[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, AND JOHNS HOPKINS UNIVERSITY MEDICAL SCHOOL]

Sulfanilamide Derivatives. I

BY ROGER ADAMS, P. H. LONG AND A. J. JOHANSON[1]

The intensive study of sulfanilamide derivatives during the past few years has been with the objective of discovering compounds of higher activity, lower toxicity and more advantageous physical properties. The work described in this communication involved especially the preparation of a variety of *p*-acylamidobenzenesulfonalkanolamides and *p*-aminobenzenesulfonalkanolamides in order to determine, (1) the effect of the alkanolamine, (2) the effect of the acyl radical, and (3) the effect of changes in water solubility on the toxicity and antistreptococcal activity of the molecules. A few of these compounds have been described by other investigators[2] since the initiation of the research but they are included in order to show the general comparisons. The description of certain simple amides,[3] morpholides and double ring compounds is also included.

The compounds were prepared by condensation of the proper substituted *p*-aminobenzenesulfonyl chloride (Table I) and an alkanolamine, ammonia, morpholine, or *p*-aminobenzenesulfonalkanolamide, according to the equation

$$RNHC_6H_4SO_2Cl + NH_2CH_2CHOHR \longrightarrow RNHC_6H_4SO_2NHCH_2CHOHR$$

The individual compounds are listed in Tables II–X.

The following general statements can be made concerning these various compounds:

(a) The aminobenzenesulfonalkanolamides are more soluble in water than sulfanilamide. The antistreptococcal activity of these compounds is from slight to moderate but lower in every instance than that of sulfanilamide. The least activity is found in the 2,3-dihydroxypropylamine derivative. The therapeutic ratio is more favorable in many of the derivatives than in sulfanilamide.

(b) The acylamidobenzenesulfonalkanolamides were less soluble in water than the unacylated analogs. The antistreptococcal activity was usually lower though not so in all instances. The toxicity, however, was greatly reduced so that in many of these compounds the therapeutic ratio was more favorable than in sulfanilamide. As the acyl group increased in size, the water solubility decreased and the antistreptococcal activity was less. The toxicity, however, remained very low except in the isobutyryl derivative.

Several compounds in the series of acylamidobenzenesulfonmorpholides showed slight to moderate activity and materially reduced water solubility.

Carbethoxyaminobenzenesulfonalkanolamides were similar in solubility, effectiveness and toxicity to the lower acyl derivatives.

The *p*-acylamidobenzenesulfonamides were less effective than sulfanilamide with the valeryl derivative somewhat more effective than the propionyl.

The substituted benzenesulfonanilide derivatives were all ineffective.

A few compounds in which an alkyl or a benzyl group was substituted for one of the hydrogens in the amino group of an aminobenzenesulfonalkanolamide showed properties not very dissimilar to those of the analogous unsubstituted amino compound.

Several 4-methoxy-3-aminobenzenesulfonamides and the analogous alkanolamides showed essentially no antistreptococcal activity.

The various compounds were also tested for antimeningococcal activity. There appeared to be no correlation with antistreptococcal activity. On the other hand, a large number of the compounds possessed antimeningococcal activity equivalent to that of sulfanilamide. Since the toxicity of most of these compounds was much less than that of sulfanilamide, the therapeutic ratio in respect to antimeningococcal activity of the new compounds is much more favorable than in sulfanilamide.

These preliminary toxicity, antistreptococcal and antimeningococcal tests were carried out in Johns Hopkins University Medical School by Dr. P. H. Long. In the tables, ++++ is the equivalence in activity to sulfanilamide.

(1) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry, 1938.

(2) Kharasch and Reinmuth, U. S. Patent 2,097,414.

(3) Miller, Rock and Moore, THIS JOURNAL, **61**, 1198 (1939).

