with 3 cc. of 5 *N* NaOH and 1.5 cc. EtOH, diluted with 30 cc. of water, and reprecipitated with AcOH. Recrystd. from 60% EtOH to plates, m.p. 178~181°. Yield, 0.9 g. *Anal.* Calcd. for $C_{20}H_{22}O_2N_2S$: N, 7.91. Found: N, 8.06.

N¹-(4'-Octylphenyl)-4-aminonaphthalenesulfonamide—1 g. of the acetyl compound was warmed with 15 cc. EtOH and 6 cc. conc. HCl for 1.5 hrs. on a water bath. The reaction mixture was poured into 30 cc. of water and the sticky amorphous precipitate was recrystallized from benzene to plates, m.p. 108~110°. Yield, 0.6 g. *Anal.* Calcd. for $C_{24}H_{30}O_2N_2S$: N, 6.83. Found: N, 6.68.

N¹-(4'-Decylphenyl)-4-aminonaphthalenesulfonamide—1 g. of the acetyl compound was hydrolyzed by the same procedures as described above. Recrystd. from benzene to fine needles, m.p. 107~109°. Yield, 0.5 g. *Anal.* Calcd. for $C_{26}H_{34}O_2N_2S$: N, 6.39. Found: N, 6.45.

Summary

1) By the condensation of alkylaniline and 4-acetylaminonaphthalenesulfonyl chloride, N¹-alkylphenyl-4-acetylaminonaphthalenesulfonamide was obtained, which was hydrolyzed to N¹-alkylphenyl-4-aminonaphthalenesulfonamide.

2) The antiviral activities of these compounds were tested *in vitro* against *Encephalitis japonica*.

3) N¹-(2'- and 4'-Methylphenyl)-4-acetylaminonaphthalenesulfonamide and N¹-(2'- and 4'-methylphenyl)-4-aminonaphthalenesulfonamide were found to be of promise.

(Received June 19, 1954)

95. Tsuneo Wachi and Takako Wada : Researches on Chemotherapeutic Drugs against Viruses.* XXI.¹⁾ Synthesis and Antiviral Effects of N¹-Acyl-4-acetylaminonaphthalenesulfonamides and N¹-Acyl-4-aminonaphthalenesulfonamides.

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As described in the preceding papers, it was shown by the present authors that among the compounds of the 4-aminonaphthalenesulfonamide series, N¹-(*p*-azobenzene)-, N¹-(*o*-azotoluene)-²⁾, N¹-(*p*-tolyl)-, and N¹-(*o*-tolyl)-4-aminonaphthalenesulfonamides³⁾ and their N¹-acetylated derivatives exerted remarkable activity *in vitro*, nearly equal to that of PANS-No. 325, but weak effects *in vivo* nearly equal to that of PAN-No. 25.

On the other hand, it was deduced by Ueda *et al.*⁴⁾ that the antiviral activity, especially *in vitro* effect, of the compounds of the 4-aminonaphthalenesulfonamide series might depend not only upon their surface-tension lowering activity, but also on their penetrating property. In taking the above into consideration, N¹-acyl-4-acetyl-amino- and N¹-acyl-4-aminonaphthalenesulfonamides were synthesized by introducing an acyl group, perhaps affording surface activity, into 4-aminonaphthalenesulfonamide. This paper describes the synthesis and antiviral activities of N¹-acyl-4-acetyl-amino- and N¹-acyl-4-aminonaphthalenesulfonamides.

Synthesis of N¹-Acyl-4-acetylaminonaphthalenesulfonamide N¹-Acyl-4-aminonaph-

* Takeo Ueda and Shigeshi Toyoshima : Researches on Chemotherapeutic Drugs against Viruses. XXI.

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1) Part XX : This Bulletin, 2, 419(1954).

2) T. Wachi : *Ibid.* 2, 415(1954).

3) T. Wachi : *Ibid.* 2, 419(1954).

4) T. Ito, *et al.* : *Ibid.*, 1, 278(1953).

thalenesulfonamides and their N^4 -acyl derivatives have not been described by either Northey⁵⁾ or Hiyama,⁶⁾ but N^1 -acyl-4-aminobenzenesulfonamides and their acetyl compounds were synthesized by Grossley *et al.*⁷⁾ By referring to the synthesis of the above N^1, N^4 -diacylsulfanilamides, the synthetic procedures for N^1 -acyl-4-acetylaminonaphthalenesulfonamides were devised.

