ceed for four hours at 20°, the sodium methylate neutralized by addition of an equivalent amount of acetic acid, and the solvent evaporated at 20° under reduced pressure. The residue crystallized from a mixture of anhydrous methanol and ether (1:1) as dense rhombic crystals; yield 76%; m. p. 193–194.5°, with slight decomposition. *Anal.* Calcd. for $C_{16}H_{20}O_8$: C, 54.85; H, 6.14; OCH_3, 9.45. Found: C, 54.90; H, 6.30; OCH_3, 9.40.

β-*d*-Xyloside of α-Hydroxypropiosyringone.—Deacetylation was effected as described for the β-*d*-xyloside of α-hydroxypropiovanillone. The residue obtained after evaporation of the methanol from the reaction mixture had to be purified with utmost care, otherwise decomposition resulted. This was effected by dissolving in a minimum amount of anhydrous methanol at 20° and cooling to −10° when the xyloside crystallized in the form of fine needles; yield 73%; m. p. 149.4–150.0°. *Anal.* Calcd. for $C_{16}H_{22}O_9$: C, 53.60; H, 6.18; OCH_3, 17.32. Found: C, 53.51; H, 6.35; OCH_3, 17.28.

Guaiacol β-*d*-Xyloside.—This was prepared by deacetylation of the acetylated xyloside by the Zemplén method.[17] The xyloside crystallized from ethyl acetate in rod-shaped crystals, yield 85%, m. p. 175.3–176.0°. *Anal.* Calcd. for $C_{12}H_{16}O_6$: C, 56.23; H, 6.29; OCH_3, 12.10. Found: C, 56.20; H, 6.43; OCH_3, 12.05.

Acetovanillone β-*d*-Xyloside.—The conditions of deacetylation were as described by Zemplén.[17] The xyloside was recrystallized, first from ethyl acetate, and then from 50% anhydrous methanol–ether, and obtained in the form of very fine hair-like crystals; yield 85%; m. p. 145.2–145.7°. *Anal.* Calcd. for $C_{14}H_{18}O_7$: C, 56.25; H, 6.08; OCH_3, 10.40. Found: C, 56.20; H, 6.41; OCH_3, 10.30.

Acknowledgment.—The authors wish to thank the National Research Council of Canada for the financial assistance given to one of them (J. H. F.).

Summary

Methods are given for the synthesis of the β-*d*-xylosides of α-hydroxypropiovanillone, α-hydroxypropiosyringone, guaiacol and acetovanillone, and their corresponding fully acetylated derivatives.

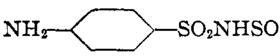
MONTREAL, CANADA RECEIVED MARCH 28, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE CALCO CHEMICAL DIVISION OF THE AMERICAN CYANAMID COMPANY]

Sulfanilamide Derivatives. VII. N^1-Alkanesulfonylsulfanilamides and Related Compounds[1]

BY M. L. CROSSLEY, E. H. NORTHEY AND MARTIN E. HULTQUIST

We were led to further investigation of sulfanilamide derivatives containing a disulfonamide linkage, $—SO_2NHSO_2—$, by the preliminary pharmacological results on disulfanilamide.[2] Long chain N^1-alkanesulfonylsulfanilamides analogous to the N^1-acylsulfanilamides[3] were of most interest, but a series of compounds was synthesized of general structure



$NH_2—C_6H_4—SO_2NHSO_2R$, where R was alkane (from 2 to 12 carbons), cycloalkane, and aralkane.

The synthesis of the intermediate sulfonyl chlorides followed the procedure of Treat B. Johnson.[4]

These were treated with N^4-acetylsulfanilamide in aqueous solution and the resulting N^4-acetyl-N^1-alkanesulfonylsulfanilamides were hydrolyzed by boiling with sodium hydroxide to remove the N^4-acetyl group. The resulting N^1-alkanesulfonylsulfanilamides were highly water soluble for the lower members of the series, but became increasingly water insoluble in the higher members. All were strongly acidic and formed neutral sodium salts.

Chemotherapeutic Properties.[5]—Preliminary results in mice against beta-haemolytic streptococci indicate that these compounds as a class are of low chemotherapeutic activity. A complete evaluation of them awaits the final results of the chemotherapeutic study.

Experimental Part

N^1-Butanesulfonylsulfanilamide.—78.3 grams (0.5 mole) of 1-butanesulfonylchloride was added to a slurry of 214 g. (1 mole) of N^4-acetylsulfanilamide and 400 cc. of water; 50% sodium hydroxide solution was added gradually to maintain a pink spot test on benzoazurine paper (*p*H 11–12) while holding the temperature at 35–40° by addition of ice. The time of adding sodium hydroxide was thirty minutes. When no more sodium hydroxide was consumed after stirring for thirty minutes, the reaction was considered

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(1) Presented in part before the Division of Medicinal Chemistry, A. C. S. Meeting, Cincinnati, Ohio, April, 1940.

(2) Crossley, Northey and Hultquist, THIS JOURNAL, **60**, 2222 (1938).

(3) Crossley, Northey and Hultquist, *ibid.*, **61**, 2950 (1939).

(4) Johnson and Sprague, *ibid.*, **58**, 1348 (1936); Sprague and Johnson, *ibid.*, **59**, 1837 (1937); Johnson and Douglass, *ibid.*, **61**, 2549 (1939); U. S. Patent 2,147,346, Feb. 14, 1939.

