occupies fully fifty-six pages. Let me ask the pharmaceutical educators and pharmacists in general if this is *fair* to the student at a school of pharmacy?

2.—Physiology occupies eleven pages and Dispensing Pharmacy only three pages! Just think of it!

3.—Posology, a Junior Study of but fifteen hours, occupies thirteen pages! Evidently, the gentleman who prepared this *outline* most certainly did *stretch* same!

4.—Last, but not least, Chapter VI, Reference Works, and Chapter VII, Text-books and Pharmaceutical Periodicals, both of which chapters occupy such a prominent place in the second edition of the Pharmaceutical Syllabus, are so full of mistakes, grammatical and otherwise, that they are certainly a disgrace to American Pharmacy. This latter fact has been so fully commented upon at the Detroit Convention, that it is unnecessary for the writer to dwell upon it any longer.

CONCLUSION.

In conclusion, I beg to state that the aim of the Pharmaceutical Syllabus is most certainly a laudable one. Let us hope that the third edition will be a great improvement upon its predecessors, and that it will prove satisfactory to our schools of pharmacy, and also to our boards of pharmacy. Up to the present time, there has been quite some confusion between the fact that the Pharmaceutical Syllabus is *sometimes adopted*, but *most generally only approved!*

Let us hope that the next edition of the Pharmaceutical Syllabus will be a master-work, which will be *adopted* by *all* the colleges of pharmacy and *all* the boards of pharmacy!

OTTO RAUBENHEIMER.

DERIVATIVES OF SALICYLIC ACID.

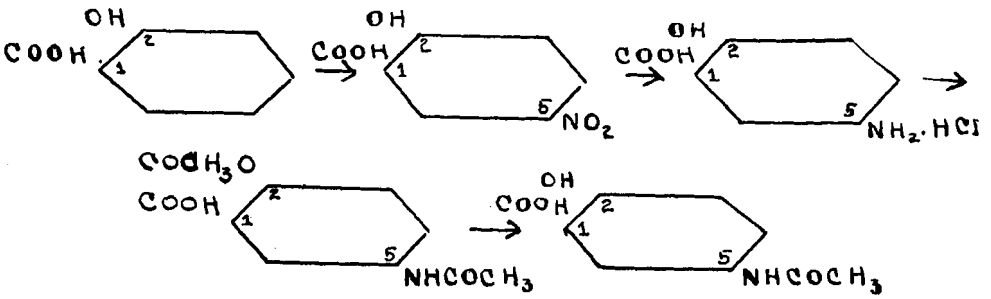
JOHN W. FORBING, PH. C., B. S.

ACETYLAMINO-SALICYLIC ACID AND ACETYLAMINOACETYL-SALICYLIC ACID FROM SALICYLIC ACID.

The following paper presents detailed methods for the production of the various acids which compose the steps of the synthesis. Interest is attached specially to acetylamino-salicylic acid $C_6 H_3 (NHCOCH_3) OHCOOH$, in that its structural formula bears a resemblance to what might be termed, a composite of the active radicles of Phenacetin, $C_6 H_4 O. C_2 H_5. NHCOCH_3$, and Aspirin $C_6 H_4 COOH.OCOCH_3$.

Acetylamino-salicylic acid forms soluble salts with, NH_4, K, Na, Ca, and Sr. If tests indicate clinical usefulness, the product would have a decided advantage over the various insoluble varieties of Analgesics and Antipyretics.

The process of synthesis is based on the nitration of salicylic acid, the production and isolation of assymetric metanitro-salicylic acid (1-2-5) with liberal yield; the conversion of the nitro-salicylic into amino-salicylic acid hydrochloride and subsequent acetylation of the Amino and hydroxyl groups:—



Pharmacological, bactericidal and clinical factors are at present being determined by the Creighton College of Medicine and will be reported in the near future.

