

[CONTRIBUTION FROM DIVISION OF INSECTICIDE INVESTIGATIONS, AGRICULTURAL RESEARCH ADMINISTRATION, BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE, UNITED STATES DEPARTMENT OF AGRICULTURE]

## Quassin. IV. A Minor Constituent of Jamaica Quassia Wood\*

BY E. P. CLARK

In the preparation of crude quassins from Jamaica quassia wood,<sup>1</sup> the mother liquors consistently yielded a small quantity of a fairly soluble material which, in the crude state, melted at about 150°. It was readily purified to a constant melting point of 166–167° by recrystallization from 16% methanol and as such had the physical characteristics of a pure compound. Analyses of several specimens gave fairly consistent values for carbon, hydrogen, methoxyl, and molecular weight, but they failed to harmonize with any possible formula. These facts indicated that if the material was an individual substance it was impure, but since its purification was complete as established by physical standards, the only conclusion tenable was that it was a complex of two or more substances which separated as mixed crystals.

With this as a working hypothesis, resolution was attempted by methods other than fractional crystallization. Selective adsorption upon aluminum oxide was the most successful in that the material was roughly separated into neoquassin, unchanged material, and a fraction which would not crystallize. The first two fractions could be readily purified, but all attempts to isolate the material in the last fraction failed.

The facts here recorded are presented for record in order to describe an unreported constituent of quassia wood and to call attention to the unique properties of the substance. Further work upon the material is not contemplated, because the small yield (0.015% of the wood) precludes any possible importance of the substance as an insecticide, the original object of the study.

### Experimental

The aqueous-methanolic mother liquors from the crystallization of crude quassins from 200 kg. of Jamaica quassia wood were concentrated under reduced pressure until a resinous material began to separate. The liquid was then filtered through norit and set aside to crystallize. A product slowly separated as long, thin, slightly colored hexagonal plates, which melted unsharply at 150°. Re-working the mother liquors gave more material, the total quantity being 30 g. A solution of 5 g. of the crystals in 15 cc. of hot methanol was diluted with 90 cc. of hot water.

The liquid was immediately filtered through norit and allowed to crystallize. The product was further purified by repeating the process three times. It then had a melting point of 166–167°, which further recrystallization failed to change. The crystals were long, colorless rods and hexagonal plates. In parallel polarized light (crossed nicols) the extinction was parallel and the elongation was negative. Many of the rods did not extinguish sharply and low polarization colors were characteristic. In convergent polarized light (crossed nicols) biaxial interference figures were rarely observable, but when they were the acute bisectrix was nearly vertical. The apparent optic axial angle in air was very small. The indices of refraction were  $\eta_\alpha$ , 1.557, usually lengthwise;  $\eta_\beta$ , indeterminate;  $\eta_\gamma$ , 1.559, usually crosswise; both  $\approx 0.002$ .

The substance contained only carbon, hydrogen, and oxygen, and analyses of three different preparations are as follows:

*Anal.* Found: C, 66.14, 65.11, 65.63; H, 7.83, 7.78, 7.59; OCH<sub>3</sub>, 11.69, 11.79, 11.79; mol. wt., 410.

**Chromatographic Separation of Neoquassin.**—A solution of 1 g. of the purified material in 30 cc. of ethyl acetate was passed through a 12 × 200 mm. column of aluminum oxide, and the chromatogram was developed with the same solvent. The eluate was collected to 50-cc. fractions, each evaporated under reduced pressure to dryness, and the residues were dissolved from the flask with small quantities of methanol. These liquids were evaporated to a small volume, diluted with 6 to 7 volumes of water, and allowed to crystallize. Five main fractions were obtained: I, m. p. 195–205°; II, m. p. 185–190°; III, m. p. 165°; IV, m. p. 155–160°, and V, m. p. 145–147°. The first two fractions contained most of the neoquassin, the third contained practically pure starting material, and the fourth and fifth fractions consisted of impure starting material. Fractions I and II were further purified by repeating the process with chloroform as a solvent. Impure neoquassin, m. p. about 215°, was obtained from the first fractions of this operation, and unchanged material in rather impure condition was obtained in the last fractions. Two recrystallizations of the impure neoquassin (solvent 35% methanol) gave a pure product, m. p. 226°. It was identified by its characteristic crystal habit and its failure to depress the melting point of an authentic sample of neoquassin. The last fractions from both the ethyl acetate and chloroform extractions were recrystallized from 16% methanol, which gave a preparation that melted at 166–167° and did not depress the melting point of the starting material.

The columns, after having been exhausted with either chloroform or ethyl acetate, were eluted with methanol. An appreciable quantity of sirupy, water-soluble material was thus obtained, but all efforts to crystallize it failed. It is impossible to state that this represents the material

(2) The crystallographic data here recorded were determined by George L. Keenan, of the Food and Drug Administration, Federal Security Agency, Washington, D. C.

