[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF TRINITY COLLEGE]

THE CONDENSATION OF AMINOANTIPYRINE. VI. A STUDY OF THE EFFECT OF EXCESS BASE ON THE REACTION OF AMINOANTIPYRINE WITH PHENOLIC COMPOUNDS IN THE PRESENCE OF OXIDIZING AGENTS

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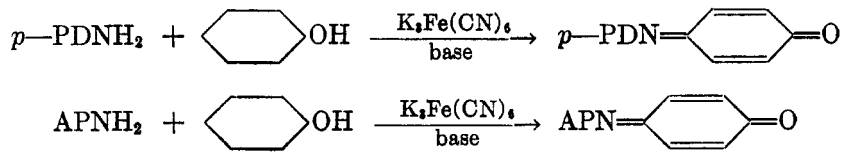
Previous work (1) has shown that potassium ferricyanide in basic solutions oxidizes a mixture of phenol and aminoantipyrine to a dye. This reaction appears to be analogous to the reactions of the *p*-diamines with phenols in which indophenols (2) are formed. If *p*-$PDNH_2$ is used to represent *p*-phenylenediamine and $APNH_2$ is used for aminoantipyrine the analogy of the reactions may be shown by the following equations:



It was recognized that this reaction of aminoantipyrine could be used as a test for certain phenolic compounds. During the course of earlier work it was noted that the tests for some phenols were erratic and led to results in variance with those already in the literature. This variance (3) of the results of the tests was particularly outstanding with solutions of *o*- and *m*-nitrophenol, and it was suspected that the amount and kind of base used produced an inhibiting effect on the reaction. The work reported in this paper was, therefore, undertaken with the object of determining this inhibiting effect and also of determining the most satisfactory base to use for general testing.

The inhibiting effect of excess base has been studied by comparison of the intensity of the colors developed in phenol solutions of various degrees of basicity. Solutions of aminoantipyrine, the oxidant, potassium ferricyanide, and the four bases, sodium bicarbonate, sodium carbonate, ammonium hydroxide, and sodium hydroxide were prepared in such a way that the first drop of the basic solution supplied the theoretically required quantity. Solutions of the phenolic compounds were used in concentrations of 1:10,000.

DISCUSSION

In general the condensations of phenolic compounds with aminoantipyrine are inhibited to a greater or lesser degree by excess base. The reactions of the nitrophenols and barbituric acid with aminoantipyrine are extremely sensitive to excess base, whereas solutions of β-naphthol are quite insensitive to an excess of

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base in these reactions. On the other hand, reactions with compounds such as α-naphthol and phenol exhibit an abnormal behavior. It will be noted that when α-naphthol is tested in the presence of sodium hydroxide there is a pronounced increase in the intensity of the color between four and five drops of base, and while it is not indicated in the table this increase is maintained even in the presence of ten drops. Between five and ten drops of sodium carbonate solution

TABLE I

EFFECT OF EXCESS BASES ON THE CONDENSATION REACTION OF PHENOLS WITH AMINOANTIPYRINE[a]

