after distillation of the dihalide was decolorized with Norit. The residue, left by evaporation of the solvent under an air blast, was extracted with petroleum ether (b.p. 90–120°) and the solvent removed from the extract under an air blast. The product was sublimed at a pressure of 0.1 mm. while the temperature of the heating jacket was slowly raised to 240°. The sublimate was recrystallized once from an ethanol-water mixture and then twice from petroleum ether (b.p. 90–120°) to give 3.10 g. (26.5%) of white plates, m.p. 89–90°. The infrared spectrum of the material exhibits an absorption band at 3381 cm.$^{-1}$, attributable to a hydroxyl group.

Anal. Calcd. for $C_{22}H_{29}BrO_2$: C, 65.17; H, 7.21; Br, 19.71. Found: C, 65.43; H, 7.20; Br, 19.69.

***p*-Hydroxy-*p*′-(ω-bromo-*n*-decyloxy)-bibenzyl.**—Ten grams of *p,p*′-dihydroxybibenzyl and 60.0 g. of decamethylene bromide were employed, the mixing time being 3 hours after which the mixture was heated under reflux for 40 minutes. The unchanged diphenol amounted to 1.6 g., the dihalide to 49.8 g. The residue after distillation of the dihalide was extracted with 200 ml. of boiling petroleum ether (b.p. 90–120°). The cool extract deposited white crystals melting at 79–87°. The product was sublimed at a pressure of 0.05–0.09 mm. while the temperature of the heating jacket was slowly raised to 230°. The yield was 2.36 g. (19.0%) of white sublimate melting at 90–94°. Recrystallization from an ethanol-water mixture, from methanol and, finally, from petroleum ether (b.p. 90–120°) gave white plates, m.p. 93–94.5°. The infrared spectrum of the compound exhibits an absorption band at 3387 cm.$^{-1}$, attributable to a hydroxyl group.

Anal. Calcd. for $C_{24}H_{33}BrO_2$: C, 66.50; H, 7.67; Br, 18.44. Found: C, 66.48; H, 7.89; Br, 18.70.

Cyclization of *p*-Hydroxy-*p*′-(ω-bromo-*n*-octyloxy)-bibenzyl.—A 1-l., three-necked, creased flask was fitted with a stainless steel stirrer driven by a 10,000 r.p.m. motor, controlled by a variac, and the high-dilution apparatus described by Leonard and Sentz.[20] A solution of 1.34 g. (0.0033 mole) of *p*-hydroxy-*p*′-(ω-bromo-*n*-octyloxy)-bibenzyl in 55 ml. of isoamyl alcohol was added in high dilution, over a period of 2 hours and with stirring, to a suspension of 3.00 g. (0.0218 mole) of anhydrous potassium carbonate in 250 ml. of refluxing isoamyl alcohol. After the addition was complete, the mixture was boiled under reflux, with stirring, for an additional hour, cooled and filtered. After the solvent was removed from the filtrate by distillation *in vacuo*, the residue was taken up in boiling ethanol and decolorized with Norit. The cold solution deposited an amorphous white solid which, since it melted over a wide range even after repeated reprecipitation, was assumed to be polymeric. Evaporation of the mother liquor under an air blast left only a yellow oil which was taken up in acetone. The acetone was removed on a steam-bath and the residue distilled *in vacuo* in a short-path still. The yield was 0.32 g. (30%) of yellow oil, collected at a bath temperature of 230–240° under a pressure of 0.3 mm. The material gives a negative Beilstein halogen test and its infrared spectrum exhibits no absorption band ascribable to a hydroxyl group. After standing several weeks, the oil crystallized in yellow needles which were dissolved in a minimum quantity of petroleum ether (b.p. 30–60°). The solution when cooled in a solid carbon dioxide–acetone-bath deposited white needles which were quickly collected on a filter. Following this procedure the material was recrystallized once more from petroleum ether (b.p. 30–60°) and, finally, once from *n*-hexane to give white needles, m.p. 56.5–58°. The infrared spectrum of the cyclic diether exhibits, in addition to those listed in the table, absorption bands at 1236 and 1248 cm.$^{-1}$, attributable to a phenyl–oxygen group, and at 1018 cm.$^{-1}$, attributable to a carbon–oxygen grouping.

