

that the silver chloride was non-radioactive. From this preliminary experiment and the half-life of radioactive chlorine, it was possible to calculate the most advantageous dilution for any subsequent time. With the strength of the sample of radioactive chlorine that was available to us, it was possible to remain in the optimum counting range for six hours even though the first count was not made until two hours after irradiation of the sample.

In Table I and Fig. 2 we show the data for typical determinations.

TABLE I

Results from two experiments. For both, the solutions were 0.0187 molar silver chloride and 0.5 molar ammonium hydroxide. Each count is the result of a ten minute period of counting.

Sample	Time, min.	Dil.	Net count per minute	Net count times the dil.
1a	0	200	158.8 ± 4.5	31760 ± 900
1b	125	20	147.2 ± 4.4	2944 ± 88
1c	280.5	2	81.2 ± 3.6	162.4 ± 7.2
2a	0	80	134.0 ± 4.0	10520 ± 320
2b	82	20	101.3 ± 3.7	2026 ± 74
2c	193	2	134.0 ± 4.0	268.0 ± 8
2	241	1	102.5 ± 3.7	102.5 ± 3.7
2	305.5	1	41.9 ± 2.8	41.9 ± 2.8

The use of this method for any material that can be brought into solution is obvious. It may be worthwhile to point out that the diluent should be chemically identical with the stock radioactive solution in order to eliminate any errors due to differential absorption.

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5,7-Diiodo-8-hydroxyquinoline

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5,7-Diiodo-8-hydroxyquinoline, which is of therapeutic interest, has been prepared previously by the interaction of iodine and sodium iodide with 8-hydroxyquinoline in alkaline solution.¹ Although the yield is satisfactory, the procedure requires working in rather dilute solution, thus involving the use of large-scale equipment even for semi-commercial production. A different procedure was therefore developed which is distinctly more economical with respect to ease of manipulation and materials required.

A solution of 2105 g. (14.5 moles) of 8-hydroxyquinoline in 5800 cc. of 15% (by weight) hydrochloric acid is added in a slow stream with stirring

(1) British Patent 351,605.

at laboratory temperature to 4872 g. (30.0 moles) of iodine monochloride dissolved in 6000 cc. of 15% hydrochloric acid. Stirring is continued for four hours longer and the mixture then allowed to stand for twelve hours. The product is washed by decantation with 5% hydrochloric acid to remove excess iodine monochloride, followed by a washing with water and finally with a 2% solution of sodium hydrosulfite to reduce traces of free iodine. An additional amount of product may be recovered by combining the liquors of the first two washings and allowing them to stand for several days. The total yield of product melting at 198–200° is 4900–5300 g. or 83.5–92.5% of the theoretical, the purity of which is approximately 98.5% as determined by iodine analysis.

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On a Relation between the Dissociation Constants of Substituted Aliphatic Acids and the Distance between the Dissociating and the Substituted Groups

BY JESSE P. GREENSTEIN

A relationship between the dissociation of a substituted acid and the distance between the carboxyl and substituted groups was suggested by MacInnes¹ in 1928 in which pK_{∞} represents the

$$pK = pK_{\infty} + S(1/d) \quad (1)$$

value of the dissociation constant for an acid whose substituent is removed an infinite length along the chain, and d has the value 1 for an α -, 2 for a β - and 3 for a γ -substitution. This inverse linear relationship held for the hydroxy and the chloro substituted acids, and was extended by subsequent authors²⁻⁴ to the variously substituted amino acids, diamines, dicarboxylic acids and amino acid esters.

In the endeavor to introduce physical quantities into equation (1), an interesting relation developed. If in place of d in the equation there is substituted the square of the distance, l^2 , in Ångströms, from the center of the group dipole to the carboxyl center on the assumption of an extended chain, there is found for the substituted aliphatic acids an inverse linear relationship between pK and l^2 .

(1) MacInnes, THIS JOURNAL, 50, 2587 (1928).

(2) Edsall and Blanchard, *ibid.*, 55, 2337 (1933).

(3) Greenstein, *J. Biol. Chem.*, 96, 499 (1932).

(4) Schmidt, Appleman and Kirk, *ibid.*, 81, 723 (1929).