colorless solid which after recrystallization from methyl alcohol melted at 64°. The filtrate, on suitable treatment, yielded more of the same substance, the total yield being about 60%. It is much more easily obtained by direct addition of dimethyl malonate to benzalacetone. Thus a methyl alcoholic solution containing 2.4 g. of ketone and 3 g. of ester was allowed to stand at room temperature for several days during which it was kept alkaline by successive additions of a few drops of a dilute solution of sodium methylate. On evaporation it deposited a pale yellow solid, which became colorless on recrystallization. When the substance was heated alone or mixed with the product from the cyano ester the melting point was 64°.

Analysis. Calc. for $C_{15}H_{18}O_5$: C, 64.7; H, 6.5. Found: C, 64.4; H, 6.3.

The substance has neither the composition nor the properties of a dihydro-resorcinol derivative. As it does not reduce permanganate it cannot be an unsaturated compound such as would be formed by addition to the carbonyl group of the ketone. It must, therefore, have the structure assigned to it.

Summary

1. In the presence of a small quantity of sodium alcoholate, benzalacetone combines with cyano-acetic esters and malonic esters. The products are saturated compounds formed by addition to the double linkage of the ketone.

2. In more concentrated solutions of the alcoholate the addition products undergo further condensation to hydro-resorcinol derivatives. The reaction, therefore, takes place in the manner stated by Vorländer, and Haworth's interpretation is incorrect.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

ASYMMETRIC DYES

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During the past 5 years, 35 asymmetric dyes have been synthesized in this Laboratory and studied with reference to the possibility of selective dyeing. We have held the opinion that selective absorption of an optically active form from a racemic mixture by silk, wool or living tissue would constitute evidence of chemical, rather than physical, union between the dye and the substance which it colors. Interest in this type of investigation has been stimulated by the observation that optically active forms of other types of asymmetric compounds show specific biochemical reactions.[1]

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[1] Neuberg and Wohlgemuth, *Ber.*, **34**, 1745 (1901). Piutti, *Compt. rend.*, **103**, 134 (1886). Mayor, *Ber.*, **37**, 1225 (1904).

Willstätter recognized the importance of finding out whether the asymmetric molecules of protein-like substances such as silk and wool would accomplish the resolution of a racemic dye by combining with one form only, but at that time there were no asymmetric dyes in existence.[2]

Porter and Hirst[3] prepared several asymmetric dyes by treating *p*-aminobenzophenone with Grignard reagents, diazotizing the condensation products, and coupling with various amines and phenols. They reported the selective absorption by wool of the levo form of one of their dyes. They were unable to obtain reproducible results of a quantitative character.

Ingersoll and Adams have prepared optically active derivatives of *d*- and *l*-phenylamino-acetic acid and obtained evidence of selective absorption of one of them by wool.[4]

The work reported in this paper represents a successful attempt to accomplish the resolution of a racemic dye by the selective action of wool.

Two new series of asymmetric dyes were produced. The members of the first group were made by producing asymmetric amines through the condensation of bromo acid bromides with acetanilide, then diazotizing these products and coupling with various aromatic amines and naphthols. The dyes of the second series were prepared from amino-mandelic acid by diazotizing the acid and coupling with aromatic amines and with naphthols.

Optically active compounds were obtained by resolving racemic aminomandelic acid into its *d* and *l* forms before diazotization. The resolution was accomplished by fractional crystallization of the cinchonine salts. Dyes derived from *d*- and *l*-*m*-mandelic acid and β-naphthol melt at 210° and have specific rotations of +47°. ± .5° and —47°. ± .5°.

When wool is dyed in a racemic mixture of these dyes, the solution containing the unused portion of the compound is levorotatory. Both forms of the dye are taken up by the wool but they are absorbed at different rates. By using an excess of wool and extending the time of contact to 72 hours the residual dye in solution was almost a pure levorotatory compound.

