-monomethylaminobiphenyl. The product was distilled at 30 mm. pressure through a Claisen flask to give: fractions 1 and 2, 26.5 g., 33–130°; 3–7, 161.8 g., 130–190°; 8 and 9. 84.0 g., 190–225°; 10, residue, 13.0 g.

Fractions 1 and 2 contained acetic acid and acetic anhydride. Fractions 3–7 are 2-dimethylaminobiphenyl, 0.82 mole, and 8–10 are 2-(N-methyl)-acetamidobiphenyl, m. p. 79–87°, 0.43 mole. This represents a ratio of 66% of dimethylaminobiphenyl to 34% of monomethyl compound.

Fractions 3–7 were redistilled through an efficient fractionating column of the total condensation, variable take-off type[9] having twelve theoretical plates. Acetic anhydride was not present in the first fractions and no appreciable residue was obtained. The purified 2-dimethylaminobiphenyl boiled at 115–116° (2–3 mm.); $n^{20}\text{D}$ 1.6052–1.6058.

Purification of a portion of fractions 8–10 by crystallization from a petroleum hydrocarbon (70–95°) gave 2-(N-methyl)-acetamidobiphenyl, m. p. 98–99°.

Anal. Calcd. for $C_{15}H_{15}NO$: C, 80.0; H, 6.71; N, 6.22. Found: C, 80.6; H, 6.77; N, 6.30.

Two similar reactions gave checking yields and comparable ratios of 2-dimethylaminobiphenyl and 2-(N-methyl)-acetamidobiphenyl.

Method 2.—A mixture was made of 67 g. of 2-aminobiphenyl, 74 g. of absolute methyl alcohol and 7 g. of concd. sulfuric acid. This was heated in an autoclave for five hours at 205–210° and 420–490 lb. pressure. The resulting mixture was brought to *p*H 11 with a 10% sodium hydroxide solution and the oil which formed was extracted with ether. The solvent was removed in a Claisen flask and the oil distilled at 143–147° (10 mm.); wt. 65.6 g., 85% yield. Several similar reactions gave 82–85% yield.

Treatment of this product with acetic anhydride and careful fractionation through an efficient column gave 2-dimethylaminobiphenyl, b. p. 118–120° (2.5 mm.), $n^{20}\text{D}$ 1.6046–1.6050, and a residue of 2-(N-methyl)-acetamidobiphenyl, m. p. 83–91°. Purification by crystallization from a low-boiling petroleum hydrocarbon resulted in crystals, m. p. 98–99°. which when mixed with the same material obtained above gave an identical melting point. The ratio of 2-dimethylaminobiphenyl to monomethyl compound was 87:13.

It was thought that the discrepancy in the boiling point and refractive index of 2-dimethylaminobiphenyl from the values obtained by Method 1 might be due to the presence of traces of 2-monomethylaminobiphenyl. A second treatment of the purified material with acetic anhydride followed by redistillation produced no change in the constants.

Preparation of 2-(N-Methyl)-acetamidobiphenyl.—A solution was made of 31.5 g. of 2-acetamidobiphenyl, m. p. 119–120°, in 200 cc. of dry xylene. To this was added 5 g. of metallic sodium and the mixture heated at 120–130° for three hours. A clear xylene solution was decanted from the excess of sodium and treated with 25 g. of methyl iodide. The mixture was refluxed and within fifteen minutes a white precipitate was formed. The xylene then was removed by heating and a thick white paste resulted. This was treated with 100 cc. of water and dilute acetic acid added to bring the *p*H to 6. The remaining xylene was removed by steam distillation until the density of the oil was greater than that of the water solution. The two phases were brought to room temperature, the upper aqueous portion decanted, and the oil washed with 300 cc. of water. This treatment converted the oil to a solid, m. p. 90–95°, wt. 28.2 g., 84% yield. One purification with Norite and two recrystallizations from a petroleum fraction (70–95°) gave crystals, m. p. 96–98°. A mixed m. p. with 2-(N-methyl)-acetamidobiphenyl (above) gave no depression in the melting point.

Stability of 2-(N-Methyl)-acetamidobiphenyl toward Hydrolysis.—Treatment of 2.5 g. of 2-(N-methyl)-acetamidobiphenyl in methyl alcohol solution with 5 cc. of concd. hydrochloric acid during fifteen minutes at reflux temperature[6] gave only unreacted 2-(N-methyl)-acetamidobiphenyl. Addition of 5 cc. of concd. hydrochloric acid to 1.5 g. of the same material resulted in a clear solution which when refluxed for fifteen minutes again gave the unhydrolyzed starting material. The reaction of 4 g. of the 2-(N-methyl)-acetamidobiphenyl, dissolved in 150 cc. of alcohol, with 3 cc. of a 30% sodium hydroxide solution at reflux temperature for ten hours,[7] produced only unreacted 2-(N-methyl)-acetamidobiphenyl.

Oxidation of 2-Dimethylaminobiphenyl.—A mixture of 2-dimethylaminobiphenyl, cupric sulfate, phenol, salt and water was treated in the usual manner.[8] A colored base thus was obtained corresponding to a Methyl Violet which has a phenyl group ortho to each of the three methylamino groups. It has the properties characteristic of Methyl Violet, resulting from oxidized dimethylaniline, *i. e.*, it forms a blue-violet solution with organic acids and alcohols, dissolves in concd. hydrochloric acid to give a reddish-brown solution which turns green and then blue on continued dilution with water, and forms insoluble tannic acid and phosphomolybdic acid salts.

Acknowledgment.—The authors are indebted to the General Printing Ink Corporation for permission to publish this work.

Summary

2-Dimethylaminobiphenyl was oxidized with cupric chloride to give a triphenylated Methyl Violet dyestuff indicating the existence of an active hydrogen in the 5 position.

The preparation of 2-dimethylaminobiphenyl by the reaction of 2-aminobiphenyl either with dimethyl sulfate or with methyl alcohol also gave the monomethyl compound, which was separated as 2-(N-methyl)-acetamidobiphenyl.

The stability of 2-(N-methyl)-acetamidobiphenyl toward hydrolysis is in agreement with the similar stability of N-methylacetanilide.

NEW YORK, N. Y. RECEIVED FEBRUARY 10, 1944

---

(8) Rowe, "Colour Index," Society of Dyers and Colorists, First Ed., 1924, p. 174.

(9) Whitmore and Lux, THIS JOURNAL, 54, 3448 (1932).