TABLE I

SUBSTITUTED *p*-AMINOBENZENESULFONYL CHLORIDES

No.	Sulfonyl chloride	M. p., °C.	Formula	Nitrogen analyses, % Calcd.	Found
1	*p*-Propionamidobenzene-	113	$C_9H_{10}O_3NSCl$	5.66	5.89
2	*p*-*n*-Butyramidobenzene-	120–121	$C_{10}H_{12}O_3NSCl$	5.35	5.53
3	*p*-Isobutyramidobenzene-	131–132	$C_{10}H_{12}O_3NSCl$	5.35	5.53
4	*p*-*n*-Valeramidobenzene-	115–116	$C_{11}H_{14}O_3NSCl$	5.08	5.32
5	*p*-Isovaleramidobenzene-	120–121	$C_{11}H_{14}O_3NSCl$	5.08	5.22
6	*p*-Methylacetamidobenzene-	136–137	$C_9H_{10}O_3NSCl$	5.66	5.81
7	*p*-Ethylacetamidobenzene-	142–143	$C_{10}H_{12}O_3NSCl$	5.35	5.39
8	*p*-Carbethoxyamidobenzene-	103	$C_9H_{10}O_4NSCl$	5.32	5.39
9	4-Methoxy-3-acetamidobenzene-[4]	149			

Experimental

Substituted (*p*)-Aminobenzenesulfonyl Chlorides.—*p*-Acetamidobenzenesulfonyl chloride was prepared by the method of Stewart.[4] A series of *p*-acylamidobenzenesulfonyl chlorides (Table I) was synthesized in essentially the same manner, by the reaction of chlorosulfonic acid with the appropriate anilide. In each case, 1 mole of the anilide was added to 5 moles of chlorosulfonic acid at 10–20° with stirring. The reactions were, with the exception of numbers 6 and 7, allowed to proceed, with stirring, from one to five hours at room temperature followed by a final period of from one to five hours at 50–60°. In the cases of numbers 6 and 7 the mixtures gradually were heated to 80° and the reactions continued at that temperature for three hours.

p-Carbethoxyaminobenzenesulfonyl chloride was prepared by adding 1 mole of phenylurethan to 5 moles of chlorosulfonic acid and stirring for five hours at room temperature followed by heating at 60° for one hour.

In no case was hydrogen chloride evolution as extensive as with *p*-acetamidobenzenesulfonyl chloride. Most of the sulfonyl chlorides tended to separate when poured into the ice–water mixture, as sticky gummy masses, light tan in color. After standing from fifteen minutes to one hour, these masses solidified and could be filtered. In most cases the solidification could be hastened by transferring the gum to a fresh ice–water mixture, and stirring and kneading.

4-Methoxy-3-acetamidobenzenesulfonyl chloride[5] was prepared in the same manner as the *p*-acetamidobenzenesulfonyl chloride except that the mixture was stirred at room temperature for twenty hours and then poured into the ice–water mixture.

The crude, moist sulfonyl chlorides were used directly in the condensation reactions. Small portions were purified for characterization by recrystallization from benzene and were obtained as small white crystals. In contrast to Stewart's acetyl compound, these sulfonyl chlorides were all found to be very soluble in hot benzene.

Although no exact determinations were made on a pure basis, the yields, excepting in the cases of numbers 6 and 7 in Table I, appeared to be about the same as with the acetyl compound. The yields of numbers 6 and 7 were not more than 15 to 20% of theoretical.

(4) Stewart, *J. Chem. Soc.*, **121**, 2558 (1922); "Org. Syntheses," Coll. Vol. I, p. 8.

(5) German patent 573,193 (1931); *Friedlaender*, **19**, (I), 699 (1934).

Condensation of the Substituted *p*-Aminobenzenesulfonyl Chlorides with Amino Compounds.—The substituted *p*-aminobenzenesulfonyl chlorides were condensed with the various amino compounds using molar portions of each and one of the following as a condensing agent to take up hydrogen chloride: (1) an additional mole of the amine (plus a small excess to neutralize hydrochloric and sulfuric acids not removed from the crude sulfonyl chloride in the washing process); (2) potassium hydroxide in 10 to 20% aqueous solution, in sufficient quantity to maintain alkalinity throughout the reaction (about 1.5 moles); (3) an excess (3 or 4 moles) of pyridine; (4) in the case of the unsubstituted sulfonamides a large excess of concentrated aqueous ammonia.

For the preparation of *p*-acetamidobenzenesulfon-(β-hydroxyethyl)-amide and *p*-acetamidobenzenesulfon-di-(β-hydroxyethyl)-amide and all the morpholides, method 1 was found satisfactory. Method 3 was most satisfactory for the substituted benzenesulfonanilide derivatives. All the other compounds were prepared using method 2.