Assymetric metanitro-salicylic acid (1-2-5) is obtained by the following process:— 160 gm. potassium nitrate is placed in a 2000 cc. flask with 200 gm. sodium salicylate, and a solution of the salts is made with 600 cc. of water; 250 cc. of concentrated sulphuric acid is gradually and cautiously added, controlling the re-action by the affusion of cold water. After complete addition of sulphuric acid, the contents of the flask are poured into a spacious, porcelain evaporating-dish and 20 cc. of fuming nitric acid added, and the mixture allowed to stand for two hours. It is then heated on the water-bath for about one hour, in order to complete re-action, and allowed to stand in a cool place for twelve hours. The crystalline mass which separates out, is removed by means of a Buechner funnel and vacuum pump, and pressed free from mother-liquor. The mass is then dissolved, by boiling it in a solution of 130 gm. of sodium hydroxide in 750 cc. of water. The resultant dark-red solution is allowed to cool. There separates a reddish-brown mass composed principally of di-sodium-metanitro-salicylate, $C_6 H_3 (NO_2) O Na COO Na.5H_2O$. The mass is placed in a funnel, exhausted by vacuum and pressed. (The filtrate may be reserved, and vicinal nitro-salicylic acid, with a m. p. 118°, may be obtained by acidifying with HCl, boiling with purified animal charcoal, filtering hot, removing the cream-yellow crystalline mass which separates out on cooling, and purifying by conversion, into the K-salt. The K-salt is very soluble in boiling aqueous solution and, on cooling, crystallizes out in long, yellow, silky needles.)

The di-sodium-metanitro-salicylate mass is purified by solution in 500 cc. of boiling water, removal from source of heat and adding 200 cc. of methyl alcohol. On cooling, a bright uniformly-colored orange-red mass, crystallizes out, which is practically pure di-sodium-metanitro-salicylate.

Analysis of the mass washed with methyl alcohol, dried in air:—

Calculated for $C_6H_3(NO_2)ONaCOONa.5H_2O$.

0.5597 gm. substance—0.1589 gm. H_2O calculated—0.1508 gm. found.

0.2021 gm. substance—0.0677 gm. Na_2CO_3 calculated—0.0708 gm. found.

The mass of di-sodium-nitro-salicylate yields the acid by placing it in 500 cc. of water, acidifying with HCl with an excess of about 150 cc., boiling and filtering while still hot. The acid is practically insoluble, in boiling water containing HCl, and remains on the filter as a yellow mass. This mass is washed with water and pressed, dissolved in boiling alcohol to which is added purified animal charcoal and filtered hot. The filtrate may be evaporated on a water-bath with a yield of 72 gm. of assymetric metanitro-salicylic acid in yellow prism crystals. Melting point, 228° with charring, (agreeing with data given in Richter's Organic Chemistry, Smith, vol. 11, p. 225).

Analysis for Nitrogen:—KJELDAHL-GUNNING METHOD:—

Calculated—N, 7.66%; found—N, 7.40%.

DUMAS' METHOD, *Technic*, Weyl (*"Die Methoden der organischen Chemic, Allgemeiner Teil, s. 34"*).

Calculated—N, 7.66%; found—N, 8.16%.

With potassium bicarbonate, the acid yields a salt crystallizing from hot aqueous solution in saffron-yellow needles; this salt dried two weeks *in vacuo* over H_2SO_4 gave the following, potassium as K_2SO_4:—

0.45 g. Salt; K_2SO_4; Calculated—0.1802. Found—0.1784.

The nitro-salicylic acid obtained by the above process is converted into amino-salicylic acid by reduction with tin and HCl.

50 gm. nitro-salicylic acid crystals is placed in a flask with 250 cc. of alcohol, 100 gm. tin and 200 cc. HCl added. The acid is added in portions of 50 cc. and the heat of reaction controlled by affusion of cold water. After addition of acid, an hour, is allowed for complete reaction:—

$$C_6H_3(NO_2)OHCOOH+3\ Sn+6\ HCl=$$
$$C_6H_3(NH_2)OHCOOH+2\ H_2O+3\ SnCl_2.$$

The contents of the flask are then heated until the white precipitate which is formed, is re-dissolved, and filtered hot. The alcoholic filtrate is evaporated, on the water-bath, to about two-thirds of its volume and allowed to stand for twelve hours. At the end of this time a large proportion of the double salt of the hydrochloride of the amino-acid and $SnCl_2$ crystallizes out. The crystalline precipitate is separated and placed in 300 cc. of water and the tin separated with H_2S, filtered, and the filtrate evaporated on the water-bath. The amino-salicylic acid hydrochloride, $C_6H_3NH_2OHCOOH.HCl$, crystallizes out in shining grayish-white crystals. By this process a portion of the amino-salicylic acid hydrochloride, remains in the filtrate and may be obtained by additional precipitation of tin with H_2S as SnS and SnS_2. The solution is filtered cold, to avoid re-solution of SnS_2, and the residue of sulphides containing a portion of the sparingly soluble amino-salicylic hydrochlorides, may be heated with water and filtered hot, the filtrate giving an increased yield of the hydrochloride.