N^1 -Acyl-4-acetylaminonaphthalenesulfonamide was synthesized by condensing 4-acetylaminonaphthalenesulfonamide suspended in dried pyridine with acyl chloride, as shown in the following:

The reaction was carried out as described in the experimental part. The reaction was found to proceed smoothly with most of acyl chlorides in a good yield.

N^1 -Acyl-4-acetylaminonaphthalenesulfonamides were also found to be obtained, in smaller yield, by most of the modified methods deduced from the synthesis of N^1 -substituted sulfanilamides, e.g. by using acid anhydride in place of acyl chloride, by using sodium salt of 4-acetylaminonaphthalenesulfonamide in acetone or dioxane solution with acyl chloride, etc. However, the desired product could not be obtained by condensing 4-acetylaminonaphthalenesulfonyl chloride with acid amides under any conditions, as was found by Crossley with N^1 -acylsulfanilamides. The latter method will be discussed in detail in the near future.

The compounds obtained are summarized in Table I.

TABLE I.

R	Mol. formula	m.p. °C. (decomp.)	Appearance	N%	
				Calcd.	Found
-COCH ₃	C ₁₄ H ₁₄ O ₄ N ₂ S	(269~271)	Prisms	9.15	9.21
-COCH ₂ CH ₃	C ₁₅ H ₁₆ O ₄ N ₂ S	(241~242)	"	8.76	8.89
-CO(CH ₂) ₂ CH ₃	C ₁₆ H ₁₈ O ₄ N ₂ S	209~211	"	8.39	8.47
-CO(CH ₂) ₄ CH ₃	C ₁₈ H ₂₂ O ₄ N ₂ S	214.5~216	Needles	7.74	7.69
-CO(CH ₂) ₆ CH ₃	C ₂₀ H ₂₆ O ₄ N ₂ S	161~162	"	7.18	7.02
-CO(CH ₂) ₈ CH ₃	C ₂₂ H ₃₀ O ₄ N ₂ S	163~166.5	Prisms	6.70	6.73
-CO(CH ₂) ₁₀ CH ₃	C ₂₄ H ₃₄ O ₄ N ₂ S	192~195	Plates	6.28	6.54
-CO(CH ₂) ₁₂ CH ₃	C ₂₆ H ₃₈ O ₄ N ₂ S	152~156.6	"	5.94	5.78
-CO(CH ₂) ₁₄ CH ₃	C ₂₈ H ₄₂ O ₄ N ₂ S	169~170.5	"	5.58	5.72
-CO(CH ₂) ₁₆ CH ₃	C ₃₀ H ₄₆ O ₄ N ₂ S	169.5~170.5	"	5.28	5.39
-COCH ₂ CH(CH ₃) ₂	C ₁₇ H ₂₀ O ₄ N ₂ S	218.5~219	Prisms	8.05	8.12
-CO(CH ₂) ₈ CH=CH ₂	C ₂₈ H ₃₀ O ₄ N ₂ S	167~173	Plates	6.52	6.53
-CO(CH ₂) ₇ CH=CH(CH ₂) ₇ CH ₃	C ₃₀ H ₄₄ O ₄ N ₂ S	159.5~161	Amorphous	5.30	5.32
-COCH=CH-	C ₂₁ H ₁₈ O ₄ N ₂ S	(248~249)	Light yellow prisms	7.12	7.21
-CO-	C ₁₆ H ₁₆ O ₄ N ₂ S	(232~233)	Plates	7.62	7.58
-COCH ₂ -	C ₂₀ H ₁₈ O ₄ N ₂ S	(244~245)	Prisms	7.33	7.42

5) E. H. Northey: "Sulfanilamides and Allied Compounds" (1948).

6) M. Hiyama: J. Pharm. Soc. Japan, **72**, 1370(1952).

7) Grossley, Northey, Hultquist: J. Am. Chem. Soc., **61**, 2950(1939).

Synthesis of N¹-Acyl-4-aminonaphthalenesulfonamide N¹-Acyl-4-aminonaphthalenesulfonamides were obtained by hydrolyzing N¹-acyl-4-acetylaminonaphthalenesulfonamides with hot aqueous or ethanol solution of alkali hydroxide.