General Procedure.—The amino compound and the condensing agent were placed in an open beaker. To the mixture was added, with stirring, a quantity of the crude damp benzenesulfonyl chloride derivative estimated to contain the desired amount of pure substance. Heat usually was evolved, but the temperature of the mixture was held below 45° by means of an ice-bath. In some cases the sulfonyl chloride dissolved to form a clear yellow solution. In others, as the sulfonyl chloride dissolved, the product separated immediately in solid form or as a heavy dark oil. The mixture was heated about thirty minutes at 70–80°, cooled to room temperature and neutralized with concentrated hydrochloric acid to brilliant yellow as indicator. At this point, the product if not already in suspension in solid form or present as an oily layer in the bottom of the beaker, usually separated, either in crystalline form or as an oil which upon cooling and standing eventually solidified. Evaporation to small volume, cooling and standing caused separation in cases where precipitation did not occur directly when the mixture was neutralized.

The products were usually recrystallized from water or aqueous ethanol of various dilutions. In almost every case one or more treatments with norite was necessary to remove color.

Hydrolysis of Acetamidobenzenesulfonamides.—The compounds shown in Tables V and VI were prepared by acid hydrolysis of the corresponding acetamido compounds.

The acetamido compound (1 mole) was added to dilute

hydrochloric acid (4–6 *N*) containing at least 1.4 moles of the acid. The mixture was heated under reflux for two to five hours at 70–80°. If the material did not dissolve completely on heating, a small quantity of ethanol was added to bring about solution. After completion of the hydrolysis, the solution was cooled and neutralized to litmus with solid sodium carbonate. In nearly every case the amine separated as a heavy oil, which after stirring, cooling and standing became solid. Purification was effected by recrystallization from water or dilute ethanol. Treatment with norite to remove color was necessary in most cases.

TABLE II

p-ACYLAMIDOBENZENESULFONAMIDES[a]

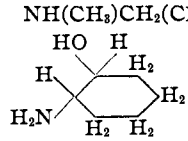
Compounds 1, 2, 3 and 4 have been described recently by Miller, Rock and Moore.[3] The melting points reported differed considerably from those given here. Compound 4 has also been described in French Patent 820,546: *C. A.*, **32**, 2958 (1938).

No.	Acyl group	M. p., °C.	Anti-strep. activity	Anti-mening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1[b]	CH_3CH_2CO	226.5–227.5	++	+++	$C_9H_{12}O_3N_2S$	12.28	12.23
2[c]	$CH_3CH_2CH_2CO$	236–237	+	++++	$C_{10}H_{14}O_3N_2S$	11.57	11.61
3[d]	$(CH_3)_2CHCO$	248–249	±	++++	$C_{10}H_{14}O_3N_2S$	11.57	11.18
4[e]	$CH_3CH_2CH_2CH_2CO$	209–210	+++		$C_{11}H_{16}O_3N_2S$	10.94	10.95

[a] White microcrystalline powders very slightly soluble in water. Yields varied from 53 to 86%. [b] Recrystallized from 25% ethanol. [c] Recrystallized from a mixture of acetone and 95% ethanol. [d] Recrystallized from an acetone–water mixture. [e] Recrystallized from 50% ethanol.

TABLE III

p-ACETAMIDOBENZENESULFONALKANOLAMIDES[a]

No.	Alkanolamine	M. p., °C.	Anti-strep. activity	Anti-mening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	$NH_2CH_2CH_2OH$	150–151	0	++++	$C_{10}H_{14}O_4N_2S$	10.81	10.86
2[b]	$NH(CH_2CH_2OH)_2$	158–159	0	+	$C_{12}H_{18}O_4N_2S$	9.27	9.53
3	$NH_2CH_2CH_2CH_2OH$	133.5–135	0	+	$C_{11}H_{16}O_4N_2S$	10.30	10.45
4[c]	$NH_2CH_2CHOHCH_3$	166–167	+	0	$C_{11}H_{16}O_4N_2S$	10.30	10.61
5	$NH_2CH_2COH(CH_3)_2$	185–187	±	++	$C_{12}H_{18}O_4N_2S$	C, 50.35 H, 6.29	51.01 6.44
6	$NH_2CH_2CHOHCH_2OH$	132–133	0	0	$C_{11}H_{16}O_5N_2S$	9.72	10.07
7	$NH(CH_3)CH_2(CHOH)_4CH_2OH$	87–91	0	±	$C_{15}H_{24}O_8N_2S$	7.14	6.93
8		218	0	0	$C_{14}H_{20}O_4N_2S$	8.97	8.88

[a] White crystalline powders of varying solubility in water. With the exception of number 8, all recrystallized from water. Number 8 from dilute ethanol. Yields from 50 to 75%. [b] Kolloff, THIS JOURNAL, **60**, 950 (1938). [c] U. S. Patent 2,097,414, Oct. 26 (1937).

