thus of interest to study the behavior of mixtures of zein–detergent complex (ZD) and either O or A. Figure 2 shows that O removes a part of the detergent from ZD yielding an OI boundary whereas A yields only an additive pattern. This is again in complete agreement with the idea that O forms the all-or-none complex much more readily than A. Again similar results were obtained in the two buffer systems; however, glycine yielded better resolution of ZD and A whereas resolution of ZD and O was superior in veronal.

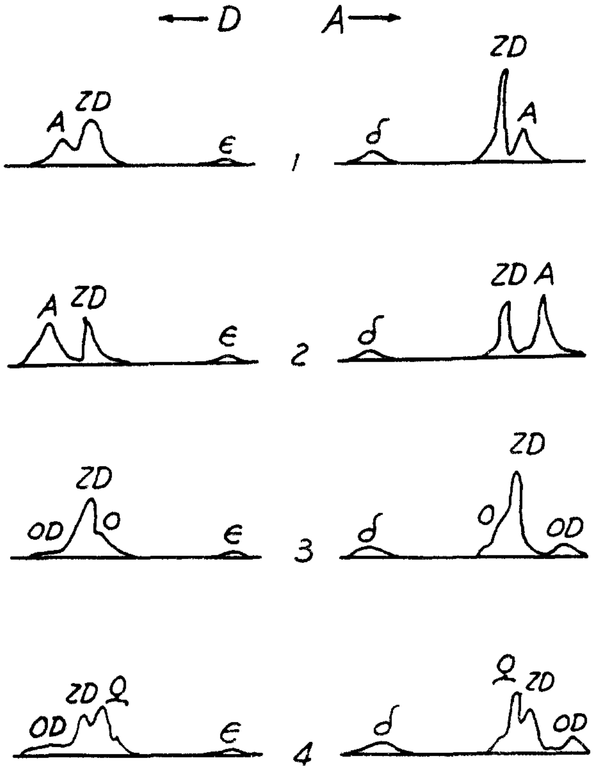

Fig. 2.—Electrophoretic analyses of mixtures of zein-SDBS (ZD) and ovalbumin (O) or bovine serum albumin (A). Runs 1 and 2, ZD plus A in glycine–NaCl buffer (*p*H 10.0, Γ/2 0.10); Z/A ratio 69/31 and 36/64, respectively. Runs 3 and 4, ZD plus O in veronal–NaCl buffer (*p*H 8.9, Γ/2 0.10); Z/O ratio 67/33 and 34/66, respectively.

Experimental

The albumin–detergent complexes were prepared from O and A by mixing 3 parts O and 2 parts A, respectively, with 1 part dodecylbenzene sodium sulfonate[7] (by weight) followed by isoelectric precipitation and redispersion of the precipitate in alkaline buffer. The complexes could also be prepared by adding a slight excess of detergent to O and A and removing the excess by prolonged dialysis against water.[8] The electrophoretic properties of the complexes prepared by either technique were substantially the same.

The zein–detergent complex was prepared by dissolving excess zein in detergent solution. Since the zein is insoluble in water a complex is formed which corresponds to the minimum detergent ratio for solubility.[9] This complex could also be prepared by dissolving zein in excess detergent and removing the excess detergent by dialysis. This procedure proved to be time consuming and tedious, however.

Electrophoretic analyses were carried out in an 11-ml. cell of the Tiselius type using a Philpot–Svenson type optical system. In the glycine–NaCl buffer O typically had a mobility of 7.4–8.3 × 10^{-5}, A 8.8–9.6 × 10^{-5} and the detergent complexes 9.6–11.3 × 10^{-5} cm.^{2} volt^{-1} sec.$^{-1}$.

Acknowledgment.—The authors are indebted to Armour and Company and to the Corn Products Refining Company for supplying the crystalline bovine serum albumin and the zein, respectively.

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[7] Santomerse No. 3, Monsanto.

[8] Neither the composition of the complexes nor their electrophoretic mobility was found to be appreciably dependent on the extent of this dialysis. It is felt that most of the ions removed are lower homologs of the detergent which are not strongly bound[5] and that the activity of true detergent ions in equilibrium with the complex is so low that removal is negligible under these conditions.