Anal. Calcd. for $C_{22}H_{28}O_2$: C, 81.44; H, 8.70; mol. wt., 324.4. Found: C, 81.25; H, 8.74; mol. wt. (Rast), 312.

Cyclization of *p*-Hydroxy-*p*′-(ω-bromo-*n*-hexoxy)-bibenzyl.—A solution of 1.03 g. (0.00276 mole) of *p*-hydroxy-*p*′-(ω-bromo-*n*-hexoxy)-bibenzyl in 60 ml. of isoamyl alcohol was added, in high dilution, over a period of 2.25 hours, to a stirred suspension of 3.00 g. (0.0218 mole) of anhydrous potassium carbonate in 300 ml. of refluxing isoamyl alcohol. After the addition was complete, the mixture was boiled under reflux, with stirring, for an additional 30 minutes and worked up as described previously. The yield was 0.21 g. (26%) of yellow oil, collected at a bath temperature of 195–280° under a pressure of 0.3 mm. Since a Beilstein halogen test indicated that the oil was not halogen free, the material was redistilled at a bath temperature of 205–220° under a pressure of 0.3 mm. to give a light-yellow, halogen-free oil. The infrared spectrum of the material exhibits no absorption band ascribable to a hydroxyl group. The oil was dissolved in *n*-hexane and the solution cooled in a solid carbon dioxide–acetone-bath. A white solid separated which was dissolved in *n*-hexane and reprecipitated by cooling as before. The resulting white solid melted at 43–44.5°. The infrared spectrum of the diether exhibits, in addition to those listed in the table, an absorption band at 1248 cm.$^{-1}$, attributable to a phenyl–oxygen group, and a second weak, broad band at 1005–1040 cm.$^{-1}$, attributable to a carbon–oxygen grouping.

Anal. Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16; mol. wt., 296.4. Found: C, 80.90; H, 8.41; mol. wt. (Rast), 266.

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[20] N. J. Leonard and R. C. Sentz, THIS JOURNAL, **74**, 1704 (1952).

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Heterocycles Containing *p*-Phenylene Units. II. Amines

BY REYNOLD C. FUSON AND HERBERT O. HOUSE[1]

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A method of synthesis of heterocycles of type II (in text) has been developed. The macrocyclic diamines in which *n* has values of 4, 6, 8 and 10 are described.

Heterocycles of type I, where X is the hetero atom and *m* has a value greater than one, are expected to be of especial interest in a study of the stereochemistry of cycles containing two *p*-phenylene units.[2] In particular heterocycles of type I where the hetero atom is nitrogen(II) are of interest. Following the introduction of either one or two appropriate nuclear substituents, the basic hetero atoms could serve as functional groups for the resolution of the compound if the rotation of the aromatic units proves to be restricted. This paper reports a synthetic route to heterocycles of type II, the method of ring closure being a modification of that previously described by several investigators.[3-8] The use of dimethylformamide

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[1] Atomic Energy Commission Predoctoral Fellow, 1951–1952.

[2] R. C. Fuson and H. O. House, THIS JOURNAL, **75**, 1325 (1953).

[3] W. Marckwald and A. F. von Droste-Huelshoff, *Ber.*, **31**, 3261 (1898); C. C. Howard and W. Marckwald, *ibid.*, **32**, 2038 (1899).

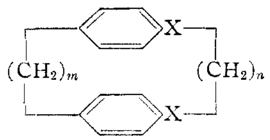
[4] O. Hinsberg and J. Kressler, *Ann.*, **340**, 110 (1905).

[5] A. Muller and P. Bleier, *Monatsh.*, **56**, 391 (1930).

[6] K. Ziegler and P. Orth, *Ber.*, **66**, 1867 (1933).

[7] A. Muller and L. Kindlmann, *ibid.*, **74**, 416 (1941).