BASE	$NaHCO_3$					Na_2CO_3					NH_4OH					NaOH				
Drops used	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Compounds tested																				
Barbituric acid	3[b]	3	3	2	2	3	1	–	–	–	3	1	–	–	–	1	–	–	–	–
o-Chlorophenol	5	5	5	5	5	5	5	5	5	3	5	5	5	5	5	5	2	1	–	–
2,6-Dibromophenol	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	1	–	–	–
m-Hydroxybenzoic acid	1	2	2	2	2	3	3	3	2	2	3	3	3	3	2	2	1	1	1	1
5-Hydroxy-1,3-dimethylbenzene	3	4	4	2	2	3	2	2	2	2	1	3	3	2	2	3	2	2	2	2
8-Hydroxyquinoline	5	5	5	5	5	5	5	5	5	2	5	5	5	5	5	5	5	5	1	1
α-Naphthol	5	5	5	5	5	5	2	2	2	2	2	2	2	2	2	2	2	2	2	5
β-Naphthol	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
o-Nitrophenol	3	3	3	3	2	3	–	–	–	–	3	–	–	–	–	–	–	–	–	–
m-Nitrophenol	1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Phenol	3	3	2	2	2	3	3	2	2	2	3	3	3	3	3	3	3	2	1	1
Phloroglucinol	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	–
1-Phenyl-3-methylpyrazolon-5	3	3	3	3	3	3	3	2	2	1	3	3	2	2	2	2	–	–	–	–
Salicylic acid	1	1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
2,4-Dichlorophenol	5	5	5	5	5	5	5	3	3	2	5	5	3	3	3	2	1	–	–	–
p-Hydroxybenzoic acid	2	3	3	2	2	3	2	2	2	2	3	3	3	3	2	2	2	1	1	1
2,4,6-Tribromophenol	5	5	5	5	5	5	5	1	1	1	5	5	1	1	1	5	–	–	–	–

[a] Most of the colors developed in the test solutions range from yellow-orange to red, but 5-hydroxy-1,3-dimethylbenzene produces a purple solution, β-naphthol a green solution, and phloroglucinol a yellow-brown to brown-red solution.

[b] The numbers used to designate the intensity of the colors developed are arbitrary: 1 indicates a weak test, 4 a very intense test, and 5 indicates the formation of a precipitate.

there is produced a similar effect on α-naphthol and phenol, although in the case of phenol the increase is not so pronounced. The decrease in the intensity of the test with excess base is not due to the dilution of the test solution.

In cases where the reaction is carried out at the threshold of sensitivity the dilution factor may be important. For salicylic acid this threshold is 1:10,000 and it will be noted in the table that this compound fails to give the test in all but the lowest concentrations of sodium bicarbonate. However, solutions of salicylic acid, 1:1,000, develop the most intense color in a solution of sodium hydroxide. This behavior is noted in an as-yet-undetermined constituent of urine.

While the reaction of 2,6-dibromophenol with aminoantipyrine is rather insensitive to excess base, the reaction of 2,4,6-tribromophenol displays a pronounced sensitivity when the stronger bases are used. It has been observed in this laboratory that condensations of compounds which have a group or atom expelled during the reaction are inhibited more by excess base than condensations of the parent compounds.

It was found that the bases, when used in excess, can be arranged in a series of increasing inhibiting effect: sodium bicarbonate < ammonium hydroxide < sodium carbonate < sodium hydroxide. This series is remarkably similar to that reported previously (4) for the efficiency of bases in promoting those coupling reactions which are accompanied by expulsion. The reaction of aminoantipyrine with a phenolic compound is best accomplished in a sodium bicarbonate solution in which slight variations in the amount of base will have the least retarding effect.

EXPERIMENTAL

The aqueous solutions for the tests reported in this paper were prepared as follows:— phenolic compound 0.100 g./l.; $K_3Fe(CN)_6$ 54.2 g./l.; aminoantipyrine 8.47 g./l.; $NaHCO_3$ 14.0 g./l.; Na_2CO_3 8.8 g./l.; conc'd NH_4OH 11.25 cc. diluted to one liter; NaOH 6.67 g./l.

To 2 cc. of the phenolic solution in a 100 × 10 mm. test tube was added the requisite quantity of base followed by one drop of the aminoantipyrine solution. After the solutions were well mixed one drop of the oxidant was added and the test tube shaken for fifteen seconds. This shaking is necessary for the formation of a precipitate in many cases. After 3 to 5 minutes the color of the solution was noted.

The dropping tubes were standardized to deliver a drop of 0.04 cc.

SUMMARY

The condensation reaction of aminoantipyrine has been shown to be sensitive to bases. The order of interference is sodium bicarbonate < ammonium hydroxide < sodium carbonate < sodium hydroxide. It is recommended that sodium bicarbonate be used as the base for the aminoantipyrine test because excesses of this reagent have the least retarding effect on the reaction.

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