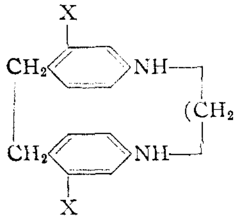
[9] J. F. Foster, *J. Phys. Chem.*, **53**, 175 (1949).

Heterocycles Containing *p*-Phenylene Units. III. Substituted Amines

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

RECEIVED JULY 16, 1953

Three substituted cyclic diamines of type I have been synthesized. The 2,2′-dimethyl-4,4′-(polymethylenediimino)-bibenzyls (Ia and Ib) were prepared from 4-nitro-1,2-dimethylbenzene following a sequence of reactions analogous to that previously reported.[2] Nitration of 4,4′-(hexamethylenediimino)-bibenzyl (Id) in sulfuric acid produced the dinitrated heterocyclic compound (Ic). In each of the three syntheses, evidence for the formation of more than one isomer (*i.e.*, *cis* and *trans* forms) was lacking.



I

Ia, X = CH_3, n = 4
Ib, X = CH_3, n = 6
Ic, X = NO_2, n = 6
Id, X = H, n = 6

Experimental[3]

Cyclization of *p*,*p*′-Diphenylsulfonamidobibenzyl and Hexamethylene Bromide.—A solution of 9.20 g. (0.0187 mole) of *p*,*p*′-diphenylsulfonamidobibenzyl and 5.00 g. (0.0204 mole) of hexamethylene bromide in 200 ml. of dimethylformamide was added, in high dilution and with stirring, over a period of 12.5 hours, to a suspension of 60.0 g. (0.43 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 12 hours and worked up as in the previous cases.[2] The residue, obtained from the chloroform extract, was recrystallized from acetic acid to give 3.18 g. (29.7%) of the cyclic disulfonamide as tan prisms melting at 201–205°. Two additional recrystallizations from acetic acid afforded the pure product as white prisms, m.p. 204–206°.

Anal. Calcd. for $C_{32}H_{34}N_2O_4S_2$: C, 66.87; H, 5.96; N, 4.86; S, 11.16. Found: C, 66.75; H, 5.75; N, 4.89; S, 11.11.

Cleavage of the Cyclic Disulfonamide.—A mixture of 2.21 g. of the cyclic disulfonamide, 5.0 g. of phenol and 75 ml. of 48% hydrobromic acid was boiled under reflux, with stirring, for 75 minutes. The isolation procedure was that outlined previously[2]; the cyclic diamine crystallized from a methanol-water mixture as white needles, m.p. 146–147°,[1] yield 0.86 g. (76%).

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[1] Atomic Energy Commission Predoctoral Fellow, 1951–1953.

[2] R. C. Fuson and H. O. House, THIS JOURNAL, **75**, 1327 (1953).

[3] 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.

N,N′-Di-*p*-tolylhexamethylenediamine.—A mixture of 40.2 g. of *p*-phenylsulfonamidotoluene,[4] 22.0 g. of hexamethylene bromide, 75.0 g. of anhydrous potassium carbonate and 300 ml. of acetone was boiled under reflux, with stirring, for 2 hours. After three-fourths of the acetone had been distilled from the reaction mixture, the residue was poured into 1 l. of water. The oily product, which partially solidified when allowed to stand, was filtered. An attempted crystallization of the solid from ethanol resulted in the deposition of an amorphous white solid which could not be induced to crystallize. The material was therefore subjected to reductive cleavage; a mixture of the amorphous substance with 15 g. of phenol and 200 ml. of 48% hydrobromic acid was boiled under reflux, with stirring, for 4 hours. The cold reaction mixture, following dilution with 100 ml. of water, was extracted with two 100-ml. portions of ethyl ether and then diluted with a sufficient amount of hot water to redissolve all the amine hydrobromide which had separated during the extraction. The acidic solution, after decolorization with Norit, was rendered alkaline with aqueous sodium hydroxide. The resulting white solid crystallized from methanol as white needles, m.p. 90.5–92°, yield 1.95 g. (8.2%). An additional recrystallization of the diamine from methanol raised the melting point to 91.5–92.5°.

Anal. Calcd. for $C_{20}H_{28}N_2$: C, 81.04; H, 9.52; N, 9.45. Found: C, 81.05; H, 9.47; N, 9.75.

