NOTES

Oxidation of Formazans to Tetrazolium Chlorides with *t*-Butyl Hypochlorite

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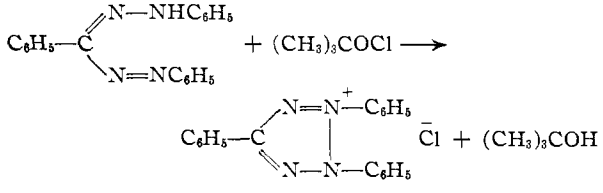
Various reagents have been used in the past for the oxidation of formazans to the corresponding tetrazolium salts. These include yellow mercuric oxide,[1] lead tetraacetate,[2] hydrogen peroxide and hydrochloric acid in the presence of vanadium pentoxide[3] and nitric acid.[4]

While *t*-butyl hypochlorite usually functions as a chlorinating agent, a few oxidation reactions have been reported. Clark[5] found that primary alcohols can be oxidized to the corresponding aldehydes. Similarly, while studying chlorination of various aromatic aldehydes Ginsberg[6] found that certain ring substituents favored conversion of the aldehyde to the corresponding acid chloride rather than ring chlorination.

This note reports the results of several experiments in which *t*-butyl hypochlorite was used as the oxidizing agent in the preparation of tetrazolium chlorides from formazans. Substantially



equimolar quantities of *t*-butyl hypochlorite and formazan are required for the oxidative conversion, which is carried out in an inert solvent. The presence of small amounts of an acidic or basic catalyst appears to increase the reaction rate but is not essential.

Experimental

2,3,5-Triphenyltetrazolium Chloride.—Triphenylformazan (6.0 g., 0.02 mole) is dissolved in 100 ml. of chloroform, a few ml. of alcoholic potassium hydroxide added and the mixture chilled to 5°. *t*-Butyl hypochlorite (8 ml. of 33% material, 0.023 mole) is added dropwise with stirring. The color changes from opaque to a clear red but is not completely discharged. The solution is filtered, evaporated on the steam-bath to about 15 cc., and acetone and ether added. The precipitate formed is filtered off, dissolved in chloroform containing 1 or 2 drops of alcohol and precipitated with a little ether. Four grams of product is obtained (60% yield). *Anal.* Calcd.: N, 16.74; Cl, 10.59. Found: N, 16.6; Cl, 10.7.

5-*n*-Hexyl-2,3-diphenyltetrazolium Chloride.—Impure C-*n*-hexyl-N,N′-diphenylformazan (4 g., 0.013 mole) is dissolved in 50 ml. of chloroform and the mixture chilled to 5°. *t*-Butyl hypochlorite (0.013 mole) is added dropwise with stirring. The solution is evaporated on the steam-bath. Ether and acetone are added and the resulting precipitate filtered off. The product is recrystallized by dissolving in acetone containing a few drops of alcohol and adding ether to precipitate the product; yield 1.5 g., 34%. *Anal.* Calcd.: C, 66.55; H, 6.76; N, 16.34. Found: C, 66.8; H, 7.0; N, 16.6.

5-α-Naphthyl-2,3-diphenyltetrazolium Chloride.—C-α-Naphthyl-N,N′-diphenylformazan (2.1 g., 0.006 mole) is dissolved in 80 ml. of dioxane and 1 ml. of glacial acetic acid is added. After cooling to 7–8°, *t*-butyl hypochlorite (0.0065 mole) in 5 ml. of dioxane is added dropwise with stirring. The solution is heated on the steam-bath for 15 minutes during which time the color became much lighter and a light colored precipitate begins to form. Addition of ether gives more precipitate which is filtered off. The combined gummy precipitates are taken up in the minimum amount of chloroform at room temperature, charcoal is added, the mixture stirred 15 minutes and filtered. Evaporation to a low volume and addition of acetone gives a precipitate which is filtered off; yield 1.4 g., 61%. *Anal.* Calcd.: N, 14.56; Cl, 9.21. Found: N, 14.4; Cl, 9.3.

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(1) H. v. Pechman and P. Runge, *Ber.*, **27**, 2920 (1894).
(2) R. Kuhn and D. Jerchel, *ibid.*, **74**, 941 (1951).
(3) W. Reid, *Angew. Chem.*, **64**, 391 (1952).
(4) F. Fichter and E. Schiess, *Ber.*, **33**, 747 (1900).
(5) B. F. Clark, Jr., *Chem. News*, **143**, 265 (1931).
(6) D. Ginsberg, This Journal, **73**, 702 (1951).

Rauwolfia Alkaloids. IX.[1] Isolation of Yohimbine from *Rauwolfia serpentina* Benth.

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Our investigations of the alkaloids of the Indian plant *Rauwolfia serpentina* Benth. have led to the isolation of yohimbine. An amorphous alkaloidal fraction (50 g.) from which reserpine had been previously removed was used as a source of material.

The weak bases were removed by ether extraction of a solution of the crude alkaloids in dilute acetic acid. Following neutralization of the aqueous layer with concentrated aqueous ammonia, the solution was extracted with ether containing 10% methanol and the solvent evaporated. The amorphous residue (5 g.) was chromatographed on alumina (Activity II/III) eluting first with increasing concentrations of acetone in benzene followed by increasing concentrations of methanol in acetone. Acetone eluted an amorphous material (127 mg., fractions 32 and 33) that yielded crystalline yohimbine (15 mg.), m.p. 224–228°, from the same solvent.

A further confirmation of the presence of yohimbine in *R. serpentina* Benth. is afforded by the earlier isolation in our laboratories (Basle, 1948), of a then unidentified alkaloid. This alkaloid was isolated as the hydrochloride by fractional crystallization of crude ajmaline hydrochloride.[2] The free base and the hydrochloride have now been shown to be identical with yohimbine and yohimbine hydrochloride. The hydrochloride, crystallized from methanol, melted at 300–302°, no depression with yohimbine hydrochloride, $[\alpha]^{22}D$ +92 ± 5° (*c* 0.92 in water). The free base was recrystallized from chloroform–petroleum ether,

(1) L. Dorfman, *et al.*, *Helv. Chim. Acta*, **37**, 59 (1954).
(2) Prepared by a modification of the method of E. Schlittler and H. Schwarz, *ibid.*, **33**, 1463 (1950).