(5) This phase of the work was carried out under the direction of W. H. Feinstone and will be reported elsewhere.

TABLE I

N^1-ALKANESULFONYLSULFANILAMIDES

Alkanesulfonyl group	Appearance	Melting range, °C.	Assay by $NaNO_2$	Assay by NaOH
Ethanesulfonyl-	Short prisms	206.5–207.5	101.0	101.0
1-Butanesulfonyl-	Plates	209.0–210.5	100.1	100.8
1-Pentanesulfonyl-	Plates	183.0–184.5	99.6	98.5
2-Ethyl-1-hexanesulfonyl-	Plates	189.0–191.0	100.5	100.0
1-Dodecanesulfonyl-	Plates	188.8–189.9	...	99.4
Cyclohexanesulfonyl-	Leaflets	230 dec.	100.0	100.3
10-*dl*-Camphorsulfonyl-	Leaflets	213.0–214.5	100.8	100.2
Phenylmethanesulfonyl-	Plates	242.0–243.5	99.8	99.4

to be complete. Dilute hydrochloric acid was added to bring the *p*H to 8–9 and the mixture was cooled to 15°. The excess N^4-acetylsulfanilamide was filtered and washed well with cold water. The mother liquor was acidified to *p*H 1 with hydrochloric acid. A sticky precipitate formed which soon crystallized to white, sandy crystals of N^4-acetyl-N^1-(1-butanesulfonyl)-sulfanilamide. A portion of the crude product was saved and purified by solution as the sodium salt, treatment with activated charcoal and reprecipitation. On attempting to recrystallize from water, partial hydrolysis of the N^4-acetyl group resulted.

The balance of the crude product was hydrolyzed with sodium hydroxide by the same procedure used for N^1-acylsulfanilamides.[3] The hydrolyzate on cooling and standing deposited coarse crystals of sodium N^1-(1-butanesulfonyl)-sulfanilamide which were salted out of solution by the excess sodium hydroxide present. The salt was twice recrystallized from concentrated aqueous solutions. Recoveries from the sodium salt mother liquors were made by acidifying to *p*H 4.0–4.5 and filtering off the free compound. This was recrystallized from water.

The other compounds listed in Table I were similarly prepared. All were assayed by the same procedures used for the N^1-acylsulfanilamides.[3] N^1-1-Dodecanesulfonylsulfanilamide was too insoluble in mineral acids to be analyzed by diazotization.

Summary

1. Sulfanilamide derivatives of the general formula, $NH_2(4)C_6H_4SO_2NHSO_2R$, were synthesized where R was alkane (2 to 12 carbons), cycloalkane and aralkane.

2. Preliminary studies in mice indicated low effectiveness of these compounds against beta-haemolytic streptococci.

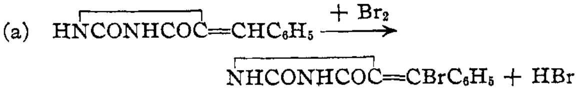
BOUND BROOK, N. J. RECEIVED APRIL 9, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MOUNT HOLYOKE COLLEGE]

Differences Observed in the Behavior of Unsaturated Hydantoins under the Action of Bromine

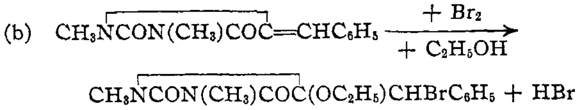
BY MARGARET J. MCLEAN AND DORIS R. SEEGER[1]

Reactions involving the addition of bromine to hydantoins possessing unsaturated side chains in the C-5-position have been reported as leading to the formation of quite different classes of compounds, the character of which seems to depend upon the conditions of the experiment. For example, unsaturated hydantoins in which a bromine atom was found to have replaced a hydrogen atom in the side chain invariably were formed when benzalhydantoin, anisalhydantoin and many similar compounds,[2] dissolved in glacial acetic acid, were treated with molecular quantities of bromine



$$\text{(a)}\quad \mathrm{HNCONHCOC{=}CHC_6H_5} \xrightarrow{+\ \mathrm{Br_2}} \mathrm{NHCONHCOC{=}CBrC_6H_5} + \mathrm{HBr}$$

In other cases[3] where reactions were carried out in chloroform or carbon tetrachloride and these solvents subsequently displaced by alcohol, saturated ethoxy-monobromo derivatives of the hydantoins were formed.



$$\text{(b)}\quad \mathrm{CH_3NCON(CH_3)COC{=}CHC_6H_5} \xrightarrow[+\ \mathrm{C_2H_5OH}]{+\ \mathrm{Br_2}} \mathrm{CH_3NCON(CH_3)COC(OC_2H_5)CHBrC_6H_5} + \mathrm{HBr}$$

The question naturally arises as to whether these differences are due to the nature of the unsaturated hydantoins involved, or solely to experimental conditions. In the latter case *all*

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(1) Acknowledgment must be made to Dr. Dorothy A. Hahn for suggesting and coöperating in this research.

(2) Wheeler, Hoffman and Johnson, *J. Biol. Chem.*, **10**, 154 (1911); Wheeler and Hoffman, *Am. Chem. J.*, **45**, 376 (1911); Johnson and Wrenshall, THIS JOURNAL, **37**, 2133 (1915); Johnson and Davidson, *ibid.*, **47**, 563 (1925).

(3) Litzinger, *ibid.*, **56**, 676 (1934); Hahn, McLean and Murphy, *ibid.*, **60**, 1927 (1938).