It was found that hydrolysis with acidic solution was unfavorable for the synthesis of N¹-acyl-4-aminonaphthalenesulfonamides, since such hydrolysis invariably afforded a considerable amount of 4-aminonaphthalenesulfonamide and naphthionic acid as by-products. The compounds obtained are summarized in Table II.

TABLE II.

R	Mol. formula	m.p. °C. (decomp.)	Appearance	N%	
				Calcd.	Found
-COCH ₃	C ₁₂ H ₁₂ O ₃ N ₂ S	(238~239)	Needles	10.60	10.51
-COCH ₂ CH ₃	C ₁₃ H ₁₄ O ₃ N ₂ S	180.5~181.5	Plates	10.09	10.07
-CO(CH ₂) ₂ CH ₃	C ₁₄ H ₁₆ O ₃ N ₂ S	155.6~156.5	Prisms	9.57	9.71
-CO(CH ₂) ₄ CH ₃	C ₁₆ H ₂₀ O ₃ N ₂ S	172~173	"	8.75	8.74
-CO(CH ₂) ₆ CH ₃	C ₁₈ H ₂₄ O ₃ N ₂ S	103~106	Needles	8.05	8.01
-CO(CO) ₂ CH ₃	C ₂₀ H ₂₈ O ₃ N ₂ S	120~121	Plates	7.45	7.51
-CO(CH ₂) ₁₀ CH ₃	C ₂₂ H ₃₂ O ₃ N ₂ S	125~127	Needles	6.93	6.81
-CO(CH ₂) ₁₂ CH ₃	C ₂₄ H ₃₆ O ₃ N ₂ S	98~101	Plates	6.47	6.50
-CO(CH ₂) ₁₄ CH ₃	C ₂₆ H ₄₀ O ₃ N ₂ S	87~89	Amorphous	6.07	6.11
-CO(CH ₂) ₁₆ CH ₃	C ₂₈ H ₄₄ O ₃ N ₂ S	105~108	Plates	5.73	5.75
-COCH ₂ CH(CH ₃) ₂	C ₁₅ H ₁₈ O ₃ N ₂ S	—	Oil	9.15	
-CO(CH ₂) ₈ CH=CH ₂	C ₂₁ H ₂₈ O ₃ N ₂ S	120~124	Needles	7.21	7.41
-CO(CH ₂) ₇ CH=CH(CH ₂) ₇ CH ₃	C ₂₈ H ₄₂ O ₃ N ₂ S	—	Oil	5.76	
-COCH=CH-	C ₁₉ H ₁₆ O ₃ N ₂ S	193~194	Light yellow needles	7.95	7.95
-CO-	C ₁₇ H ₁₄ O ₃ N ₂ S	186~187	Prisms	8.58	8.54
-COCH ₂ -	C ₁₈ H ₁₆ O ₃ N ₂ S	184~185	Plates	8.24	8.12

Most of N¹-acyl-4-acetyl-amino- and N¹-acyl-4-aminonaphthalenesulfonamides were obtained, at first, as viscous oily or amorphous substances, but after allowing to stand they solidified to crystals. In general, it was observed that lengthening of the acyl chain in the two series was attended with increased difficulty in crystallization.

Above all, it was found that N¹-acyl-4-aminonaphthalenesulfonamide, whose acyl group was an unsaturated or a branched chain, failed to crystallize. The compounds possessing higher acyl groups showed increased organic properties and N¹-acyl-4-acetyl-amino compounds were more organic in character than N¹-acyl-amino compounds: sodium salts of the latter were more easily soluble in water than those of the former.

Antiviral Activities of N¹-Acyl-4-acetylaminonaphthalenesulfonamides and N¹-Acyl-4-aminonaphthalenesulfonamides For the test of antiviral activities of these compounds *in vitro* against the Nakayama strain of *Encephalitis japonica*, the same procedures as described in Part V⁸⁾ were employed. The results are shown in Table III.

From these results, the compounds more effective *in vitro* than PANS-No. 325 were

8) T. Ueda, *et al.*: J. Pharm. Soc. Japan, **72**, 265 (1952); see p. 413 of this Bulletin.

TABLE III.