[8] A. Muller, E. Srepel, E. Funder-Fritzsche and F. Dicher, *Monatsh.*, **83**, 386 (1952).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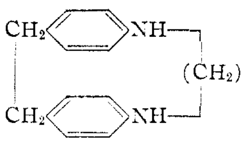
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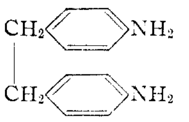
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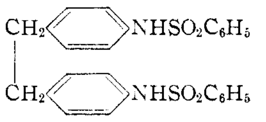
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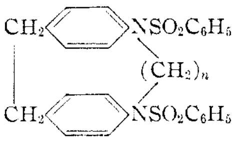
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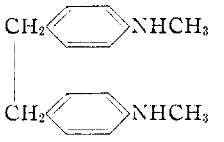
VI

as a solvent was suggested by its effectiveness as a solvent for the alkylation of potassium phthalimide.[9]

p,p'-Diaminobibenzyl (III), the preparation of which was previously described,[2] has been converted to *p,p'*-diphenylsulfonamidobibenzyl (IV). Addition of an equimolar mixture of the amide (IV) and the polymethylene bromides, in high dilution, to a suspension of anhydrous potassium carbonate in refluxing dimethylformamide has served to produce the diphenylsulfonyl derivatives (V) of the desired heterocycles (II) in which n = 4, 6, 8 and 10, only the sulfonamides in which n = 8 and 10 being characterized. Cleavage of the disulfonamides to give the cyclic diamines (II) in which n = 4, 6, 8 and 10 was effected according to the method of Snyder and Heckert.[10]

N,N'-Dimethyl-*p,p'*-diaminobibenzyl (VI), prepared by the methylation of the disulfonamide (IV) and subsequent cleavage, served as an open-chain analog whose infrared spectrum was compared with that of the heterocycles (II). The infrared spectra of the acyclic and cylic compounds differed but slightly. The variations observed, which follow the pattern previously noted in the oxygen analogs,[2] are summarized in Table I.

TABLE I

Compound	Region of absorption characteristic of aromatic systems, cm.$^{-1}$	Region of absorption characteristic of *p*-substitution, cm.$^{-1}$
VI	1614 (5)[a]	818 (10)
	1582 (1)	
	1522 (9)	
II	1615 (1)	818 (1)
(n = 4)	1516 (2)	809 (2)
II	1615 (3)	825 (1)
(n = 6)	1519 (5)	814 (2)
		805 (1, sh. band)
II	1613 (1)	823 (1)
(n = 8)	1515 (2)	815 (1)
II	1615 (3)	811 (3)
(n = 10)	1583 (1/2, sh. band)	
	1519 (5)	819 (2, sh. band)

[a] The numbers in parentheses indicate approximately the relative intensities of the bands in each of the spectra determined.

Experimental[11]

***p,p'*-Diphenylsulfonamidobibenzyl.**—To a solution of 50 g. of *p,p'*-diaminobibenzyl in 350 ml. of pyridine was added, with shaking and external cooling, 100 ml. of benzenesulfonyl chloride. The resulting mixture was boiled under reflux for 60 minutes, cooled and poured, with vigorous stirring, into 2 l. of cold water. The resulting solid was washed with water and dissolved in 1 l. of 4% aqueous sodium hydroxide. The alkaline solution decolorized with Norit, was reacidified with hydrochloric acid. The precipitated product, after being washed with water, was taken up in boiling glacial acetic acid and decolorized with Norit. The cold solution deposited 87.6 g. (75.5%) of the disulfonamide melting at 211–214°. A second recrystallization from glacial acetic acid gave white plates, m.p. 212–214°.

Anal. Calcd. for $C_{26}H_{24}N_2O_4S_2$: C, 63.39; H, 4.91; N, 5.69; S, 13.02. Found: C, 63.15; H, 5.11; N, 5.74; S, 12.88.

