[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, NORTHWESTERN UNIVERSITY DENTAL SCHOOL]

The Preparation of Amine Derivatives of 2-Chloro-1,4-naphthoquinone

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It has been found that 1,4-naphthoquinones are useful inhibitors of acid formation by oral bacteria from carbohydrates.[1,2] Buu-Hoi[3] reported that certain aryl amine derivatives of 1,4-naphthoquinones are capable of inhibiting the growth of the tubercle bacillus and Zetterberg[4] reported quantitative measurements on naphthoquinone inhibition of the growth of the tubercle bacillus. This work involves the syntheses of amine derivatives of 2-chloro-1,4-naphthoquinone of four types: aminopyridines, sulfonamides, aminoalkanes and amino acids.

All the compounds prepared have been found to be very active inhibitors of acid production by bacteria in the oral cavity. Inhibition was determined in the usual manner.[2] The 2-amino-4-methylpyridine derivative was the most effective, inhibiting at concentrations as low as 1 mg. per 100 cc. The sulfonamides were effective in concentrations as low as 5 mg. per 100 cc. and the others showed varying degrees of inhibition. The work on growth inhibition of the tubercle bacillus has not been completed and will be presented elsewhere.

(1) L. S. Fosdick, O. F. Fancher and J. C. Calandra, *Science*, **96**, 45 (1942).

(2) J. C. Calandra, O. E. Fancher and L. S. Fosdick, *J. Dent. Res.*, **23**, 31 (1944).

(3) Buu-Hoi, *Bull. soc. chim.*, **11**, 578 (1944).

(4) B. Zetterberg, *Acta Path. Microbiol. Scand.*, Suppl. LXXXII, 1949.

Experimental

A mixture of equimolecular quantities of the amine and the 2,3-dichloro-1,4-naphthoquinone in 50 cc. of ethanol was refluxed for eighteen hours. The product which separated on cooling was recrystallized from ethanol.

Derivative of	M. p., °C.	Form and color	N Analyses, % Calcd.	Found	Yield, %
Sulfapyridine[a]	262 dec.	Red-orange cryst.[b]	8.82	8.60	80
Sulfathiazole[a]	279–281 dec.	Red cryst.	9.40	9.22	72
Sulfadiazine[a]	256	Orange powd.	12.72	12.31	85
Sulfamerazine[a]	254	Red powd.	12.32	11.90	61
Sulfaguanidine[a]	272	Red powd.	9.4[c]	9.97	93
2-Aminopyridine	276–278 dec.	Yellow powd.	9.84	9.89	45
2-Amino-3-methylpyridine	176–178 dec.	Yellow powd.	5.2[c]	4.87	50
			Cl 14.54	14.79	
2-Amino-5-methylpyridine	261	Orange ndls.	9.4	10.0	55
2-Amino-4-methylpyridine	255 dec.	Golden cryst.	9.4	9.31	49
2-Amino-6-methylpyridine	120 dec.	Yellow cryst.[d]	5.2[c]	4.87	35
			Cl 14.52	15.25	
n-Decylamine[e]	90–91	Red cryst.	4.0	3.77	76
γ-Aminocaproic[f]	81–84	Red cryst.	4.11	3.80	31
Guanidine carbonate[a]	217–218	Red cryst.[g]	4.0[c]	3.77	22
Morpholine[e]	146–147	Red cryst.	5.04	5.06	95

[a] 2.5 g. of diethylaniline was added to the reaction. [b] Recrystallized from dioxane–water mixture. [c] The ratio of chloroquinone to amine was 2:1 rather than 1:1. [d] Recrystallized from ethanol–water mixture. [e] Reaction was run without solvent by shaking 4 g. of the chloroquinone and 10 cc. of the amine together for 15 min. [f] Acetone was the solvent. The solution was poured into ice-water after completion of the reaction. [g] The alcohol was evaporated to yield a black tar which was extracted with hot water to yield a black solution. After clarification with charcoal to yield a red solution, the product was obtained by evaporation *in vacuo*.

Preparation of Alkali Metal Salts.—The sodium salts of the sulfonamide derivatives were prepared by shaking them with solid sodium hydroxide in ethyl alcohol for about 15 min. and precipitating the salts with dry ethyl ether. In all cases purple products were obtained, which were easily soluble in water, but showed a great tendency to hydrolyze and also to decompose in contact with air. The potassium salts of the decylamine and aminopyridine derivatives were prepared by dissolving them in ethyl ether and adding potassium until the reaction was complete. These salts were also purple and were even more unstable than the sulfonamide salts.

Summary

1. Several amine derivatives of 2,3-dichloro-1,4-naphthoquinone were prepared and characterized.

2. Water-soluble alkali metal salts of these compounds were also prepared.

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