

Conductimetric Study of the Interaction of Hexylresorcinol and Amaranth with Quaternary Ammonium Compounds

By D. H. RODGERS

A conductimetric titration procedure was used to demonstrate interactions of hexylresorcinol and amaranth with cetylpyridinium chloride and cetyl dimethyl benzyl ammonium chloride. The conductimetric technique gives an indication of the stoichiometry and the type of interaction involved.

INTERACTION OF quaternary ammonium germicides with various substances, including anionic and nonionic surfactants, dyes, and polymeric compounds, has been reported by numerous investigators (1-4). Since hexylresorcinol may be considered a nonionic surfactant, a study was conducted to determine the nature and extent of any interaction which might occur in proposed formulations containing both hexylresorcinol and quaternary ammonium compounds.

Among the methods used to study such interactions are microbiological assay (5), dialysis (2), electrophoresis (5), and cloud point determinations (3, 5). These methods, while useful, were considered too time consuming or were inapplicable to the present problem. The conductimetric titration procedure described in this report was rapid, simple, and sensitive for the purposes of the study.

EXPERIMENTAL

Reagents.—Cetylpyridinium chloride (CPC) U.S.P., cetyl dimethyl benzyl ammonium chloride¹ (CDBAC), 1% solution of hexylresorcinol U.S.P. in methanol, 0.5% solution of amaranth U.S.P. (FD&C Red No. 2) in distilled water were employed. The reagents were not subjected to special purification.

Conductimetric Titration Procedure.—A weighed quantity of the quaternary ammonium compound, dissolved in 100 ml. of distilled water, was titrated conductimetrically with 1% hexylresorcinol in methanol or with 0.5% amaranth in water. An Industrial Instruments model RCM15 Serfass conductivity bridge and a dipping type conductivity cell having a cell constant of approximately 1 were employed. The solution was stirred continuously using a magnetic stirrer. The effects of dilution and introduction of methanol were shown to be small enough to make correction unnecessary.

RESULTS AND DISCUSSION

Figures 1 and 2 show the curves obtained with varying weights of CDBAC and CPC when titrated with hexylresorcinol. In each case, the conductivity decreased to a minimum value, then increased upon further addition of hexylresorcinol. The initial drop in conductivity was interpreted as due to the interaction of hexylresorcinol and quaternary ammonium compound, which caused a lowering of the critical micelle concentration of the latter and resulted in a decrease in concentration of quaternary ammonium ions. Presumably, at the point of minimum conductivity, the quaternary ammonium compound was associated completely with hexylresorcinol. This

point may also correspond to a maximum micelle size; however, the exact mechanism for the interaction at the minimum point is not known. The subsequent rise in conductivity was attributed to the release of gegenions (chloride) which are bound to or associated with the micelle (6). In the case of the blank titration with distilled water (Fig. 1), no change in conductivity was observed with increasing hexylresorcinol concentration, an indication that resorcinol was nonionic at the pH of the measurements. Taking the point of minimum conductivity as the end point, the reactants appeared to combine in a ratio of 2 moles of CDBAC to 1 mole of hexylresorcinol, and 1 to 1 in the case of CPC. The difference in stoichiometry between quaternaries is not readily explained. It may be due to a number of effects, such as impurity of reactants, steric effects, and difficulty of detecting the end point. No apparent phase change occurred during the titrations with hexylresorcinol.

Figure 3 shows the titration curves obtained for CPC and CDBAC when titrated with an aqueous solution of amaranth. The shape of the curves, typical of the conductimetric titration of two strong electrolytes, contrast sharply with those in Figs. 1 and 2. At the end point, the point of intersection of the two straight lines, an insoluble precipitate of the

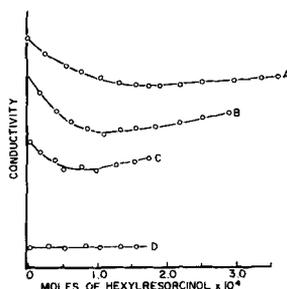


Fig. 1.—Conductimetric titration of CDBAC with hexylresorcinol. Key: A, 3.8×10^{-4} moles; B, 2.5×10^{-4} moles; C, 1.3×10^{-4} moles of CDBAC; D, distilled water.