***p,p'*-Bis-(N-methylphenylsulfonamido)-bibenzyl.**—A mixture of 10.0 g. of *p,p'*-diphenylsulfonamidobibenzyl, 55.2 g. of anhydrous potassium carbonate, 12.4 ml. of methyl iodide and 600 ml. of acetone was boiled under reflux with stirring for 3 hours. After an additional 12.4 ml. (0.20 mole) of methyl iodide was added, the mixture was boiled under reflux with stirring for 17 hours longer. The residue, obtained by removal of the acetone on a steam-bath, was mixed with 700 ml. of hot water. The product, collected on a filter, was washed thoroughly with water and recrystallized from glacial acetic acid. The yield was 9.40 g. (88.8%) of cream-colored plates melting at 233–235.5°. Recrystallization from isoamyl alcohol gave white plates, m.p. 234–235.5°.

Anal. Calcd. for $C_{28}H_{28}N_2O_4S_2$: C, 64.60; H, 5.42; N, 5.38; S, 12.32. Found: C, 64.73; H, 5.58; N, 5.51; S, 12.30.

N,N'-Dimethyl-*p,p'*-diaminobibenzyl.—A mixture of 9.40 g. of *p,p'*-bis-(N-methylphenylsulfonamido)-bibenzyl, 30 g. of phenol and 330 ml. of 48% hydrobromic acid was boiled under reflux, with stirring, for 21 hours. The mixture was diluted with twice its volume of water, cooled and filtered. The residue, while still on the filter, was washed with ethyl ether and recombined with the aqueous solution which had been extracted with two 200-ml. portions of ethyl ether. The mixture was heated to boiling and sufficient water added to bring all the dihydrobromide into solution. The hot solution was decolorized with Norit and chilled. Treatment of the resulting white plates with warm, 10% aqueous sodium hydroxide liberated the free base. The diamine, after decolorization with Norit, crystallized from a methanol–water mixture as tan needles, m.p. 87–88.5°, yield 2.09 g. (48.3%). Two additional recrystallizations of the product from methanol–water mixtures gave white needles melting at 88–89°. The infrared spectrum of the material exhibits, in addition to those listed in the table, an absorption band at 3365 cm.$^{-1}$, attributable to an NH group.

Anal. Calcd. for $C_{16}H_{20}N_2$: C, 79.98; H, 8.39; N, 11.66. Found: C, 79.98; H, 8.23; N, 11.86.

Diacetate.—A mixture of 1.09 g. of the diamine, 4.0 g. of anhydrous sodium acetate and 50 ml. of acetic anhydride was boiled under reflux for 75 minutes. The resulting mixture was poured into 400 ml. of hot water, neutralized with 10% aqueous sodium hydroxide and cooled. The solid product was recrystallized from an ethanol–water mixture to give 0.84 g. (57%) of cream-colored needles melting at 134–140°. A solution of the material in a boiling ethanol–water mixture, after decolorization with Norit, deposited upon cooling white needles, m.p. 139–142°. An additional recrystallization of the compound from an ethanol–water mixture sharpened the melting point to 141–142°.

Anal. Calcd. for $C_{20}H_{24}N_2O_2$: C, 74.35; H, 7.49; N, 8.64. Found: C, 74.27; H, 7.24; N, 8.84.

Cyclization of *p,p'*-Diphenylsulfonamidobibenzyl and Decamethylene Bromide.—The apparatus previously described,[2] in which the 1-l. flask is replaced by a 2-l. flask, was used for all the cyclizations. A solution of 10.0 g. (0.02 mole) of *p,p'*-diphenylsulfonamidobibenzyl and 6.11 g. (0.02 mole) of decamethylene bromide in 250 ml. of di-

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(9) J. C. Sheehan and W. A. Bolhofer, THIS JOURNAL, **72**, 2786 (1950).

(10) H. R. Snyder and R. E. Heckert, *ibid.*, **74**, 2006 (1952).