Experimental Part

***m*-Nitromandelic Acid.**—*m*-Nitrobenzaldehyde was made by the action of chromyl chloride and water on a solution of *m*-nitrotoluene in carbon disulfide.[5] The aldehyde was treated with potassium cyanide and acetic acid. The resulting cyanohydrin was hydrolyzed by Heller's method.[6] The reduction of the nitro compound to aminomandelic acid was accomplished by means of ferrous sulfate and barium hydroxide. A solution of 20 g. of *m*-nitromandelic acid in 200 cc. of warm water was treated with a suspension of 255 g. of crystallized barium hydroxide in 1200 cc. of water, and a solution of 184 g. of crystallized ferrous sulfate in 800 cc. of water. The suspension of barium hydroxide was obtained by heating the water until all of the base had dissolved, then cooling the solution and constantly shaking it. The reduction proceeded rapidly at 30°,

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[2] Willstätter, *Ber.*, **37**, 3758 (1904).

[3] Porter and Hirst, This Journal, **41**, 1264 (1919).

[4] Ingersoll and Adams, *ibid.*, **44**, 2930 (1922).

[5] Widmann, *Ber.*, **13**, 678 (1880).

[6] Heller, *ibid.*, **46**, 280 (1913).

the whole mass changing in color from green to brown within a few minutes. After the mixture had been vigorously stirred for an hour, it was filtered. The clear filtrate was treated with sulfuric acid until all of the barium had been precipitated and the solution was distinctly acid. The barium sulfate was removed by filtration and the filtrate evaporated on a water-bath. The product was recrystallized from hot water. The crystals melt with decomposition at 130°. The yield was about 60%.

Resolution of *m*-Amino-mandelic Acid.—A suspension of 20 g. of crystalline cinchonine and 11 g. of *m*-aminomandelic acid in 500 cc. of water was heated on the water-bath for an hour, and shaken frequently. After cooling, the solution was filtered and allowed to stand in an open vessel at room temperature. The first crystals appeared after 4 days. Later, however, seeding decreased the time to a few hours. The crystals were roset-shaped and on drying fell to a powder. They were recrystallized from hot water (25 cc. of water for each g. of the dry salt); m. p., 156.5°. The pure crystals were dissolved again in hot water and the solution was cooled to room temperature, treated with ammonium hydroxide until all the cinchonine was precipitated and the solution gave the odor of ammonia. The cinchonine was filtered off and the filtrate was freed from ammonia by evaporation at room temperature over sulfuric acid in a vacuum desiccator. It was then acidified with hydrochloric acid and the evaporation was continued at room temperature. The dextrorotatory amino acid crystallized in a few days. It was recrystallized twice from water; m. p. 130° (decomp.); $[\alpha]_D = +33.80°$. After several crops of mixed crystals had been removed from the mother liquor the levo product was obtained nearly pure by fractional recrystallization at ordinary temperatures. The yield was poor; m. p., 130° (decomp.); $[\alpha]_D = -33.65°$.

***Dextro-m*-Azo-β-naphthol-mandelic Acid.**—*d-m*-Aminomandelic acid prepared as described above was diazotized at 0° and poured into a cold alkaline solution of β-naphthol. The solution became blood red. The dye was precipitated by making the solution faintly acid, and was recrystallized from glacial acetic acid. It is soluble in bases, slightly soluble in alcohol and in acetic acid, insoluble in water; m. p., 210°; $[\alpha]_D = +49° \pm 5°$.

***Levo-m*-Azo-β-naphthol-mandelic Acid.**—This dye was prepared by the methods applied in the synthesis of the dextro compound. Its color, melting point, solubility and other properties are identical with the corresponding properties of the dextrorotatory dye; $[\alpha]_D = -49° \pm 5°$.

Dyeing Experiments

Many experiments were made with fresh, clean wool and with silk. The fibers were dyed by pure *d* and pure *l* derivatives of *m*-mandelic acid and β-naphthol, and by racemic mixtures of the dyes. The rates of absorption have not been measured, but a typical example, indicating selective absorption, may be given. A solution containing 1 g. of the racemic dye in 75 cc. of acetic acid was treated with 2.5 g. of wool at 20° for 24 hours. The solution was then filtered and its rotation measured. A 250watt nitrogen-filled Mazda lamp was used as a source of light. (This dye gives an optically clear solution, and satisfactory readings of the colored solution can be made.) At the end of 24 hours the reading was —0.66°. Fresh wool was then added. At 48 hours the reading was —0.91°. Control samples of wool in acetic acid without the dye did not develop optical activity. There was no extraction of optically active compounds from the wool.

