

ALIEN PROPERTY CUSTODIAN

COCCOCIDAL COMPOUNDS

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Alien Property Custodian

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This invention relates to new compounds with coccocidal action.

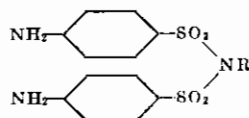
It is an object of the invention to provide new and useful derivatives of p.aminobenzene-sulfonamide such derivatives being soluble in water to a considerable extent.

It is well known that p.aminobenzene-sulfonamide is only sparingly soluble in water. Hence large volumes of its aqueous solution have to be injected in order to apply the necessary doses.

While injecting the new compounds the volume of solution can be considerably reduced.

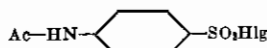
The new products can be obtained by the process which forms an object of the invention too and which is to be described hereafter.

I have found that substances of the general formula



have the properties indicated above. In this formula R stands for a group from the class comprising H, alkyl, an isocyclic and a heterocyclic ringsystem.

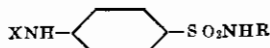
These new compounds are prepared by causing two molecules of the structure



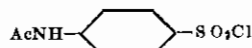
Ac standing for an acyl group and Hlg for a halogen, to react with one molecule of a substance having the general formula H_2NR , in which R stands for a group from the class comprising H, alkyl, an isocyclic and a heterocyclic compound.

It is supposed that the reaction proceeds in two steps. In the first step one of the two hydrogen atoms in the H_2NR molecule is substituted, whereas in the second step the second hydrogen atom is substituted. In both steps the substitution is caused by the splitting off of hydrogen halide from the reacting molecules.

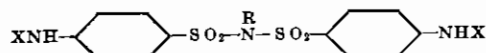
From the foregoing it follows that the first step can be avoided by taking as a starting material the product of this first step, which product is p.aminobenzene-sulfonamide or one of its acyl derivatives. Hence, the reaction between



and



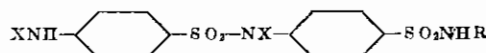
to form



falls within the scope of my invention. [Ac, X

and R have the same meaning as stated above].

In carrying out the condensation with unacylated p.aminobenzene-sulfonamide, thus X being H, the reaction may take a different course, products of the general formula



being formed.

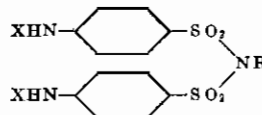
If it is desired to avoid the formation of these by products one may either start with p-acyl derivatives of p.aminobenzene-sulfonamide, in which case the amino group is protected against substitution, or carry out the reaction in an alkaline solution. I have found that in alkaline solutions the formation of by products is reduced to a great extent.

The new compounds have excellent coccocidal properties.

During the reaction generally the acyl groups are subsequently saponified.

It is a further object of my invention to provide neutral solutions of derivatives of p.aminobenzene-sulfonamide. It is well known that p.aminobenzene-sulfonamide itself is only soluble in acid solutions. Some of the new compounds obtained by the process of this invention, however, have the property of forming soluble alkali salts.

If in the general formula



R=H, this hydrogen atom can be substituted by an alkali metal. The solutions of these alkali salts can easily be adjusted to pH 7.2, the pH of normal blood. The sodium salts are especially well suited for injection. The salts have the same therapeutic value as the substances themselves.

In order to facilitate a clear understanding the following examples are given.

Example 1.—40 g of p.aminobenzene-sulfonamide are suspended in 200 cc of sodiumhydroxide of 25% strength. To the suspension, which is continuously stirred, 60 g of p.acylamino-benzene-sulfonylchloride are added in small portions. Condensation takes place with evolution of heat the hydrochloric acid liberated being neutralized by the sodium hydroxide. After the reaction has slowed down the reaction mixture is further heated for half an hour on a steam bath. After cooling part of the di-[p.amino benzene-sulfonyl] amide-sodium crystallizes; it is filtered with suction. From the mother liquor a further crop is precipitated with ethanol. Yield: 80% of the theoretical yield.

The product can be purified by recrystallisation from ethanol. In this way white needles are obtained which are easily soluble in water to at

least 20%. The pH of such a solution may be adjusted to 7.2.

Example 2.—25 g of p.acetylamino-benzene-sulfonamide, 25 g of p.acetylamino-benzene-sulfonylchloride and 140 cc of water are boiled with reflux for one hour. The acid reaction mixture is cooled down. 7 g of p.acetylamino-benzene-sulfonamide crystallize and are recovered. After neutralisation of the filtrate another 13 g crystallize and after evaporation of a large part of the solvent once more a quantity of 7 g p.acetylamino-benzene-sulfonamide is obtained. The filtrate is now evaporated to dryness.

The residue is recrystallized from ethanol.

Yield 7 g of a compound which is supposed to be di-[p.amino-benzene-sulfonyl] amide.

Example 3.—23 g of p.acetylamino-benzene-sulfonamide are boiled under reflux for one hour with 100 cc of water and 4 cc of 25%ic ammonia. The liquid reacts as acid with respect to congo and is therefore neutralized with sodium-carbonate. The solution is evaporated on a steam bath and the residue recrystallized from ethanol. Yield 7 g.

The acetyl groups appear to have been split off during the reaction.

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