The infrared spectrum of the product exhibits absorption bands at 3310 cm.$^{-1}$, attributable to an N–H group; at 1520, 1584 and 1616 cm.$^{-1}$, attributable to absorption by the aromatic nuclei; and at 804 and 819 cm.$^{-1}$, attributable to a *p*-substituted benzene ring. Thus the doubling of the *p*-substitution band, formerly noted only in the heterocycles,[2] is not a property unique to the cyclic compounds.

3-Bromo-4-phenylsulfonamidotoluene.—A solution of 15.8 g. of 3-bromo-4-aminotoluene[5] in 80 ml. of pyridine was treated with 16.0 ml. of benzenesulfonyl chloride. The solution, after having been heated on a steam-bath for 15 minutes, was poured into 500 ml. of ice-water. The product was recrystallized twice from ethanol–water mixtures; yield 25.4 g. (91.4%) of white needles, m.p. 100–102°. An additional recrystallization of the sulfonamide from the same solvent pair raised the melting point to 102–103°.

Anal. Calcd. for $C_{13}H_{12}BrNO_2S$: C, 47.85; H, 3.71; N, 4.29; S, 9.83; Br, 24.50. Found: C, 47.98; H, 3.66; N, 4.38; S, 9.98; Br, 24.53.

3,3′-Dibromo-4,4′-diphenylsulfonamidobibenzyl.—To a solution of 30.0 g. (0.0612 mole) of *p,p*′-diphenylsulfonamidobibenzyl in 150 ml. of pyridine was added dropwise, with stirring, 19.8 g. (0.123 mole) of bromine. The mixture was stirred for 30 minutes, warmed on a steam-bath for 10 minutes and diluted with 500 ml. of water. After the mixture had been acidified with hydrochloric acid, the tan solid which separated was collected on a filter. The sulfonamide was extracted with aqueous sodium hydroxide and reprecipitated from the extract with hydrochloric acid. It was treated with 150 ml. of boiling ethanol to leave a white residue, m.p. 171–178°, which was recrystallized from 1500 ml. of ethanol; yield 4.49 g. (11.3%) of white needles, m.p. 175–178°. Two additional recrystallizations of the disulfonamide from large volumes of ethanol raised its melting point to 178–180°.

Anal. Calcd. for $C_{26}H_{22}Br_2N_2O_4S_2$: C, 48.02; H, 3.41; N, 4.31; Br, 24.57; S, 9.86. Found: C, 47.84; H, 3.41; N, 4.29; Br, 24.80; S, 9.57.

Since the product had been prepared by bromination in pyridine solution, a procedure known to permit facile bromination at all free positions ortho and para to the sulfonamido group,[6] the question arose as to whether both bromine atoms were borne by the same aromatic nucleus. A comparison of the infrared spectra of the benzenesulfonamides of *p*-toluidine and of 3-bromo-4-aminotoluene with those of *p,p*′-diphenylsulfonamidobibenzyl and its bromination product served to settle the question. The spectra of both bromine-free compounds exhibit an absorption band at 1510 cm.$^{-1}$, attributable to a benzene ring bearing substituents para to one another. This absorption band is absent in both brominated sulfonamides, indicating that each ring of the dibromo-*p,p*′-diphenylsulfonamidobibenzyl has an additional substituent.

2-Nitro-4-methylaminotoluene.[7]—This nitrotoluidine derivative was obtained in 97.3% yield by nitrating a solution of N-methyl-*p*-toluidine in concentrated sulfuric acid. Two additional recrystallizations from small volumes of ethanol afforded the pure nitroamine as red-orange prisms, m.p. 54–55.5°.

3-Nitro-4-methylaminotoluene.[8]—The methylation of 3-nitro-4-acetamidotoluene[9] was effected according to the procedure of Pachter and Kloetzel.[10] The intermediate amide, when hydrolyzed with a boiling ethanol–hydrochloric acid mixture, afforded the nitrotoluidine in 17.3% yield. The product crystallized from ethanol in red needles, m.p. 84–85°.