Compound	pH	Drug concentration(%)		
		0.05	0.025	0.01
N ¹ -Octanoyl-4-acetylaminonaphthalenesulfonamide	8.2	5/10	0	0
N ¹ -Decanoyl-4-acetylaminonaphthalenesulfonamide	8.2	9/9	0	0
N ¹ -Dodecanoyl-4-acetylaminonaphthalenesulfonamide	8.2	9/9	7/10	0/10
N ¹ -Tetradecanoyl-4-acetylaminonaphthalenesulfonamide	8.2	9/9	9/9	0/10
N ¹ -Hexadecanoyl-4-acetylaminonaphthalenesulfonamide	8.2	9/10	7/8	0/10
N ¹ -Octadecanoyl-4-acetylaminonaphthalenesulfonamide	8.2	9/10	10/10	0/10
N ¹ -Decanoyl-4-aminonaphthalenesulfonamide	8.0	5/10	0/10	0
N ¹ -Dodecanoyl-4-aminonaphthalenesulfonamide	8.0	9/10	4/10	0
N ¹ -Tetradecanoyl-4-aminonaphthalenesulfonamide	8.0	9/9	5/10	0
<i>p</i> -(3-Phenylazo-4-aminonaphthalenesulfonamido)-benzoic acid(PANS-No. 325)	8.2	8/10	4/10	0/10
Cotrol	7.6	0/10		

The numerator represents the number of mice that survived and the denominator, total number injected.

N¹-octanoyl, N¹-decanoyl, N¹-dodecanoyl, N¹-tetradecanoyl, N¹-hexadecanoyl, and N¹-octadecanoyl derivatives in the series of N¹-acyl-4-acetylaminonaphthalenesulfonamides, and N¹-decanoyl, N¹-dodecanoyl, and N¹-tetradecanoyl derivatives in the series of N¹-acyl-4-aminonaphthalenesulfonamides.

The curative effects of the compounds possessing comparatively high *in vitro* effect were tested on Japanese encephalitis and Lansing viruses. The procedures for the tests were the same as described in Part XVI⁹⁾: Groups of mice, infected by intranasal inoculation of virus dilutions of the Nakayama strain or Lansing strain, were administered with above compounds. From the results of these tests, only N¹-dodecanoyl-4-acetylaminonaphthalenesulfonamide showed significant effectiveness *in vivo*, and the others showed only a weak activity.

As described above, it may be said that the compounds possessing higher acyl groups in the two series showed remarkable *in vitro* activities against the Nakayama and the Lansing strains and that the compounds of the N¹-acyl-4-acetylaminonaphthalenesulfonamide series exerted stronger activity than those of the N¹-acyl-4-aminonaphthalenesulfonamide series. These facts suggest that the mode of action of the above compounds on the viruses might essentially differ from those of sulfa drugs on bacteria, and that the activities of the above compounds might be associated with their surfactant properties.

In comparing the result on encephalitis virus with that on poliomyelitis,¹⁰⁾ it may be said that the activities of the above compounds on the Nakayama strain *in vitro* did not coincide with those on the Lansing strain. This fact shows that the virus may be differentiated from each other in susceptibility to the above compounds, though classified into the same neurotropic group.

It may be said that only N¹-dodecanoyl-4-acetylaminonaphthalenesulfonamide exerted a significant *in vivo* effect among the compounds of the two series. At present, enough evidence has not been obtained on the reason why the above compound exerted both *in vitro* and *in vivo* effect exclusively.

However, it was found by Ueda *et al.*¹⁰⁾ that N¹-dodecanoyl-4-acetylaminonaphthalenesulfonamide possesses a specific surfactant property, i.e. strong surface tension-lowering and penetrating activities. Thus, this fact suggests that the compound with such surfactant activity might be able to penetrate into nervous tissues of the host and attach itself to the virus in the cells.

9) T. Ueda, S. Toyoshima, T. Wachi: This Bulletin, 1, 379(1953).

10) In preparation.

As for the mode of action of the compound against the virus, various criteria may be raised. However, it might be possible to obtain some effective compounds by introducing this concept of surface chemistry into the synthesis of N¹-substituted 4-aminonaphthalenesulfonamides and screening the resulting surfactant compounds by *in vitro* and *in vivo* tests.

Chemotherapeutic effect⁹⁾ of N¹-dodecanoyl-4-acetylaminonaphthalenesulfonamide, named PANS-No. 610, has already been examined in detail and recognized as a useful protective and curative drug against diseases caused by small virus such as the Japanese encephalitis and poliomyelitis virus.