Acetyaminoacetyl-salicylic acid is prepared as follows: 20 gm. amino-salicylic acid hydrochloride, is placed in a 100 cc. round-bottom flask and an excess of acetic anhydride added. The flask is connected with an upright condenser and heated on an oil-bath to 140°-145° for one hour. The following re-action takes place:

$$C_6H_3(NH_2)OHCOOH.HCl + (CH_3CO)_2O =$$
$$C_6H_3NHCOCH_3.O.COCH_3COOH + HCl + H_2O.$$

HCl is liberated and acetylation takes place with the gradual formation of a clear solution. The product of the re-action is poured into 150 cc. of water, and the greater amount of the acetic acid formed, due to excess of the anhydride used, is driven off by boiling and the water replaced. On cooling, clusters of white crystals of acetylaminoacetyl-salicylic acid separate and are collected on filter and washed with cold water.

These crystals were purified for analysis by re-crystallization from alcohol.

Calculated for $C_6H_3NHCOCH_3O.COCH_3COOH$—N, 5.97%.

Found, 5.94, 6.07%.

This acid (acetylaminoacetyl-salicylic) has a melting point of 181°.

I found it impossible to produce a potassium salt of this acid. This acid gives no hydroxyl re-action with ferric chloride. On combining molecular weights of the acid and $KHCO_3$ the hydroxyl is opened and acetic acid liberated and the K-salt of acetylamino-salicylic acid is formed. If this re-action takes place in the presence of ethyl alcohol, ethyl acetate is formed. The following equations account for action taking place:

$$C_6H_3(CH_3CONH)O.COCH_3.COOH+KHCO_3=C_6H_3(CH_3CONH).OHCOOK+CH_3COOH+CO_2.$$

$$C_6H_3(CH_3CONH)O.COCH_3COOH+KHCO_3+C_2H_5OH=C_6H_3(CH_3CONH)OHCOOK+COCH_3.O.C_2H_5+CO_2+H_2O.$$

Both acetylamino-salicylic acid and its potassium salt give a rich blue-coloration with ferric chloride.

If acetylaminoacetyl-salicylic acid is neutralized with potassium carbonate the K-salt of acetylamino-salicylic acid separates from a hot aqueous solution as a fine white powder. The K-salt, free from H_2O, gave the following results on analysis, determining potassium as K_2SO_4 and assuming the formula to be $C_6H_3(NHCH_3CO)OH.COOK$:—

0.5621 gm. K-salt; K_2SO_4; found—0.2163. Calculated—0.2098.

0.0143 gm. K-salt; K_2SO_4; found—0.0407. Calculated—0.0427.

If sodium acetate be added to acetylaminoacetyl-salicylic acid as a condensing agent, in order to introduce, by means of acetic anhydride, an acetyl radicle in the carboxyl group, there results a compound, crystallizing from water acidulated with HCl in silver-lustred laminæ. This compound is undoubtedly the acetester of acetylaminoacetyl-salicylic acid; m. p. 245°. It is unstable and shortly after preparation gives acid re-action with potassium carbonate and a wine-coloration with ferric chloride. It crystallizes from alcohol in colorless prisms.

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TRANSATLANTIC TELEPHONY.

Mr. Marconi announces that an attempt to talk by wireless telephone from Carnarvon, Wales, to New York probably will be made within the next three months. Godfrey Isaacs, manager of the Marconi Company, testifying before the Dominion's Royal Commission on Imperial Communications, had said this feat probably would be accomplished before the end of the year, and he added: "I do not hesitate to express the opinion that if Marconi is able to telephone to New York he will, when the stations for wireless communication between this country and Buenos Aires are built, telephone to that city at the same time that he telegraphs."

Sir Rider Haggard, who is a member of the commission, anxious to follow up this peep into the future, asked Mr. Isaacs:

"You expect the time when a subscriber can have a telephone in his house by which he can telephone all over the world?"

Mr. Isaacs answered that he would not like to go so far as that. Many difficulties first would have to be overcome. It might be possible to go to a particular station in London and telephone to New York. There were great things yet to be revealed in the wireless business."—*Boston Transcript.*