2,2′-Dinitro-4,4′-(hexamethylenediimino)-bibenzyl (Ic).—To a solution of 2.00 g. of 4,4′-(hexamethylenediimino)-bibenzyl in 30 ml. of concentrated sulfuric acid, cooled in an ice-bath, was added, dropwise and with stirring, 2.5 ml. of concentrated nitric acid. After the addition was complete, the ice-bath was removed and stirring continued for 30 minutes. The reaction mixture was poured into 300 ml. of water, and the resulting mixture filtered. The crude product, which separated when the filtrate was made alkaline with aqueous sodium hydroxide, crystallized from propanol as red prisms, m.p. 229–231°, yield 2.29 g. (87.8%). Recrystallization of the heterocyclic compound from ethanol raised its melting point to 231–232°.

Anal. Calcd. for $C_{20}H_{24}N_4O_4$: C, 62.49; H, 6.30; N, 14.55. Found: C, 62.54; H, 6.31; N, 14.76.

The infrared spectrum of the cyclic compound, although similar to that of 2-nitro-4-methylaminotoluene, differs markedly from the spectrum of the isomeric 3-nitro-4-methylaminotoluene.

N-Methyl-N-(4-methyl-3-nitrophenyl)-glycine.—A mixture of 8.1 g. of 2-nitro-4-methylaminotoluene, 5.0 g. of chloroacetic acid, 5.3 g. of anhydrous sodium carbonate, 200 ml. of water and 100 ml. of ethanol was heated on a steam-bath, with stirring, for 2 hours. After the mixture had been cooled, the unchanged amine, amounting to 7.7 g., was collected on a filter. The *p*H of the filtrate was adjusted to 3 to liberate the amino acid, a yellow solid melting at 147–149°. The yield was 0.40 g. or 74% of the theoretical amount based upon the unrecovered amine. Two recrystallizations from water gave the pure amino acid as golden-yellow needles, m.p. 150.5–151.5°.

Anal. Calcd. for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.50. Found: C, 53.57; H, 5.35; N, 12.74.

N,3,4-Trimethylacetanilide.—To a mixture of 10.1 g. of crude 3,4-dimethylacetanilide,[11] 20 g. of powdered potassium hydroxide and 250 ml. of refluxing acetone was added 15.0 ml. of methyl iodide in 45 ml. of acetone (methylation procedure of Pachter and Kloetzel[10]). The mixture, after being boiled under reflux, with stirring, for 5 minutes, was filtered. The filtrate was concentrated almost to dryness and then diluted with 300 ml. of water. The oil, which separated, solidified on standing and was collected on a filter. A solution of the product in a boiling methanol–water mixture, after decolorization with Norit, was chilled to give 3.68 g. (35.5%) of light tan needles melting at 68–76°. Two additional recrystallizations from petroleum ether (b.p. 30–60°) gave long, white needles, m.p. 75–76°.

Anal. Calcd. for $C_{11}H_{15}NO$: C, 74.51; H, 8.53; N, 7.90. Found: C, 74.80; H, 8.63; N, 8.01.

4,4′-Dinitro-2,2′-dimethylbibenzyl.[12]—A solution of 120.1 g. of 4-nitro-1,2-dimethylbenzene[13] in 2 l. of 30% methanolic

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[4] O. Wallach and T. Huth, *Ber.*, **9**, 424 (1876).

[5] J. R. Johnson and L. T. Sandborn, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, pp. 111–113.

[6] F. Bell, *J. Chem. Soc.*, 2338 (1931).

[7] J. Pinnow, *Ber.*, **28**, 3039 (1895); J. B. Cohen and H. G. Crabtree, *J. Chem. Soc.*, **119**, 2055 (1921).

[8] L. Gattermann, *Ber.*, **18**, 1482 (1885); G. T. Morgan, E. Jobling and R. T. F. Barnett, *J. Chem. Soc.*, **101**, 1209 (1912).

[9] G. Bacharach, THIS JOURNAL, **49**, 1522 (1927); T. L. Davis and K. C. Blanchard, *ibid.*, **51**, 1801 (1929).

[10] I. J. Pachter and M. C. Kloetzel, *ibid.*, **74**, 1321 (1952).

[11] H. E. Zaugg, *ibid.*, **67**, 1861 (1945).

[12] A. G. Green, A. H. Davies and R. S. Horsfall, *J. Chem. Soc.*, **91**, 2076 (1907).

