Summary

By avoiding so far as possible the disturbing effects of a change taking place subsequent to the formation of a mixture of neutral red and leuco neutral red, there were established potentials apparently characteristic of a reversible system. The "normal potential" at 30° was estimated to be +0.240 volt. The curve relating P_H and the potentials of the half-reduced solutions, E_0', has a slope $\Delta E_0'/\Delta P_H = -0.09$ in acid solution and a slope $\Delta E_0'/\Delta P_H = -0.06$ in alkaline solution. Closely crowded inflections of the curve in an intermediate zone of P_H indicate dissociation exponents for reductant of 6.16 and 5.30 and for oxidant of 6.80 (approximate only).

Similar approximate data for simple neutral red are: $E_0 = +0.237$; $pK_{r_1} = 5.96$; $pK_{r_2} = 4.95$ and $pK_0 = 6.32$.

For dimethylaminomethylphenazine E_0 is roughly +0.208 and $\Delta E_0'/\Delta P_H = -0.06$ in acid solutions of P_H number < 5.

Interference with stability of potentials is attributed to the formation of a substance which because of its characteristic and brilliant fluorescence is called the "fluorescent material." This was isolated in crystal form. Although it has the elementary composition attributed to leuco neutral red, it differs from leuco neutral red in the values of its dissociation constants and in other particulars. Among its several peculiar properties is its resistance to oxidation in neutral or mildly alkaline solution. In distinctly acid solution it was oxidized to neutral red. Its oxidative titration in acid solution yields a value of E_0' characteristic of the neutral red system.

Because of the instability of the reversible system, neutral red can be used as an oxidation–reduction indicator only for rough comparisons. One rough comparison is made between the indications of neutral red as an oxidation–reduction indicator and electrode behavior in bacterial cultures. This comparison clarifies the "neutral red reaction" well known to bacteriologists.

The data suggest an "orthoquinone" structure for neutral red base.

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NOTE

Preparation of Epichloro- and Epibromohydrins.—In the preparation of 3-chloro- and 3-bromocrotonic acids[1] large amounts of epichloro- and epibromohydrins are required. Because all of the methods known for their preparation in the scientific literature give either low yields or are inconvenient, it was necessary to work out new procedures. The best yield is reported when dichlorohydrin is treated with powdered sodium hydroxide in ethereal solution,[2] but this method is not economical.

[1] Géza Braun, THIS JOURNAL, **52**, 3167 (1930).

[2] "Organic Syntheses," John Wiley and Sons, Inc., New York, 1923, Vol. III, p. 47.

On the other hand, very good methods are reported in the patent literature: the epichlorohydrin is obtained in high yields when dichlorohydrin is treated with calcium hydroxide[3] or with very dilute sodium hydroxide solution.[4] The calcium hydroxide method seemed to be more advantageous, therefore this process was modified to laboratory conditions.

(a) The conversion of dichlorohydrin into epichlorohydrin with calcium hydroxide in the presence of water takes place easily even at room temperature. A number of experiments were carried out under various conditions and it was found that this conversion is about 75% in one operation, but it is not advisable to complete the reaction by raising the temperature or loss in epichlorohydrin will occur; it is best to remove the epichlorohydrin by fractional distillation and treat the residue again with calcium hydroxide. This can easily be done without loss of time, for the operations are very simple. The yield of epichlorohydrin is as high as 80%, in larger amount (4–5 kg.) up to 90% of the theoretical.

(b) The conversion of dibromohydrin with calcium hydroxide into epibromohydrin in the manner described above is much simpler than that of dichlorohydrin. The operation is almost complete in one treatment, and the yield of epibromohydrin is as high as 90% of the theoretical.

