figures indicated that this compound was a mixed acid anhydride.

Anal. Calcd. for $C_{32}H_{24}O_7N_2$: C, 70.07; H, 4.38; N, 5.11. Found: C, 70.25; H, 4.35; N, 5.23.

I hereby desire to thank Professor Hata for his interest in the work.

Summary

The preparation of 5-propionyl- and 7-*o*-carboxylic-benzoyl-8-hydroxyquinoline and 8,8'-dihydroxydiquinolylphthalide has been reported.

TOKYO, JAPAN RECEIVED SEPTEMBER 4, 1934

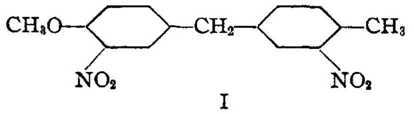
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF KITASATO INSTITUTE]

Nitration of 4,4'-Dimethoxydiphenylmethane

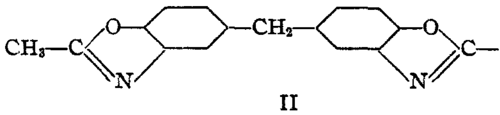
BY KONOMU MATSUMURA

It was a matter of interest to know whether nitro groups enter the 5,5' or 6,6' positions of 4,4'-dimethoxydiphenylmethane on di-nitration, because of *p*-methoxybenzyl and methoxyl groups both are *o*-*p*-directors. Moreover, the 6,6'-dinitro derivative might provide a convenient material for the preparation of 3,6-dimethoxyacridone which in turn is an intermediate for acridine compounds of therapeutic importance.[1]

Upon nitration of 4,4'-dimethoxydiphenylmethane with fuming nitric acid, however, the product was found to be 5,5'-dinitro-4,4'-dimethoxydiphenylmethane (I).



I



II

The 4,4'-dihydroxydinitrodiphenylmethane of Staedel in which the positions of the dinitro groups have not been established,[2] on methylation gave 4,4'-dimethoxydinitrodiphenylmethane which was found to be identical with that (I) obtained by dinitration of 4,4'-dimethoxydiphenylmethane, and, on the other hand, the 4,4'-dihydroxydinitrodiphenylmethane of Staedel on reduction followed by acetylation and subsequent distillation afforded a dioxazole derivative (II).

This established the orientation of both the nitro groups as being in the ortho positions to the methoxyl as well as to the hydroxyl groups.

Experimental

4,4'-Dimethoxydiphenylmethane.—The following modification of Ter Meer's method was found to be the best.[3] To the cooled solution (8°) of methylal (35.5 g.) and anisole (110 g.) in glacial acetic acid (110 g.) was added a cooled solution of concd. sulfuric acid (17 g.) in glacial acetic acid (135 g.). The resulting homogeneous solution, after standing for twenty-four hours at 8°, was poured into ice water (3 liters). The separated oil was fractionated in a Claisen flask. The portion (102 g.) which distilled at 320–340° (*ca.* 80% being distilled at 338°, 762 mm.) and solidified at room temperature (30°) was taken. Upon pressing on a porous plate, 85 g. of colorless crystals, m. p. 51–52°, was obtained.[4]

Nitration of 4,4'-Dimethoxydiphenylmethane.—Fuming nitric acid (12 g.) was gradually added to the cooled solution (10°) of 4,4'-dimethoxydiphenylmethane (5 g.) in glacial acetic acid (10 g.) with stirring at a temperature not exceeding 30°. The product, after pouring into ice water, formed yellowish white plates from alcohol, m. p. 164.5–165.5°; yield, 1.7 g. The alcoholic mother liquor, on evaporation, gave a yellow oil (4.6 g.) from which, on oxidation with chromic acid, no definite product could be isolated. It is soluble in glacial acetic acid and alcohol but difficultly in ether.

Anal. Calcd. for $C_{15}H_{14}O_6N_2$: C, 56.60; H, 4.40; N, 8.81. Found: C, 56.85; H, 4.19; N, 8.88.

5,5'-Dinitro-4,4'-dimethoxybenzophenone.—Chromic oxide (3 g.) was added to the hot solution of 5,5'-dinitro-4,4'-dimethoxydiphenylmethane (1.5 g.) in glacial acetic acid (30 g.) and the solution refluxed for four hours. The product gave almost colorless flat needles from dilute acetic acid (60%), m. p. 193°; yield, 1.25 g. It is soluble in alcohol and benzene but almost insoluble in ether.

Anal. Calcd. for $C_{11}H_{12}O_7N_2$: C, 54.22; H, 3.61; N, 8.43. Found: C, 54.41; H, 3.60; N, 8.41.

Methylation of Dinitro-4,4'-dihydroxydiphenylmethane.—A mixture of powdered disodium salt prepared from 1.45 g. of Staedel's dinitrodihydroxydiphenylmethane, dimethyl sulfate (2 cc.) and toluene (1 cc.) was refluxed for one hour. The product formed bundles of yellow needles from alcohol, m. p. 163–164°; yield, 1.2 g. The mixed melting point with the specimen obtained by nitration of 4,4'-dimethoxydiphenylmethane showed no depression.

Anal. Calcd. for $C_{15}H_{14}O_6N_2$: N, 8.81. Found: N, 8.94.

---

(1) Matsumura, THIS JOURNAL, **51**, 816 (1929).

(2) Staedel, *Ann.*, **283**, 163 (1894).

(3) Ter Meer, *Ber.*, **7**, 1200 (1874).