[13] A. W. Crossley and N. Renouf, *ibid.*, **95**, 202 (1909); P. Karrer, B. Becker, F. Benz, P. Frei, H. Salomon and K. Schopp, *Helv. Chim. Acta*, **18**, 1435 (1935); S. F. Birch, R. A. Dean, F. A. Fidler and R. A. Lowry, THIS JOURNAL, **71**, 1362 (1949).

potassium hydroxide, cooled to 7° in an ice-bath, was stirred vigorously while a rapid stream of air was introduced. After 2 hours the ice-bath was removed. The stirring accompanied by the introduction of air was continued for an additional 10 hours. The mixture was diluted with 1 l. of hot water and filtered with suction. The residue, while still on the filter, was washed first with boiling water and then with ethanol. The product crystallized from acetic acid as yellow needles, m.p. 225–227.5°, yield 85.1 g. (71.5%). Recrystallization of the dinitro compound from acetic acid raised the melting point to 227–228.5°.

4,4'-Diamino-2,2'-dimethylbibenzyl.—A mixture of 87.9 g. of 4,4'-dinitro-2,2'-dimethylbibenzyl, 200 g. of powdered iron, 500 ml. of ethanol and 500 ml. of water was heated to boiling. To this boiling mixture was added dropwise, with stirring, a solution of 12.1 ml. of concentrated hydrochloric acid in 100 ml. of 50% aqueous ethanol. The resulting mixture, after having been boiled under reflux, with stirring, for 16 hours, was made alkaline by the addition of 30 ml. of 6 *N* aqueous sodium hydroxide in 500 ml. of ethanol. The mixture was filtered while hot. The cold filtrate deposited 36.5 g. of tan needles, m.p. 164–167°. Concentration of the mother liquor afforded an additional crop of the diamine; total yield 43.5 g. (62%). A boiling ethanolic solution of the product, after decolorization with Norit, was chilled to give the pure diamine as white needles melting at 169–170.5°.

Anal. Calcd. for $C_{16}H_{20}N_2$: C, 79.98; H, 8.39; N, 11.66. Found: C, 79.90; H, 8.12; N, 11.82.

4,4'-Diphenylsulfonamido-2,2'-dimethylbibenzyl.—A solution of 23.3 g. of 4,4'-diamino-2,2'-dimethylbibenzyl and 45 ml. of benzenesulfonyl chloride in 200 ml. of pyridine was heated to boiling. The solution, after having been allowed to cool, was poured, with stirring, into 1.5 l. of cold water. The crude sulfonamide was dissolved in warm, dilute, aqueous sodium hydroxide, the alkaline solution decolorized with Norit and the product reprecipitated with hydrochloric acid. The disulfonamide crystallized from ethanol as tan prisms; m.p. 172–174°, yield 42.3 g. (82.1%). It was obtained as colorless prisms, m.p. 173–174°, by slowly cooling a decolorized solution of the crude product in boiling ethanol.

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, 64.65; H, 5.37; N, 5.33; S, 12.17.

Most attempts to recrystallize the material from ethanol resulted in the deposition of an alternative crystalline form, large rectangular prisms melting at 159–160° with a simultaneous transition to the higher melting form. The substance would melt completely only if it were plunged into a bath heated to a temperature of 161° or more. When the recrystallizing solvent was benzene or acetic acid, the lower-melting crystalline form resulted. The infrared spectra of the two forms are identical and the composition of the lower-melting form corresponds to that of the desired product.

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, 64.74; H, 5.59; N, 5.31; S, 12.26.

2,2'-Dimethyl-4,4'-(hexamethylenediimino)-bibenzyl (Ib).—A solution of 30.9 g. (0.0593 mole) of 4,4'-diphenylsulfonamido-2,2'-dimethylbibenzyl and 15.0 g. (0.0614 mole) of hexamethylene bromide in 200 ml. of dimethylformamide was added in high dilution and with stirring, over a 13-hour period, to a suspension of 150 g. (1.08 moles) 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, cooled, diluted with 1 l. of water and poured into 3 l. of cold water. The crude product was taken up in boiling chloroform, the solution decolorized with Norit and the solvent removed on a steam-bath. A mixture of the residue, a viscous yellow oil, with 20 g. of phenol and 150 ml. of 48% hydrobromic acid was boiled under reflux, with stirring, for 1 hour. The cyclic diamine, isolated in the usual fashion,[2] crystallized from ethanol as white needles, m.p. 185.5–187.5°, yield 5.05 g. (26.4%). An additional recrystallization of the compound from ethanol sharpened the melting point to 186.5–187.5°.