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(1) E. P. Clark, *THIS JOURNAL*, 59, 927 (1937).

associated with neoquassin in the original substance, for it may represent a decomposition product resulting from the operation involved, or it is possible the unknown component was not eluted from the adsorbent. Both considerations seem doubtful, for a methanolic solution of the original material was rapidly and quantitatively passed through a column of aluminum oxide without separation or apparent change. However, a solution of neoquassin added to a solution of the uncrystallizable material failed to effect a synthesis of the original substance.

### Summary

A hitherto unrecorded constituent of Jamaica quassia wood is described. It has the physical properties of an individual compound, but in reality consists of a complex of neoquassin and one or more unknown materials, which apparently separate as mixed crystals.

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## Local Anesthetics. II. Alkoxybenzoates of 2-Monoalkylamino-2-methyl-1-propanols and 2-Monoalkylamino-1-butanols<sup>1,2</sup>

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In a recent paper from this Laboratory,<sup>3</sup> the preparation of  $\beta$ -monoalkylaminoethanol esters of alkoxybenzoic acids was described. Goldberg, Ringk and Spoerri<sup>4</sup> reported aminobenzoates of  $\beta$ -monoalkylaminoethanols in which branching occurs on the alpha carbon of the amino alcohol.

We have mono-alkylated 2-amino-2-methyl-1-propanol and 2-amino-1-butanol, which are now on the market, and have been engaged in the preparation of esters of these amino alcohols with alkoxybenzoic, alkoxybenzoic, alkoxybenzoic, diphenylacetic, acetyltropic, acetylmandelic and *p*- and *m*-nitrobenzoic acids, with the expectation of reducing the latter to the aminobenzoate esters. The recent report of Kremer and Waldman<sup>5</sup> on *p*-nitrobenzoic and *p*-aminobenzoic esters of 2-monoalkylamino-2-methyl-1-propanols makes it desirable to report the results thus far obtained. This paper takes up the preparation of 2-monoalkylamino-2-methyl-1-propanols, 2-monoalkylamino-1-butanols and the alkoxybenzoates of these amino alcohols.

Alkylation of 2-amino-2-methyl-1-propanol and 2-amino-1-butanol with the lower alkyl halides usually was carried out by heating equimolar quantities of the amino alcohol and alkyl bromide in a sealed tube or under reflux at 100° for two hours. For the introduction of the amyl, hexyl, heptyl, allyl and benzyl radicals, usually the mo-

lar quantity of amino alcohol was doubled and in the introduction of the latter two groups, chlorides were used instead of bromides. The reaction product was dissolved in dilute hydrochloric acid, separated from unchanged alkyl halide, in case the reaction was not complete, and treated with excess concentrated sodium hydroxide. The alkylation product rose to the surface of the hot solution as an oil. The oil was vacuum distilled and the distillate redistilled at atmospheric pressure. The 2-monoalkylamino-2-methyl-1-propanols except the allyl, solidified on cooling. Several of the 2-monoalkylamino-1-butanols showed a tendency to crystallize, reaching a maximum in the case of 2-monobenzylamino-1-butanol. The crystals of this compound, on separation, reverted to a mixture of liquid and crystals.

In a previous paper from this Laboratory,<sup>3</sup> the preparation and isolation of  $\beta$ -monoalkylaminoethyl alkoxybenzoate hydrochlorides was described. The same general procedure, with some modifications, was used to obtain hydrochlorides of alkoxybenzoates of 2-monoalkylamino-2-methyl-1-propanols and 2-monoalkylamino-1-butanols.

### Experimental

Examples are given of the preparation of 2-*n*-amylamino-2-methyl-1-propanol and of the condensation of this amino alcohol with *p*-ethoxybenzoyl chloride.

**2-*n*-Amylamino-2-methyl-1-propanol.**—A mixture of 113 g. (0.75 mole) of *n*-amyl bromide and 134 g. (1.5 moles) of 2-amino-2-methyl-1-propanol was heated in two sealed tubes for two hours at 100°. The contents of the tubes were combined and dissolved in 500 ml. of water and 80 ml. of concentrated hydrochloric acid. No oil remained undissolved. To the acid solution was added a solution of 100 g. of sodium hydroxide in 100 ml. of water. The oil which rose to the surface was vacuum distilled, yielding

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(3) J. Stanton Pierce, J. M. Salsbury and J. M. Fredericksen, THIS JOURNAL, **64**, 1691-1694 (1942).

(4) Goldberg, Ringk and Spoerri, *ibid.*, **61**, 3582-3584 (1939).

(5) Kremer and Waldman *ibid.* **64**, 1089-1090 (1942)