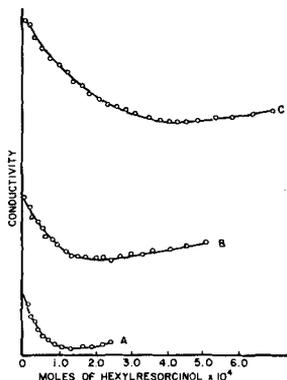


Fig. 2.—Conductimetric titration of cetylpyridinium chloride with hexylresorcinol. Key: A, 1.40×10^{-4} moles; B, 2.80×10^{-4} moles; C, 5.60×10^{-4} moles of cetylpyridinium chloride.

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¹ Fine Organics, Inc., Lodi, N. J.

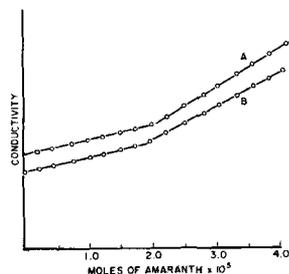


Fig. 3.—Conductimetric titration of CPC and CDBAC with amaranth. Key: A, 5.6×10^{-5} moles of CPC; B, 5.06×10^{-6} moles of CDBAC.

quaternary ammonium-dye reaction product was formed. Before the end point was reached, the reaction product was kept in solution by the solubilizing effect of the excess quaternary amine and by the charge on the colloidal particles. Both CPC and CDBAC reacted in a ratio of slightly less than 3 moles of quaternary amine to 1 mole of amaranth. The slight departure from the theoretical ratios probably is due to the impurity of the compounds used.

SUMMARY

Data are given to show an interaction between hexylresorcinol or amaranth and two quaternary ammonium germicides. The shape of the titration curves with hexylresorcinol suggest the interaction to be a loose reversible one, probably due to the formation of a mixed micelle (2). In contrast, the interaction of amaranth with the quaternary ammonium compounds is a metathesis reaction of two salts. The conductimetric titration method was found to be a simple and convenient technique for screening compounds for possible interaction with quaternary ammonium compounds.

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Neurodepressive Agents I

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A group of new 3,4,5-trimethoxybenzylamines has been synthesized for pharmacological evaluation. To a degree, all compounds have displayed a depressant effect. Some analgesic, ganglionic blocking, and vasodilating actions have also been exhibited.

IN RECENT YEARS, several papers have been published describing the activity of 3,4,5-trimethoxybenzylamides (1-11) and related compounds. It is noteworthy that these compounds appear to be sedatives for anxiety, agitation, and psychomotor restlessness of the chlorpromazine type instead of the reserpine type, although they contain a structural part (3,4,5-trimethoxybenzyl moiety) of the original reserpine molecule. It has been postulated that chlorpromazine and reserpine act by two distinctly different mechanisms—reserpine by trophic stimulation and chlorpromazine by ergotropic inhibition (12). By using molecular models, the structural similarity of the active sites of reserpine and chlorpromazine has been pointed out by Nieforth (13).

In this study, the 3,4,5-trimethoxybenzylamines were prepared by condensing 3,4,5-trimethoxybenzaldehyde with an amine to form an anil, which was not isolated, then reducing it with sodium borohydride to the corresponding secondary amine (Table I).

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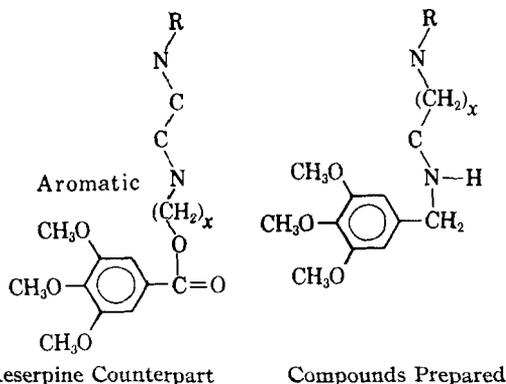
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It is suggested that by having a 3,4,5-trimethoxybenzyl base and creating two nitrogen atom sites, then varying the distance between these two, we may be able to create a depressive effect with these two aliphatic nitrogen centers, despite the fact that in chlorpromazine and reserpine one nitrogen is aromatic.

EXPERIMENTAL

General Procedure.—One-tenth mole of 3,4,5-trimethoxybenzaldehyde and 0.1 mole of the desired amine were mixed with 100 ml. of xylene and refluxed for 20 hours with a water separator attached to the condenser. After the theoretical amount of water was separated, the xylene was distilled off under reduced pressure. The compound was then taken

Schematic Sketch of the Molecules



Reserpine Counterpart

Compounds Prepared