Experimental

General Method of Synthesis of N¹-Acyl-4-acetylaminonaphthalenesulfonamides—1.1~1.2 moles of dry, finely pulverized 4-acetylaminonaphthalenesulfonamide was added into 500 cc. of dry pyridine. Agitation was started, the mixture was heated to 90°, and 1 mole of acyl chloride was added in portions through a long-stemmed funnel. The mixture was cooled from outside to prevent the temperature from exceeding 110°. The temperature was held at 100~110° for 15 mins. to complete the reaction. The resulting pyridine solution was poured into a mixture of 5 L. of water and 500 cc. conc. HCl, the product was filtered, and washed well with water. The crude N¹-acyl-4-acetylaminonaphthalenesulfonamide was dissolved in water adjusted to pH 9 with NaOH. The solution was treated with decolorizing carbon and the product was reprecipitated by acidification, and recrystallizations afforded N¹-acyl-4-acetylaminonaphthalenesulfonamide.

General Method of Synthesis of N¹-Acyl-4-aminonaphthalenesulfonamides—1 mole of the N¹-acyl-4-acetyl amino compound was added into a mixture of 480 cc. 5 N NaOH and 400 cc. EtOH. The mixture was warmed on a water bath for 1 hr. to effect hydrolysis of the N⁴-acetyl group. The hydrolyzed solution was diluted with an equal amount of water, neutralized to about pH 9, and treated with activated carbon. The clarified solution was acidified, the crude product was filtered, and by recrystallizations N¹-acyl-4-aminonaphthalenesulfonamide was obtained.

N¹-Acetyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 70% EtOH to prisms, m.p. 269~271°(decomp.). Yield, 77%. *Anal.* Calcd. for C₁₄H₁₁O₄N₂S: N, 9.15. Found: N, 9.21.

N¹-Propionyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 30% EtOH to prisms, m.p. 241~242°(decomp.). Yield, 55%. *Anal.* Calcd. for C₁₅H₁₆O₄N₂S: N, 8.76. Found: N, 8.89.

N¹-Butanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 30% EtOH to prisms, m.p. 209~211°. Yield, 55%. *Anal.* Calcd. for C₁₆H₁₈O₄N₂S: N, 8.39. Found: N, 8.47.

N¹-Hexanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 60% EtOH to needles, m.p. 214.5~216°. Yield, 66%. *Anal.* Calcd. for C₁₈H₂₂O₄N₂S: N, 7.74. Found: N, 7.69.

N¹-Octanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 60% EtOH to needles, m.p. 161~162°. Yield, 68%. *Anal.* Calcd. for C₂₀H₂₆O₄N₂S: N, 7.18. Found: N, 7.02.

N¹-Decanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 70% EtOH to prisms, m.p. 163~166.5°. Yield, 85%. *Anal.* Calcd. for C₂₂H₃₀O₄N₂S: N, 6.70. Found: N, 6.73.

N¹-Dodecanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 80% EtOH to plates, m.p. 192~195°. Yield, 80%. *Anal.* Calcd. for C₂₄H₃₄O₄N₂S: N, 6.28. Found: N, 6.54.

N¹-Tetradecanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 80% EtOH to plates, m.p. 152~156.5°. Yield, 90%. *Anal.* Calcd. for C₂₆H₃₈O₄N₂S: N, 5.94. Found: N, 5.78.

N¹-Hexadecanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 80% EtOH to plates, m.p. 169~170.5°. Yield, 70%. *Anal.* Calcd. for C₂₈H₄₂O₄N₂S: N, 5.58. Found: N, 5.72.

N¹-Octadecanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 80% EtOH to plates, m.p. 169.5~170.5°. Yield, 90%. *Anal.* Calcd. for C₃₀H₄₆O₄N₂S: N, 5.28. Found: N, 5.39.

N¹-Isovaleroyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 50% EtOH to prisms, m.p. 218.5~219°. Yield, 60%. *Anal.* Calcd. for C₁₇H₂₀O₄N₂S: N, 8.05. Found: N, 8.12.

N¹-Undecylenoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 70% EtOH to plates, m.p. 167~173°. Yield, 95%. *Anal.* Calcd. for C₂₈H₃₀O₄N₂S: N, 6.52. Found: N, 6.53.