(11) All melting points are corrected. The infrared spectra were determined and interpreted by Miss Helen Miklas. The microanalyses are by Mrs. Katherine Pih, Mrs. Esther Fett and Mr. Joseph Nemeth.

methylformamide was added, in high dilution and with stirring, over a period of 23 hours, to a suspension of 55.2 g. (0.40 mole) of anhydrous potassium carbonate in 500 ml. of refluxing dimethylformamide. After the addition was complete, the mixture was boiled under reflux, with stirring, for an additional 5.5 hours, cooled and poured, with stirring, into 2 l. of water. The water-insoluble material, collected on a filter, was extracted with 300 ml. of boiling chloroform and the extract decolorized with Norit. The residue, a brown oil obtained from the extract by removal of the solvent on a steam-bath, was taken up in boiling glacial acetic acid and decolorized with Norit. The cold solution deposited 1.88 g. (14.6%) of white plates melting over the range 180–192°. The material was subsequently recrystallized once from glacial acetic acid, twice from isoamyl alcohol, and, finally, once from *n*-butyl alcohol to give 1.14 g. (8.9%) of white plates melting at 191.5–192.5°.

Anal. Calcd. for $C_{36}H_{42}N_2O_4S_2$: C, 68.55; H, 6.71; N, 4.44; S, 10.16. Found: C, 68.71; H, 6.93; N, 4.46; S, 10.36.

Cleavage of the Cyclic Disulfonamide.—A mixture of 0.40 g. (0.00063 mole) of the cyclic disulfonamide, 5.0 g. of phenol and 75 ml. of 48% hydrobromic acid was boiled under reflux with stirring for 5.5 hours. The resulting mixture was diluted with an equal volume of water and extracted with two 100-ml. portions of ethyl ether. The aqueous layer, after being decolorized with Norit, was made alkaline with a solution of 50 g. of sodium hydroxide in 150 ml. of water. The solid which separated was recrystallized from a methanol–water mixture to give 0.11 g. (50%) of white needles melting at 96–97°. The infrared spectrum of the compound exhibits, in addition to those listed in the table, an absorption band at 3250 cm.$^{-1}$, attributable to an NH group.

Anal. Calcd. for $C_{24}H_{34}N_2$: C, 82.23; H, 9.70; N, 8.00; mol. wt., 350.5. Found: C, 82.01; H, 9.84; N, 8.22; mol. wt. (Rast), 348.

Cyclization of *p,p'*-Diphenylsulfonamidobibenzyl and Octamethylene Dibromide.—A solution of 10.0 g. (0.02 mole) of *p,p'*-diphenylsulfonamidobibenzyl and 5.55 g. (0.02 mole) of octamethylene dibromide in 300 ml. of dimethylformamide was added, in high dilution and with stirring, over a period of 38 hours, to a suspension of 55.2 g. (0.40 mole) of anhydrous potassium carbonate in 500 ml. of refluxing dimethylformamide. After the addition was complete, the mixture was boiled under reflux, with stirring, for an additional 8 hours and worked up as described previously. The residue, obtained from the chloroform extract, was taken up in boiling *n*-butyl alcohol and decolorized with Norit. The cold solution deposited 1.96 g. (15.9%) of tan prisms melting with decomposition over the range 230–255°. The compound was then recrystallized once from *n*-butyl alcohol, twice from glacial acetic acid and finally twice from isoamyl alcohol to give 0.60 g. (4.9%) of white prisms melting with decomposition at 256–258°.

Anal. Calcd. for $C_{34}H_{38}N_2O_4S_2$: C, 67.73; H, 6.36; N, 4.65; S, 10.64. Found: C, 67.88; H, 6.48; N, 4.64; S, 10.71.

Cleavage of the Cyclic Disulfonamide.—A mixture of 0.30 g. (0.00050 mole) of the cyclic disulfonamide, 5.0 g. of phenol and 75 ml. of 48% hydrobromic acid was boiled under reflux with stirring for 6 hours. Following the procedure outlined above, the cyclic diamine was isolated as white needles, m.p. 123–124°, yield 0.12 g. (75%). The infrared spectrum of the diamine exhibits, in addition to those listed in Table I, an absorption band at 3220 cm.$^{-1}$, attributable to an NH group.

Anal. Calcd. for $C_{22}H_{30}N_2$: C, 81.92; H, 9.38; N, 8.70; mol. wt., 322.5. Found: C, 81.90; H, 9.15; N, 8.59; mol. wt. (Rast), 318.

