

The Preparation and Properties of Certain Acyl Derivatives of Sulfamide

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A method for preparing sulfamide that can be adapted to commercial production has been described (1). Since there is a similarity in the structure and in the chemical properties between urea and sulfamide, and since some acyl derivatives of urea possess valuable pharmacological properties, this availability of sulfamide made it desirable to prepare acyl derivatives of sulfamide and to test their physiological action. This paper concerns only the preparation of these derivatives.

It was found that the N-acyl and the N,N'-diacyl sulfamides were formed by the action of acylating agents in the proper mole quantities. The diacylsulfamides were formed by the action of the acylating agent on sulfamide without a solvent. It was necessary, however, to use a solvent (ethyl acetate) to prepare the monosubstituted sulfamides.

Seven new compounds were prepared and characterized:

1. N-Acetylsulfamide, m.p. 157° decomp.
2. N-Propionylsulfamide, m.p. 148° decomp.
3. N-Butyrylsulfamide, m.p. 145° decomp.
4. N,N'-Diacetylsulfamide, m.p. 165° decomp.
5. N,N'-Dipropionylsulfamide, m.p. 171° decomp.
6. N,N'-Dibutyrylsulfamide, m.p. 159° decomp.
7. N,N'-Diisovaleryl sulfamide, m.p. 157° decomp.

All of these compounds decomposed at their melting points, which were dependent upon the rate of heating. N,N'-Diacetylsulfamide, although melting sharply, melted at various temperatures from 144-170°. A technique similar to that used by Cortese and Bauman (2) was used to characterize the compounds. The melting point was taken as the temperature at which the compound melts completely in 30 ± 1 seconds.

Experimental

The preparations which follow are typical ones for each of the two types of compounds which were prepared—the monosubstituted and the disubstituted sulfamides. In the synthesis of the disubstituted compounds, dipropionyl- and dibutyrylsulfamide, the only difference in the procedure from that given is in the amounts of anhydride added. The diisovaleryl sulfamide was formed from isovaleryl bromide and sulfamide. In all cases the amount of acylating agent was about 1.1 times the theoretical quantity. The monopropionyl- and monobutyrylsulfamide

were refluxed for four and three hours respectively instead of twenty minutes as given for the acetyl compound.

Preparation of N-Acetylsulfamide:

Six grams of sulfamide (m.p. 92-93°) is dissolved in boiling ethyl acetate (150-175 ml.) in a 500 ml. round bottom flask fitted with a reflux condenser. A dropping funnel is inserted in a loosely fitted one-hole stopper and attached to the top of the condenser. Six ml. (6.4 gms.) of acetic anhydride to which had been added a few drops of conc. sulfuric acid is mixed with fifteen ml. of ethyl acetate and transferred to the dropping funnel. This mixture is allowed to drop slowly into the refluxing ethyl acetate solution.

When all the acetic anhydride-ethyl acetate mixture has been added, a calcium chloride drying tube is attached to the top of the reflux condenser instead of the dropping funnel. The mixture is refluxed for twenty minutes, then 100 ml. of ethyl acetate distilled off. The remaining solution is transferred to a 125 ml. florence flask and allowed to cool. Small white crystals are deposited on the sides of the flask. Weight of crude product, 4.5 gms. (52%). Small needles precipitate upon crystallization from absolute ethyl alcohol. After three crystallizations from absolute alcohol, the product melts with decomposition at 157°. It is soluble in water, alcohol, and acetone. Analysis: N calculated, 20.29; N found, 20.05, 20.10.

Preparation of N,N'-Diacetylsulfamide:

Twelve ml. (12.9 gms.) of acetic anhydride, to which had been added a few drops of conc. sulfuric acid, is added slowly and with stirring to six grams of sulfamide (m.p. 92-93°) in a 125 ml. erlenmeyer flask. A very vigorous reaction takes place with the evolution of heat. The reaction mixture is warmed on a steam bath for one hour with intermittent stirring. On cooling, the mass solidifies and is crystallized from 60% ethyl alcohol. White needles are formed. Yield 5 gms. (55%). The product melts with decomposition after three crystallizations from 60% ethyl alcohol at 165°. Analysis: N calculated, 15.55; N found, 15.37, 15.15.

Summary

1. Mono- or disubstituted sulfamides may be prepared from the action of an acylating agent or sulfamide. In the latter case, no solvent is necessary.

2. Seven N-substituted sulfamides were prepared and characterized.

Literature Cited

1. Degering and Gross, *Ind. Eng. Chem.*, **35**, (1943).
2. Cortese and Bauman, *J. Am. Chem. Soc.*, **57**:1394 (1935).