(4) Beck gives m. p. 48–49°, b. p. 330–340° and Ter Meer gives m. p. 52°, b. p. >360° for their products [Beck, *Ann.*, **194**, 323 (1878), and Ter Meer, Ref. 3].

5,5′-Diamino-4,4′-dihydroxydiphenylmethane.—The reduction of 5,5′-dinitro-4,4′-dihydroxydiphenylmethane (2.9 g.) was effected on treating it with the solution of stannous chloride (15 g.) and concd. hydrochloric acid (13 cc.) in glacial acetic acid (50 cc.) at 80° for two hours. The product gave colorless needles from ether, m. p. 220–222° (dec.) with preliminary darkening.

Anal. Calcd. for $C_{13}H_{14}O_2N_2$: C, 67.83; H, 6.09; N, 12.17. Found: C, 67.98; H, 6.32; N, 12.27.

The hydrochloride gave colorless prismatic needles, m. p. >305°. *Anal.* Calcd. for $C_{13}H_{14}O_2N_2 \cdot 2HCl$: HCl, 24.09. Found: HCl, 23.34.

5,5′-Tetraacetyldiamino-4,4′-diacetoxydiphenylmethane.—A mixture of 5,5′-diamino-4,4′-dihydroxydiphenylmethane (0.65 g.), anhydrous sodium acetate (0.7 g.) and acetic anhydride (13 g.) was refluxed for fifteen hours. The product formed prismatic needles from dilute alcohol, m. p. 142–143°; yield, 0.8 g.

Anal. Calcd. for $C_{25}H_{26}O_8N_2$: N, 5.81. Found: N, 5.90.

4,5,4′,5′-Dimethylbenzoxazolmethane (II).—On submitting the acetyl compound (0.7 g.) to distillation, the distillate soon turned to colorless prisms (0.4 g.). It was water washed and crystallized from ether into colorless prisms, m. p. 103–105°. It is easily soluble in the usual organic solvents but insoluble in dilute acid and alkali.

Anal. Calcd. for $C_{17}H_{14}O_2N_2$: C, 73.38; H, 5.04; N, 10.07. Found: C, 73.16; H, 5.12; N, 10.05.

The author thanks Professor Hata for his interest in the work.

Summary

It was ascertained that 4,4′-dimethoxydiphenylmethane on treatment with fuming nitric acid gives 5,5′-dinitro-4,4′-dimethoxydiphenylmethane.

TOKYO, JAPAN RECEIVED SEPTEMBER 17, 1934

[CONTRIBUTION FROM THE PHYSICO-CHEMICAL LABORATORY OF THE NEW YORK STATE AGRICULTURAL EXPERIMENT STATION]

The Optical Rotation and Dissociation of Casein[1]

BY D. C. CARPENTER

In studies dating from 1927, the writer[2] was able to show, by use of the ultracentrifuge, that casein prepared by the classical methods, respectively, of Hammarsten and of Van Slyke and Baker, was a mixture of protein molecules of different molecular weights. It was also shown that these different protein species could be separated from one another by fractionation from suitable solvents and the molecular weights of the pure monomolecular species established. The species were found to have molecular weights, respectively, of 96,000,[3] 188,000 and 375,000. Subsequent work[4] on the content of various amino acids in the 96,000 species, showed that a value of 98,000 for the molecular weight was compatible with the analyses. These molecular weight values obtained by two totally different lines of attack are in excellent agreement with one another. Serological tests[5] on the three protein species separated from casein showed that they were different from one another.

With reference to the old "casein" being a complex mixture, work in Sörensen's laboratory[6] has substantiated our own findings and lately Cherbuliez[7] has separated crude casein into four fractions by ammonium chloride and acetone. Groh[8] has fractionated crude casein by three different procedures. The homogeneity of the various individual fractions obtained by the various workers above has been ascertained only in the materials described by the writer, and it is therefore impossible to say whether clear-cut separations have been obtained by these other workers or not.

Recently Jones and Gersdorff[9] have shown that dissolving crude casein in very dilute alkali and reprecipitating with dilute acid reduces the cystine content of the protein. After five successive repetitions of the operation of dissolving in alkali followed by reprecipitation with acid, these workers record a decrease in cystine content from an initial value of 0.336 to 0.033%. In the course of our work on casein with the ultracentrifuge, we have found that it was impossible

---

(1) Approved by the Director of the New York Agricultural Experiment Station for publication as Journal Paper No. 45.

(2) T. Svedberg, L. M. Carpenter and D. C. Carpenter, THIS JOURNAL, **52**, 241 and 701 (1930).

(3) D. C. Carpenter, unpublished data.

(4) D. C. Carpenter, THIS JOURNAL, **53**, 1812 (1931).

(5) D. C. Carpenter and G. J. Hucker, *J. Infect. Dis.*, **47**, 435 (1930).

(6) Linderström-Lang, *Z. physiol. Chem.*, **176**, 76 (1928); *Compt. rend. trav. Lab. Carlsberg*, **17**, No. 9 (1929).

(7) E. Cherbuliez and M. L. Schneider, *Helv. Chim. Acta*, **15**, 597 (1932); E. Cherbuliez and F. Meyer, *ibid.*, **16**, 600 (1933).

(8) J. Groh, E. Kardos, K. Denes and V. Serenyi, *Z. physiol. Chem.*, **226**, 32–44 (1934).

(9) D. B. Jones and C. E. F. Gersdorff, *J. Biol. Chem.*, **104**, 99 (1934).