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

ASYMMETRIC DYES.

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Differential stains are among the most important aids employed in bacteriological and histological work. Although no definite relationship has been established between the chemical structures of dyes and their functions as vital stains, still we considered it a reasonable assumption that selective action in staining might be demonstrated if experiments were made with dyes representing great diversity in structure. In our search for evidence in support of this assumption we have found one racemic mixture upon which wool acts selectively, absorbing more of the levo than of the dextro form of the dye.

The most exhaustive research in this field has been conducted by H. M. Evans,[1] who has reached the conclusion that staining in living tissue with benzidine dyes is a physical rather than a chemical phenomenon. In this opinion Evans is supported by Schulemann[2] and others.

In no instance recorded, however, has an optically active dye been employed as a vital stain. Inasmuch as specificity in enzyme action is closely related to the asymmetric structure of the substrate, it seemed to us worth while to investigate the action of dyes having at least one asymmetric carbon atom in each molecule. We have, therefore, synthesized a group of asymmetric dyes and have made some preliminary experiments on dyeing with them. The results of these experiments, including partial resolution of a racemic dye with concomitant dyeing of wool, give some support to our theory, and the work is being repeated on a quantitative basis. No experiments have yet been made on living tissue.

We desire to present in this paper only a description of the dyes synthesized. The dyes were derived from *p*-amino-benzophenone which was prepared from benzoyl chloride and phthalanilid in the presence of zinc chloride.[3] From this ketone several amino-diphenylalkyl carbinols were prepared by the Grignard reaction. The carbinol carbon was thus rendered asymmetric. *p*-Amino-benzohydrol[4] was prepared also by reducing the ketone in alcoholic solution by means of sodium amalgam. These amines were diazotized and coupled as indicated below.

In preparing the alkyl derivatives of amino-benzophenone it is necessary to use an excess of alkyl magnesium iodide, for the reagent acts quan-

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[1] Evans, *Sci.*, **39**, 443 (1914).

[2] Schulemann, *Deut. Med. Woch.*, **40**, 1839 (1914).

[3] Dobner, *Ann.*, **210**, 260 (1881).

[4] Kippenberg, *Ber.*, **30**, 1136 (1897).

titatively upon the amino group before the carbonyl group is attacked; and unless both parts of the molecule have been acted upon, the original ketone is regenerated by hydrolysis. The addition products formed between the amino-benzophenone and alkyl magnesium iodide were hydrolyzed by pouring into cold saturated solutions of ammonium chloride. The carbinols were obtained from the ether layer and recrystallized from hot ligroin.

p-Amino-diphenylmethyl-carbinol.

The compound was formed by the action of methyl magnesium iodide on *p*-amino-benzophenone. It is a colorless crystalline body melting at 101°. It appears among the reaction products as a red oil and crystallizes only when quite pure. It is soluble in alcohol, chloroform, acetone and in hot ligroin. The ligroin solution on cooling yields the crystals in the pure state.

Calc. for $C_6H_5C(OH)(CH_3)C_6H_4NH_2$: C, 78.87; H, 7.04; N, 6.58. Found: C, 78.80; H, 7.14; N, 6.56.

The corresponding ethyl derivative crystallizes in colorless plates melting at 103°. It dissolves in glacial acetic acid from which it may be precipitated by the addition of water. Crystallization from hot ligroin affords the best means of purification.

Calc. for $C_6H_5C(OH)(C_2H_5)C_6H_4NH_2$: C, 79.25; H, 7.49; N, 6.17. Found: C, 79.00; H, 7.52; N, 6.16.

Diphenyl-methylcarbinol-*p*-azo-β-naphthol.

The amine described above was diazotized and coupled with β-naphthol with the production of a red dye. The compound is soluble in hot alcohol from which it crystallizes on cooling. It is soluble in the ordinary organic solvents and practically insoluble in water, dilute acids and alkalies. It melts at 190°.

Calc. for $C_6H_5C(OH)(CH_3)C_6H_4N{=}NC_{10}H_6OH$: C, 78.30; H, 5.44; N, 7.61. Found: C, 78.30; H, 5.40; N, 7.65.

Diphenyl-methylcarbinol-*p*-azodimethyl-aniline.

Success in preparing this dye depends largely upon the control of the hydrogen-ion concentration. Dimethyl-aniline hydrochloride was dissolved in 0.1 *N* hydrochloric acid. The primary amine was diazotized in acid of the same concentration to which an equivalent quantity of sodium acetate had been added. The dye has a deep red color in acid solution and is yellow in alkaline solution. It may be purified by crystallization from hot alcohol. M. p. 177°.