Experimental Part

(a) **Epichlorohydrin.**—In a 5-liter round-bottomed flask 1350 g. (1 liter) of dichlorohydrin, 840 g. of calcium hydroxide (technical, 88%) and 840 cc. of water were vigorously shaken for fifteen minutes at room temperature. The mixture was a thick paste at the beginning, but the epichlorohydrin soon separated from the calcium salts as a thin liquid. No formation of heat was observed. Then the mixture was distilled at first under 40–50 mm., then under 10 mm. pressure, gradually raising the temperature up to 100°. The receiver was cooled with ice and salt to −2° to prevent loss of epichlorohydrin. The distillate was transferred into a separatory funnel, the aqueous layer poured back into the distilling flask and the distillation repeated as above. A third distillation in a similar manner still yielded some epichlorohydrin. The united lower layers of the distillates (570 + 220 + 20 = 810 cc.) were fractionated under 50 mm. pressure at 75° and separated into two fractions, (a) distillate and (b) residue. The residue (about 160–180 cc.) contained a large percentage of dichlorohydrin and was poured back into the original distilling flask, together with 150 cc. of water, and distilled once under reduced pressure as above. The lower layer of the distillate was united with fraction (a) and distilled under reduced or ordinary pressure.

From the first distillate the water was removed, it was dried with an-

[3] Griesheim, German Patent 246,242.

[4] Bayer, German Patent 239,077.

hydrous sodium sulfate, poured back into the distilling flask and the crude epichlorohydrin thus freed from water fractionated again. After a small forerun the pure epichlorohydrin distilled at 30–32° under 10 mm. pressure; the yield was 770 g. of epichlorohydrin or 80% of the theoretical. The epichlorohydrin thus obtained boiled at 115–117° and had a specific gravity of 1.18 at 20°.

(b) **Epibromohydrin.**—One liter (2140 g.) of dibromohydrin was suspended in 1.5 liters of water and then gradually under shaking 420 g. of calcium hydroxide was added in the course of fifteen minutes. Then 420 g. of calcium hydroxide was added at once and the epibromohydrin distilled under reduced pressure in the same manner as is described in the case of epichlorohydrin. The united lower layers of two distillations (690 + 70 = 760 cc.) were fractionated under 50 mm. pressure and the medium fraction, after drying with anhydrous sodium sulfate, fractionated again. The yield of epibromohydrin (b. p. 61–62° under 50 mm. pressure or 134–136° at ordinary pressure) was 1200 g. or 90% of the theoretical. The product had a specific gravity of 1.665.

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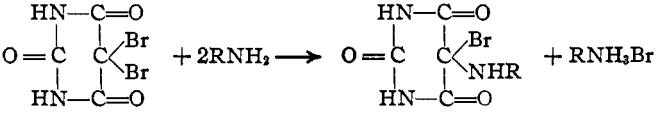
COMMUNICATIONS TO THE EDITOR

THE REACTION OF DIBROMOBARBITURIC ACID WITH AMINES

Sir:

In a recent communication Nightingale and Schaefer[1] describe the reaction of 5,5-dibromobarbituric acid with primary and secondary amines. The reaction is said to yield a series of 5-bromo-7-alkyl uramils.



Such a reaction seems improbable in view of the general properties of the class of "persubstituted" halogen compounds.[2] Such compounds act as brominating agents, the active halogen being replaced by hydrogen. To quote a single example, bromonitromalonic ester reacts with dimethylamine to form the amine salt of nitromalonic ester and N-bromodimethylamine.[3] Baeyer[4] and Biltz and Hamburger[5] obtained the ammonium

[1] Nightingale and Schaefer, THIS JOURNAL, **54**, 236 (1932).

[2] *Cf.* a summary by Schmidt, Ascherl and von Knilling, *Ber.*, **59**, 1876 (1926), which includes over seventy references to the literature.

[3] Willstätter and Hottenroth, *Ber.*, **37**, 1776 (1904).

[4] A. Baeyer, *Ann.*, **130**, 134 (1864).

[5] Biltz and Hamburger, *Ber.*, **49**, 641 (1916).