The morphine obtained by the U. S. P. XI method contains about 4% of non-phenolic alkaloids. If this correction is applied the results are as follows:

U. S. P. XI after Correcting for Non-phenolic Alkaloids.	New Method Free from Non-phenolic Alkaloids.
Morphine alkaloid	Morphine alkaloid
10.83%	11.65%

The following results were obtained with one sample of opium:

Morphine Alkaloid by U. S. P. XI Method.	Temperature during Precipitation.	Morphine Alkaloid by New Method.	Temperature during Precipitation.
13.59%	17° to 26° C.	14.19%	17° to 26° C.
Corrected for non-phenolic alkaloids			
13.05%	....	....	....

The results obtained by the new method were 0.38% to 0.6% higher than by the U. S. P. XI method. After correcting for the non-phenolic alkaloids the difference is 0.82% to 1.14%.

In all assays by the U. S. P. XI and the new method, the volume of methanol used was 75 cc.

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BROMOALKYL DERIVATIVES OF SALICYLIC ACID.*

BY E. MONESS AND W. G. CHRISTIANSEN.[1]

An unsaturated alkyl chain containing bromine has frequently been found of considerable value in producing a sedative effect in barbituric acid derivatives. Pernocton, for example, is secondary-butyl-β-bromoallyl barbituric acid. A combination of the sedative bromoalkyl group with the antipyretic and analgesic salicylic acid grouping offered interesting possibilities. We therefore prepared bromoallyl salicylate (I), and its acetyl derivative (II). The former was made by condensing sodium salicylate with 2,3-dibromopropene, and the latter by acetylating the condensation product. Biological tests revealed that both compounds were somewhat superior to acetyl salicylic acid in antipyretic activity, but were almost three times as toxic. The advantage of enhanced antipyretic action was therefore outweighed by increased toxicity.

Having in mind the preparation of α-bromoacrylyl salicylic acid we made three attempts at the preparation of intermediates:

(1) α-bromoacrylyl chloride from potassium α-bomoacrylate and thionyl chloride.

(2) α-bromoacrylyl chloride from potassium α-bromoacrylate and phosphorus oxychloride

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by the method used by Moureu (1) in the preparation of acrylyl chloride.

(3) α,β-dibromo-propionyl salicylic acid from salicylic acid and α,β-dibromo-propionyl chloride.

All three attempts were unsuccessful, yielding only resinous polymerization products.

EXPERIMENTAL.

Preparation of Bromoallyl Salicylate.—40 Gm. sodium salicylate (over 100% excess) which had been dried under a vacuum of 6–8 mm., and at a temperature of 170° C. for three hours, was placed in a flask with 25 Gm. dibromopropene and 45 cc. of acetone. The mixture was heated on the steam-bath, under reflux, for ten hours. After distilling off the acetone and unreacted dibromopropene, the oily residue was taken up in water and extracted with ether. This extract was washed with water, dilute sodium carbonate solution, and again with water, dried over anhydrous sodium sulfate and purified through charcoal. This gave a colorless ether solution. The ether was distilled off and the oil which remained was distilled *in vacuo*.

Yield—16 Gm. of a light yellow oil, b. p. 125–130° C./1–2 mm.
Molecular Weight: Found, 262; calculated for $C_{10}H_9O_3Br$, 257.

Preparation of Acetyl, Bromoallyl Salicylate.—6.9 Gm. bromoallyl salicylate was dissolved in 2.7 Gm. pyridine and cooled with an ice-salt mixture. Into this was stirred, drop by drop, over a period of thirty minutes, 2.7 Gm. of acetyl chloride. The liquid gradually turned into a semi-solid crystalline paste due to the formation of pyridine hydrochloride. The reaction mixture was then heated on the steam-bath for ten minutes and taken up in 150 cc. of ice water. The compound separated out as a dark brown oil, which was extracted with ether, and the extract dried and purified as before. The ether was then evaporated off, yielding a yellow oil which was dried *in vacuo* for two days at room temperature. There was not enough of it to warrant fractionation *in vacuo*, and a molecular weight determination was made without further treatment.

Molecular Weight: Found, 280; calculated, 299.

This low value is undoubtedly due to the presence of traces of solvent. The substance is otherwise pure. Ferric chloride produces no color. (The non-acetylated bromoallyl salicylate gives a deep purple with ferric chloride.) There is no unoccupied carboxyl as proved by the absence of acidity to phenolphthalein.

Attempted Preparation of α-Bromoacrylyl Chloride.—10 Gm. of the potassium salt of α-bromoacrylic acid (3) was refluxed on the steam-bath for two hours with a large excess of thionyl chloride. It was cooled, and diluted with dry ether, filtered from the white salt, and the ether distilled off. On distilling *in vacuo* an oil was obtained which was a mixture of thionyl chloride, and what was possibly α-bromoacrylyl chloride. When an attempt was made to fractionate this at atmospheric pressure, a few cc. of pure thionyl chloride came off, and then the distillation stopped. The substance in the flask proved nondistillable, becoming first viscous and then hard.

The same negative result was obtained when phosphorus oxychloride was used instead of thionyl chloride. Since α-bromoacrylic acid is known to be very un-

stable (2), it is not surprising to find the corresponding acid chloride extremely unstable.

Attempted Preparation of α,β-Dibromopropionyl Salicylic Acid.—5 Gm. salicylic acid was dissolved in 5 Gm. pyridine, and the solution cooled in an ice-salt bath. To this was added slowly, drop by drop, and with stirring, 11 Gm. of α,β-dibromo-propionyl chloride. A gummy mass soon formed, and it became impossible either to continue efficient stirring or to control the temperature. The mass was brown at first, but soon became purple. After all the acid chloride had been added the reaction mixture was heated on the steam-bath for five minutes. There was considerable foaming, accompanied by darkening of the reaction mixture. It was stirred into ice water, and a purple precipitate was obtained. It was isolated as a purple powder weighing 4 Gm. However, it was found to contain considerable water when heated on the steam-bath, and when completely dry was a semi-solid tarry substance. This on cooling solidified into a glassy substance which when powdered, was of a dark purple color. The powder was boiled with benzol, a large part remaining undissolved. The benzol solution was evaporated to dryness, leaving a brown glassy residue. On analysis this substance showed only a trace of bromine. Either the desired compound was not formed, or hydrolyzed in the attempt at purification.

The testing of the bromoalkyl salicylates for toxicity and antipyretic activity was done in the Biological Research Laboratories of E. R. Squibb & Sons and we gratefully acknowledge their assistance.

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A STUDY OF PRECIPITATION IN FLUIDEXTRACT OF UVA URSI I.*[1]

THE CRYSTALLINE NATURE OF THE PRECIPITATE IN FLUIDEXTRACT OF UVA URSI.

BY H. L. TISHER[2] AND C. O. LEE.[3]

INTRODUCTION.

Fluidextracts are a troublesome class of preparations because they precipitate badly upon standing. Years ago Lloyd said, "Physicians object to even muddy fluidextracts. Pharmacists feel annoyed and discouraged when they find their bottles partly filled with sediment, and this trouble (sediment) is the rule and not the exception"(3).

The causes for the formation of precipitates in fluidextracts are many, the chief of which is, perhaps, the fact that they are highly concentrated preparations. The subject has attracted many investigators.

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[1] An abstract of a thesis submitted to the faculty of Purdue University in partial fulfilment of the requirements for the degree of Master of Science by H. L. Tisher.

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