TABLE IV

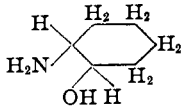
p-ACYLAMIDOBENZENESULFONALKANOLAMIDES[a]

No.	Acyl group	Alkanolamine	M. p., °C.	Anti-strep. activity	Anti-mening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	CH_3CH_2CO	$NH_2CH_2CHOHCH_3$	148	0	+++	$C_{12}H_{18}O_4N_2S$	9.79	9.87
2	CH_3CH_2CO	$NH_2CH_2COH(CH_3)_2$	172–172.5	+	+++	$C_{13}H_{20}O_4N_2S$	9.33	9.45
3	$CH_3CH_2CH_2CO$	$NH_2CH_2CH_2OH$	139	0	+	$C_{12}H_{18}O_4N_2S$	9.79	9.79
4	$CH_3CH_2CH_2CO$	$NH(CH_2CH_2OH)_2$	114–115	0	+	$C_{14}H_{22}O_5N_2S$	8.48	8.44
5	$CH_3CH_2CH_2CO$	$NH_2CH_2CHOHCH_3$	127–128	0	++	$C_{13}H_{20}O_4N_2S$	9.33	9.65
6	$CH_3CH_2CH_2CO$	$NH_2CH_2COH(CH_3)_2$	166	±	++++	$C_{14}H_{22}O_4N_2S$	8.91	8.80
7	$(CH_3)_2CHCO$	$NH_2CH_2CH_2OH$	116.5	++	+	$C_{12}H_{18}O_4N_2S$	9.79	9.68
8	$(CH_3)_2CHCO$	$NH_2CH_2CHOHCH_3$	144	±	+++	$C_{13}H_{20}O_4N_2S$	9.33	9.23
9	$(CH_3)_2CHCO$	$NH_2CH_2COH(CH_3)_2$	173	±	++++	$C_{14}H_{22}O_4N_2S$	8.91	9.10
10	$CH_3(CH_2)_3CO$	$NH_2CH_2CHOHCH_3$	121.5	±	++++	$C_{14}H_{22}O_4N_2S$	8.92	8.89
11	$CH_3(CH_2)_3CO$	$NH_2CH_2COH(CH_3)_2$	136–136.5	±	+++	$C_{15}H_{24}O_4N_2S$	8.54	8.56
12	$(CH_3)_2CHCH_2CO$	$NH_2CH_2COH(CH_3)_2$	146–147	0	0	$C_{15}H_{24}O_4N_2S$	8.54	8.63

[a] White microcrystalline powders, slightly soluble in water. Recrystallized from 25 to 50% aqueous ethanol. Yields ranged from 30 to 60%.

TABLE V

p-AMINOBENZENESULFONALKANOLAMIDES[a]

No.	Alkanolamine	M. p., °C.	Antistrep. activity	Antimening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	$NH_2CH_2CH_2OH$	95–97	++	+++	$C_8H_{12}O_3N_2S$	12.98	13.16
2[b]	$NH(CH_2CH_2OH)_2$	109–110	++	±	$C_{10}H_{16}O_4N_2S$	10.77	10.52
3	$NH_2CH_2CH_2CH_2OH$	123–124	±	++++	$C_9H_{14}O_3N_2S$	12.18	12.18
4	$NH_2CH_2CHOHCH_3$[c]	115–116	+	++++	$C_9H_{14}O_3N_2S$	12.18	12.20
5	$NH_2CH_2COH(CH_3)_2$	102–103	0	++++	$C_{10}H_{16}O_3N_2S$	11.48	11.69
6	$NH_2CH_2CHOHCH_2OH$	102–104	0	++++	$C_9H_{14}O_4N_2S$	11.39	11.11
7		141–142	0	0	$C_{12}H_{18}O_3N_2S$	10.36	10.22

[a] White crystalline powders soluble in water, number 7 only slightly. Yields varied from 48 to 67%. Recrystallized from water with the exception of number 7, which was recrystallized from 20% aqueous ethanol. [b] *Cf.* Kolloff.