Cyclization of *p,p'*-Diphenylsulfonamidobibenzyl and Hexamethylene Bromide.—A solution of 10.0 g. (0.02 mole) of *p,p'*-diphenylsulfonamidobibenzyl and 5.0 g. (0.02 mole) of hexamethylene bromide in 300 ml. of dimethylformamide was added, in high dilution and with stirring over a period of 24.5 hours to a suspension of 55.2 g. (0.40 mole) of anhydrous potassium carbonate in 500 ml. of refluxing dimethylformamide. After the addition was complete, the mixture was boiled under reflux, with stirring, for an additional 4 hours and worked up as described previously. The viscous residue obtained from the chloroform extract could not be induced to crystallize and was therefore subjected to reductive cleavage. The crude disulfonamide was mixed with 10 g. of phenol and 100 ml. of 48% hydrobromic acid and the mixture, after being boiled under reflux with stirring for 17 hours, worked up as in the previous cases. Recrystallization from a methanol–water mixture gave 0.96 g. (16.0%) of colorless crystals melting at 145–147°. A second recrystallization from a methanol–water mixture gave white needles, m.p. 146–147°. The infrared spectrum of the compound exhibits, in addition to those listed in Table I, absorption bands at 3310 and 3245 cm.$^{-1}$, attributable to an NH group.

Anal. Calcd. for $C_{20}H_{26}N_2$: C, 81.59; H, 8.90; N, 9.52; mol. wt., 294.4. Found: C, 81.61; H, 8.86; N, 9.68; mol. wt. (Rast), 279.

Diacetate.—A mixture of 0.60 g. of the cyclic diamine, 2.0 g. of anhydrous sodium acetate and 25 ml. of acetic anhydride was boiled under reflux for 60 minutes. The resulting mixture was poured into 250 ml. of hot water, neutralized with 10% aqueous sodium hydroxide and cooled. The diacetate was recrystallized from an ethanol–water mixture to give 0.42 g. (55%) of white needles, m.p. 172–173°. A second recrystallization of the compound from an ethanol-water mixture raised the melting point to 173–174°.

Anal. Calcd. for $C_{24}H_{30}N_2$: C, 76.14; H, 7.99; N, 7.40. Found: C, 76.29; H, 8.04; N, 7.66.

Cyclization of *p,p'*-Diphenylsulfonamidobibenzyl and Tetramethylene Dibromide.—A solution of 10.0 g. (0.02 mole) of *p,p'*-diphenylsulfonamidobibenzyl and 4.41 g. (0.02 mole) of tetramethylene dibromide in 300 ml. of dimethylformamide was added, in high dilution and with stirring, over a period of 72.5 hours, to a suspension of 55.2 g. (0.40 mole) of anhydrous potassium carbonate in 500 ml. of refluxing dimethylformamide. After the addition was complete, the mixture was boiled under reflux, with stirring, for an additional 4 hours and worked up as described previously. The residue, obtained from the chloroform extract, was taken up in boiling *n*-butyl alcohol and decolorized with Norit. After the volume of the solution had been reduced under air blast, an amorphous white solid separated. It was recrystallized from isoamyl alcohol; yield 0.38 g. of an amorphous white solid melting over the range 198–217°. Since the solid could not be obtained in good crystalline form, it was subjected to reductive cleavage. The crude disulfonamide was mixed with 5.0 g. of phenol and 75 ml. of 48% hydrobromic acid and the mixture was boiled under reflux, with stirring, for 4.5 hours. The heterocycle was isolated as outlined previously; yield 0.07 g. (1.4%) of colorless crystals melting at 170–172.5°. An additional recrystallization from a methanol–water mixture gave white plates, m.p. 171–172.5°. The infrared spectrum of the material exhibits, in addition to those listed in Table I, an absorption band at 3240 cm.$^{-1}$, attributable to an NH group.

Anal. Calcd. for $C_{18}H_{22}N_2$: C, 81.16; H, 8.33; N, 10.52; mol. wt., 266.4. Found: C, 81.04; H, 8.20; N, 10.76; mol. wt. (Rast), 280.

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