Anal. Calcd. for $C_{22}H_{30}N_2$: C, 81.92; H, 9.38; N, 8.70; mol. wt., 323. Found: C, 81.66; H, 9.23; N, 8.72; mol. wt. (Rast), 352.

Concentration of the mother liquor yielded no additional material having the composition of the cyclic diamine.

The diacetate of the heterocyclic compound was prepared by boiling, under reflux for 4 hours, a mixture of 0.50 g. of the diamine, 1.0 g. of anhydrous sodium acetate and 20 ml. of acetic anhydride. After the excess acetic anhydride had been hydrolyzed the mixture was poured into 300 ml. of dilute, aqueous sodium hydroxide. The product separated as an oil which solidified when chilled. A solution of the compound in boiling ethanol was decolorized with Norit, the solvent removed and the residue taken up in boiling petroleum ether (b.p. 30–60°). The diamide crystallized from the cold solution as white cubes, m.p. 126–127°, yield 0.48 g. (74%).

Anal. Calcd. for $C_{26}H_{34}N_2O_2$: C, 76.83; H, 8.43; N, 6.89. Found: C, 76.93; H, 8.51; N, 6.79.

The infrared spectrum of the product closely resembles the spectrum of N,3,4-trimethylacetanilide.

2,2'-Dimethyl-4,4'-(tetramethylenediimino)-bibenzyl (Ia).—A solution of 6.10 g. (0.0117 mole) of 4,4'-diphenylsulfonamide-2,2'-dimethylbibenzyl and 3.24 g. (0.0150 mole) of tetramethylene bromide in 100 ml. of dimethylformamide was added in high dilution and with stirring, over a period of 7.5 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 7 hours and then worked up as in the previous case. A mixture of the crude cyclic disulfonamide, a viscous, yellow oil obtained from the chloroform extract, with 5.0 g. of phenol and 75 ml. of 48% hydrobromic acid was boiled under reflux, with stirring, for 1 hour. The cyclic diamine crystallized from a methanol–water mixture as white needles, m.p. 174–176°, yield 0.19 g. (5.5%). Recrystallization of the heterocyclic compound from aqueous methanol raised the melting point to 175.5–176.5°.

Anal. Calcd. for $C_{20}H_{26}N_2$: C, 81.59; H, 8.90; N, 9.52; mol. wt., 294. Found: C, 81.70; H, 8.94; N, 9.68; mol. wt. (Rast), 318.

No other product could be isolated from the mother liquor.

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The Conformation of 2-(2,3-Dimethoxyphenyl)-cyclohexane-1,2-diol, a *cis*-Glycol

BY DAVID GINSBURG[1]

RECEIVED JULY 13, 1953

It has been shown that hydroxylation of the double bond of 1-(2,3-dimethoxyphenyl)-cyclohexene by performic acid and by osmium tetroxide leads to the same glycol, 2-(2,3-dimethoxyphenyl)-cyclohexane-1,2-diol, presumed to be a *cis*-glycol.[2] It is generally believed that the performic acid and osmium tetroxide hydroxylation methods lead to *trans*- and to *cis*-glycols, respectively. Clearly, in the case under discussion one conformation is considerably more stable than the other and therefore only one glycol is isolated.

It seems reasonable to assume that in the present case, the bulkier dimethoxyphenyl group at C_2 of the cyclohexane ring and the hydroxyl group at C_1 will both assume the equatorial conformation and will thus be *trans* with respect to each other. The hydroxyl group at C_2 must necessarily adopt the polar conformation and constitute with the adjacent hydroxyl group, a *cis*-glycol system. Although both *cis*- and *trans*-2-phenylcyclohexane-1,2-diol are known, it has been shown that the

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[1] U. S. Public Health Service Postdoctoral Fellow at Harvard University 1952–1953. On leave of absence from the Weizmann Institute, Rehovoth, Israel.

[2] E. D. Bergmann, R. Pappo and D. Ginsburg, *J. Chem. Soc.*, 1369 (1950).