TABLE VI

p-ALKYL- AND *p*-ARALKYLAMINOBENZENESULFONALKANOLAMIDES[a]

No.	Alkyl or aralkyl group	Alkanolamine	M. p., °C.	Antistrep. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	CH_3	$NH_2CH_2CHOHCH_3$	90–91	..	$C_{10}H_{16}O_3N_2S$	11.48	11.40
2	$C_2H_5(COCH_3)$	$NH_2CH_2COH(CH_3)_2$	134	..	$C_{14}H_{22}O_4N_2S$	8.92	8.81
3	C_2H_5	$NH_2CH_2COH(CH_3)_2$	131.5	0	$C_{12}H_{20}O_3N_2S$	10.29	10.36
4	$CH_2C_6H_5$	$NH_2CH_2CH_2OH$	115–116	±	$C_{15}H_{18}O_3N_2S$	9.15	9.05

[a] White crystalline solids slightly soluble in water. Yields varied from 35 to 60%. All were recrystallized from water except number 4 for which benzene containing 5% methanol was used.

TABLE VII

SUBSTITUTED *p*-CARBETHOXYAMINOBENZENESULFONAMIDES[a]

No.	Amide	M. p., °C.	Antistrep. activity	Antimening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1[b]	$NH_2CH_2CH_2OH$	176	+	++++	$C_{11}H_{16}O_5N_2S$	9.72	9.65
2[c]	$NH_2CH_2CHOHCH_3$	132	±	++	$C_{12}H_{18}O_5N_2S$	9.27	9.26
3[d]	$NH(CH_2CH_2)_2O$	157–158	0	++	$C_{13}H_{18}O_5N_2S$	8.91	8.89
4[e]	NH_3	241–242	+	+	$C_9H_{12}O_4N_2S$	11.48	11.58

[a] White microcrystalline solids, very slightly soluble in water. Estimated yields varied from 50 to 86%. [b] Recrystallized from 60% ethanol. [c] Recrystallized from hot water. [d] Recrystallized from 50% ethanol. [e] Recrystallized from acetone and water (1:1).

TABLE VIII

p-ACYLAMIDOBENZENESULFONMORPHOLIDES AND *p*-AMINOBENZENESULFONMORPHOLIDE[a]

No.	Acyl group	M. p., °C.	Antistrep. activity	Antimening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	CH_3CO	165–166	+	++	$C_{12}H_{16}O_4N_2S$	9.86	9.77
2	CH_3CH_2CO	189–190	+	+	$C_{13}H_{18}O_4N_2S$	9.40	9.49
3	$CH_3CH_2CH_2CO$	191–193	+	++	$C_{14}H_{20}O_4N_2S$	8.97	8.75
4	$(CH_3)_2CHCO$	147	±	±	$C_{14}H_{20}O_4N_2S$	8.97	8.93
5	H	217	±	±	$C_{10}H_{14}O_3N_2S$	11.57	11.51

[a] White crystalline solids usually as small glistening plates. Very slightly soluble in water. Yields varied from 50 to 82%. Recrystallized from 20 to 50% ethanol.

TABLE IX

SUBSTITUTED BENZENESULFONANILIDE DERIVATIVES:[a]

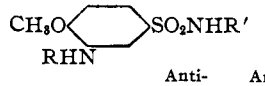
$RNHC_6H_4SO_2NHC_6H_4SO_2NHR'$

No.	R	R'	M. p., °C.	Antistrep. activity	Antimening. activity	Formula	Nitrogen analyses, % Calcd.	Found
1	CH_3CO	$CH_2CHOHCH_3$	127–128	0	0	$C_{17}H_{21}O_6N_3S_2$	9.88	9.58
2	H	$CH_2CHOHCH_3$	123–125	0	++++	$C_{15}H_{19}O_5N_3S_2$	10.97	11.00
3	CH_3CO	$CH_2COH(CH_3)_2$	213	0	0	$C_{18}H_{23}O_6N_3S_2$	9.52	9.46
4	H	$CH_2COH(CH_3)_2$	184–185	±	++++	$C_{16}H_{21}O_5N_3S_2$	10.52	10.74
5	C_2H_5OCO	$CH_2CHOHCH_3$	175–177	0	++++	$C_{18}H_{22}O_7N_3S_2$	9.19	8.99

[a] White microcrystalline powders very slightly soluble in water. Yields varied from 60 to 77%. Recrystallized from 30 to 50% ethanol.