Other Compounds.—Incidentally, in the course of this investigation, the following compounds, not mentioned above, were prepared and analyzed.

***p*-Azo-β-naphthol-mandelic Acid,** $HO\cdot C_{10}H_6\cdot N:N\cdot C_6H_4\cdot CHOH\cdot COOH$.—From diazotized *p*-aminomandelic acid and β-naphthol; it is a bright red dye, insoluble in acids but soluble in bases and in hot alcohol; m. p., 118°. Calc.: N_2, 8.7. Found: 8.45, 8.23.

***p*-Azo-resorcinol-mandelic Acid,** $(HO)_2C_6H_3\cdot N:N\cdot C_6H_4\cdot CHOH\cdot COOH$.—A red dye, soluble in bases, slightly soluble in alcohol and in acetic acid; m. p., 154° (decomp.). Calc.: N_2, 9.72. Found: 10.95, 11.14.

***p*-Azo-dimethylaniline-mandelic Acid,** $(CH_3)_2N\cdot C_6H_4\cdot N:N\cdot C_6H_4\cdot CHOH\cdot COOH$.—A brown dye, insoluble in bases but soluble in acids and slightly soluble in water. It becomes bright red in acid solution; m. p., 125–129° (decomp.). Calc.: N_2, 14.05. Found: 14.21, 13.95.

***m*-Azo-resorcinol-mandelic Acid,** $(HO)_2C_6H_3\cdot N:N\cdot C_6H_4.CHOH\cdot COOH$.—A red dye, soluble in alcohol, water and in bases; m. p., over 280°.

***m*-Azo-dimethylaniline-mandelic Acid,** $(CH_3)_2N\cdot C_6H_4\cdot N:N\cdot C_6H_4\cdot CHOH\cdot COOH$.—A reddish-purple dye, soluble in acids and in alcohol but insol. in bases; m. p., 158°.

***m*-Azo-phenol-mandelic Acid,** $HO\cdot C_6H_4\cdot N:N\cdot C_6H_4\cdot CHOH\cdot COOH$.—A bright yellow compound, soluble in bases and in hot alcohol, but insoluble in acids; m. p., 119°. Calc.: N_2, 10.33. Found: 10.56.

β-Naphthol-azo-α-hydroxy-propionophenone, $CH_3\cdot CHOH\cdot CO\cdot C_6H_4\cdot N:N\cdot C_{10}H_7H$.—A red dye made by condensing α-bromopropionyl bromide with acetanilide, hydrolyzing the condensation product, diazotizing the resulting *p*-aminopropionophenone and coupling with β-naphthol. It is soluble in alcohol, ether and bases, and insoluble in water and in acids; m. p., 132°. Calc.: N_2, 9.00. Found: 9.39, 9.34, 9.37.

β-Naphthol-azo-α-hydroxybutyrophenone, $CH_3\cdot CH_2\cdot CHOH\cdot CO\cdot C_6H_4\cdot N:N\cdot C_{10}H_7OH$.—A red dye from *p*-aminobutyrophenone and β-naphthol. It is soluble in bases, alcohol, or acetone and insoluble in acids; m. p., 72°.

β-Naphthol-azo-α-hydroxy-*iso*valerophenone, $(CH_3)_2CH\cdot CHOH\cdot CO\cdot C_6H_4\cdot N:N\cdot C_{10}H_7OH$.—A red dye from the condensation product of α-bromo-*iso*valeryl bromide and acetanilide by hydrolysis, diazotization of the amine and coupling with β-naphthol. It is soluble in benzene, ether or bases and is insoluble in acids; m. p., above 265°.

Summary

Representatives of 2 series of asymmetric dyes have been prepared, analyzed and described.

A dye derived from *m*-aminomandelic acid and β-naphthol has been obtained in pure optically active forms.

The dextro form of this dye combines with wool faster than does the corresponding levo form.

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