Calc. for $C_6H_5C(OH)(CH_3)C_6H_4 - N = N - C_6H_4N(CH_3)_2$: C, 76.48; H, 6.72; N, 12.17. Found: C, 76.40; H, 6.65; N, 12.15.

Naphthol sulfonic acid and naphthylamine sulfonic acid derivatives were synthesized for the production of water-soluble dyes. Corresponding compounds were prepared from *p*-amino-diphenyl-ethylcarbinol and from

TABLE I.
Properties of Dyes.

		M. p.	Color	Water.	Acids.	Bases	Alcohol.
(1)	$C_6H_5CHOHC_6H_4N_2C_{10}H_6OH$	169.5°	red	insol.	insol.	insol.	sol.
(2)	$C_6H_5CCH_3OHC_6H_4N_2C_{10}H_6OH$	190°	red	insol.	insol.	insol.	sol. (hot)
(3)	$C_6H_5CC_2H_5OHC_6H_4N_2C_{10}H_6OH$	149°	crimson	insol.	insol.	insol.	s. sol.
(4)	$C_6H_5CHOHCH_4N_2C_6H_4N(CH_3)_2$	145°	red	sl. sol.	sol.	insol.	sol.
(5)	$C_6H_5CCH_3OHC_6H_4N_2C_6H_4N(CH_3)_2$	177°	yellow	insol.	sol.	sol.	sol. (hot)
(6)	$C_6H_5CC_2H_5OHC_6H_4N_2C_6H_4N(CH_3)_2$	138–9°	orange	sol.	sol.	sol.	sol.
(7)	$C_6H_5CHOHC_6H_4N_2C_{10}H_4OH(SO_3H)_2$	162°	red	insol.	sol.	insol	sol.
(8)	$C_6H_5CC_2H_5OHC_6H_4N_2C_{10}H_5OHHSO_3$	120–2°	dark red	v. sol.	sol.	sol.	sol.
(9)	$C_6H_5C(CH_3)OHC_6H_4N_2C_{10}H_5OHHSO_3$	150–2°	red	v. sol.	sol.	sol.	sol.

p-amino-benzhydrol. They are very much alike in properties, but vary in color from yellow to crimson.

The first 3 compounds listed in this table constitute examples of alkali-insoluble phenols (naphthols). The insolubility of these dyes lends support to the theory of Torrey and Kipper,[1] *viz.*, that phenols are generally insoluble if in each molecule there is a long side chain *ortho* to the hydroxyl group and at least one other substituent in the ring. In this case the C_4H_4 residue of the naphthalene constitutes the auxiliary substituent. The behavior of these dyes in dilute alkalies is in harmony also with Adams'[2] more recent theory concerning the solubility of phenols.

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THE OXIDATION OF ETHYL ALCOHOL BY MEANS OF POTASSIUM PERMANGANATE.

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A preliminary report of a portion of the work included in this paper has already been made.[3] The influence of the alkali on the oxidation of organic and inorganic compounds by means of potassium permanganate has been studied by other early investigators (Margueritte, Pelouze, Bussey, Hempel and Berthelot) in addition to those mentioned in the preliminary article.

Among the objects of this investigation were the following: (1) to ascertain what are the reaction products when ethyl alcohol is oxidized both in neutral and in alkaline potassium permanganate solutions under known conditions of temperature; (2) to study the effect of temperature, of change in the initial concentration of the alkali present, and their combined effect on the character of the reaction products; (3) to study the mechanism of the oxidation of ethyl alcohol under these variable conditions.[4]

It has been definitely established that acetic acid is the only product obtained when ethyl alcohol is oxidized by an aqueous solution of potassium permanganate, but that acetic acid, oxalic and carbonic acids are also formed when the oxidation is conducted in the presence of potassium hydroxide the concentration being above certain minimum values (p. 1282), Hepter,[5] studying the action of potassium permanganate on organic compounds in acid and alkaline solution, found that substances

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[1] Torrey and Kipper, THIS JOURNAL, 30, 840 (1908).

[2] Adams, *Ibid.*, 41, 247 (1919).

[3] THIS JOURNAL, 38, 375 (1916).

[4] *Ibid.*, 38, 377 (1916).

[5] *Z. anal. Chem.*, 51, 409–29 (1912).