TABLE X

DERIVATIVES OF 4-METHOXY-3-AMINOBENZENESULFONAMIDE:[a]



No.	R	R′	M. p., °C.	Anti-strep. activity	Anti-mening. activity	Formula	Nitrogen analyses, % Calcd,	Found
1	CH_3CO	H	225.5	0	±	$C_9H_{12}O_4N_2S$	11.47	11.34
2	CH_3CO	CH_2CH_2OH	152–153	0	0	$C_{11}H_{16}O_5N_2S$	9.72	9.85
3	CH_3CO	$CH_2CHOHCH_3$	146–147	0	0	$C_{12}H_{18}O_5N_2S$	9.27	9.36
4	CH_3CO	$CH_2COH(CH_3)_2$	125	0	±	$C_{13}H_{20}O_5N_2S$	8.86	9.09
5	H	H	142–142.5	0	0	$C_7H_{10}O_3N_2S$	13.86	13.53
6	H	$CH_2CHOHCH_3$	102	0	0	$C_{10}H_{16}O_4N_2S$	10.77	10.90

[a] Usually small glistening white crystals. Yields varied from 60 to 84%. Slightly soluble in water. Recrystallized from water, excepting number 4 which was recrystallized from dilute ethanol.

Summary

A variety of *p*-acylamidobenzenesulfonamides, *p*-acylamidobenzenesulfonalkanolamides, *p*-aminobenzenesulfonalkanolamides, *p*-alkyl- and *p*-aralkylaminobenzenesulfonalkanolamides, *p*-carbethoxyaminobenzenesulfonamides, *p*-acylamidobenzenesulfonmorpholides, *p*-aminobenzenesulfonmorpholide, *p*-acyl- and *p*-aminobenzenesulfonanilides and derivatives of 4-methoxy-3-aminobenzenesulfonamide have been prepared.

All show less antistreptococcal activity than sulfanilamide but practically all are much less toxic.

The antimeningococcal activity of many is equivalent to that found in sulfanilamide.

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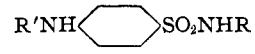
Sulfanilamide Derivatives. II

BY ROGER ADAMS, P. H. LONG AND ALLENE JEANES[1]

In the previous paper[2] it was demonstrated that the acyl groups in acylamidobenzenesulfonalkanolamides greatly reduced the toxicity of the molecule. The antistreptococcal activity was generally lower than that of sulfanilamide but the therapeutic ratio in many instances was more favorable. Consequently, a variety of other substituted acyl substituents has been introduced either directly or indirectly into the molecule. The compounds studied are shown below.



where R = $-CH_2CHOHCH_3$ and

R′ = $HOOC(CH_2)_2CO-$ I

$C_2H_5OOC(CH_2)_2CO-$ II

$CH_3CHOAcCO-$ III

where R = $-CH_2CH_2OH$ and

R′ = $HOCH_2CH_2NHCO(CH_2)_2CO-$ IV

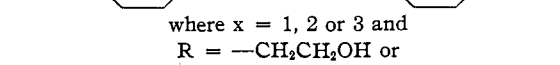
CH_3OCH_2CO- V

where R = H and

R′ = $NH_2CO(CH_2)_2CO-$ VI

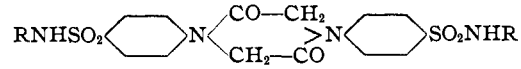
$CH_3CHOAcCO-$ VII

$CH_3CHOHCO-$ VIII

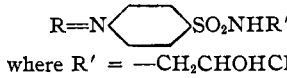


where x = 1, 2 or 3 and

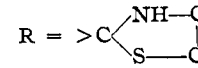
R = $-CH_2CH_2OH$ or $-CH_2CHOHCH_3$

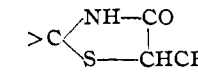


where R = H or $-CH_2CH_2OH$ or $-CH_2CHOHCH_3$

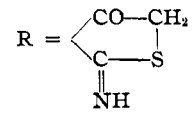


where R′ = $-CH_2CHOHCH_3$ and

R =  IX

 X

where R′ = H and

R =  XI

All the compounds were prepared either (1) by introduction of the sulfonyl chloride grouping into

(1) The authors are indebted to The Chemical Foundation for grants which made possible the work described in this communication.

(2) Adams, Long and Johanson, THIS JOURNAL, **61**, 2342 (1939).