[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY]

Some Colored Local Anesthetics

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Several attempts have been made to give staining properties to physiologically active substances as a means of observing their action in the organism. Ehrlich and Einhorn[1] prepared some colored local anesthetics but no evidence could be found of their having used them. Fulton prepared a large number of such compounds, none of which could be regarded as entirely satisfactory from the standpoint of their color.[2]

The present investigation involves the preparation of a number of compounds in an effort to find some which may prove of value for physiological or pharmacological studies.

A series of compounds was prepared by diazotizing procaine and coupling with various dye intermediates. In order to obtain products with colors in the longer wave length range, some of these were converted into disazo dyes. It was found that the presence of any acidic group in the molecule destroys the anesthetic effect.

The anesthetic action of the dyes was determined only qualitatively by their effect on the tongue. The color was observed on wool dyed from a bath at *p*H 7.5. The results are given in Table I.

TABLE I

No.	Dye, diazotized procaine +	Color	M. p., °C.	Solubility in water	Anesthetic activity
1	H-acid	Purple	dec. 250	Soluble	–
2	Salicylic acid	Pale yellow	dec. 250	Sl. sol.	–
3	Resorcinol	Orange	dec. 250	Sl. sol.	–
4	Methyl salicylate	Pale yellow	196.5	Sl. sol.	?
5	Methyl anthranilate	Bright yellow	216–219	Soluble	+
6	*p*-Bromoaniline	Light brown	109–110	Sl. sol.	+
7	α-Naphthylamine	Brown-red	190 dec.	Soluble	+
8	α-Naphthylamine + α-naphthylamine	Brown-red	dec. 250	Sl. sol.	+
9	Methyl anthranilate + α-naphthylamine	Orange-red	dec. 250	Soluble	+
10	Diazotized *p*-nitroaniline + procaine	Yellow	169–172	Sl. sol.	+

Experimental

Basic Monazo Dyes (Nos. 1, 5, 6, 7).—Approximately 0.5 g. of procaine hydrochloride was dissolved in 10 cc. of water and 1 cc. of concd. hydrochloric acid. The solution was cooled to 0° and molar sodium nitrite solution was added with vigorous mechanical stirring until a positive test was obtained with starch–potassium iodide paper. The diazonium salt solution was added to a solution prepared by dissolving the equivalent quantity of the amine in 10 cc. of water and the minimum amount of hydrochloric acid, and adding 1 g. of sodium acetate. Coupling was allowed to proceed with mechanical stirring until a spot test for diazonium salt with alkaline H-acid was negative. The dye was filtered out, in some cases after saturation with sodium chloride, and crystallized from 90% alcohol.

TABLE II

ANALYSES

No.	N, % Calcd.	N, % Found	Cl, % Calcd.	Cl, % Found
1	8.97	8.41	5.69	5.40
2	9.95	9.83	8.42	8.38
3	10.67	10.53	9.02	8.88
4	9.65	9.47	8.15	8.00
5	12.89	12.47	8.17	7.90
6	12.29	12.15	43.69	43.36[a]
7	13.05	12.67	8.32	9.19
8	14.45	13.49	6.11	6.52
9	14.27	13.76	6.03	6.05
10	16.61	16.41	8.42	8.31

[a] Cc. of 0.1 *N* silver nitrate per g.

Basic Disazo Dyes (8, 9).—The appropriate monazo dye was diazotized and coupled as described above.

Acid Monazo Dyes (2, 3, 4).—Approximately 0.5 g. of procaine hydrochloride was diazotized as before and added to a solution of the equivalent quantity of the phenol in 12.5 cc. of 4% sodium hydroxide. The mixture was allowed to react and the dye was isolated and purified as before.

Summary

1. A number of azo dyes derived from procaine have been prepared.

2. Several of these compounds are local anesthetics.

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(1) Ehrlich and Einhorn, *Ber.*, **27**, 1870 (1894).

(2) Fulton, *Am. J. Physiol.*, **57**, 153 (1921).