N¹-Oleinoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 85% EtOH to amorphous powder, m.p. 159.5~161°. *Anal.* Calcd. for C₃₀H₄₄O₄N₂S: N, 5.30. Found: N, 5.32.

N¹-Cinnamoyl-4-acetylaminonaphthalenesulfonamide—Dissolved as Na salt in 60% EtOH and precipitated by AcOH to light yellow prisms, m.p. 248~249°(decomp.). Yield, 47%. *Anal.* Calcd. for C₂₁H₁₈O₄N₂S: N, 7.12. Found: N, 7.21.

N¹-Benzoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 70% EtOH to plates, m.p. 232~233°(decomp.). Yield, 38%. *Anal.* Calcd. for C₁₉H₁₆O₄N₂S: N, 7.62. Found: N, 7.58.

N¹-Phenylacetyl-4-acetylaminonaphthalenesulfonamide—Dissolved as Na salt in 60% EtOH and precipitated by AcOH to prisms, m.p. 244~245°(decomp.). Yield, 16%. *Anal.* Calcd. for C₂₃H₁₈O₄N₂S:

N, 7.33. Found: N, 7.42.

N¹-Acetyl-4-aminonaphthalenesulfonamide—Recrystd. from hot water to needles, m.p. 238~239°(decomp.). Yield, 54%. *Anal.* Calcd. for C₁₂H₁₂O₃N₂S: N, 10.60. Found: N, 10.51.

N¹-Propionyl-4-aminonaphthalenesulfonamide—Recrystd. twice from dil. EtOH to plates, m.p. 180.5~181.5°. Yield, 46%. *Anal.* Calcd. for C₁₃H₁₄O₃N₂S: N, 10.09. Found: N, 10.07.

N¹-Butanoyl-4-aminonaphthalenesulfonamide—Recrystd. twice from dil. AcOH to prisms, m.p. 155.6~156.5°. Yield, 57%. *Anal.* Calcd. for C₁₄H₁₆O₃N₂S: N, 9.57. Found: N, 9.71.

N¹-Hexanoyl-4-aminonaphthalenesulfonamide—Recrystd. twice from dil. EtOH to prisms, m.p. 172~173°. Yield, 62%. *Anal.* Calcd. for C₁₆H₂₀O₃N₂S: N, 8.75. Found: N, 8.74.

N¹-Octanoyl-4-aminonaphthalenesulfonamide—Recrystd. 4 times from toluene to needles, m.p. 103~106°. Yield, 34%. *Anal.* Calcd. for C₁₈H₂₄O₃N₂S: N, 8.05. Found: N, 8.01.

N¹-Decanoyl-4-aminonaphthalenesulfonamide—Recrystd. 3 times from toluene to plates, m.p. 120~121°. Yield, 28%. *Anal.* Calcd. for C₂₀H₂₈O₃N₂S: N, 7.45. Found: N, 7.51.

N¹-Dodecanoyl-4-aminonaphthalenesulfonamide—Recrystd. 5 times from toluene and from 80% EtOH to needles, m.p. 125~127°. Yield, 60%. *Anal.* Calcd. for C₂₂H₃₂O₃N₂S: N, 6.93. Found: N, 6.81.

N¹-Tetradecanoyl-4-aminonaphthalenesulfonamide—Recrystd. 3 times from 80% EtOH to plates, m.p. 98~101°. Yield, 30%. *Anal.* Calcd. for C₂₄H₃₆O₃N₂S: N, 6.47. Found: N, 6.50.

N¹-Hexadecanoyl-4-aminonaphthalenesulfonamide—Recrystd. 3 times from 80% EtOH to amorphous powder, m.p. 87~89°. Yield, 26%. *Anal.* Calcd. for C₂₆H₄₀O₃N₂S: N, 6.07. Found: N, 6.11.

N¹-Octadecanoyl-4-aminonaphthalenesulfonamide—Recrystd. 4 times from 80% EtOH to plates, m.p. 105~108°. Yield, 22%. *Anal.* Calcd. for C₂₈H₄₄O₃N₂S: N, 5.73. Found: N, 5.75.

N¹-Undecylenoyl-4-aminonaphthalenesulfonamide—Recrystd. 3 times from toluene to needles, m.p. 120~124°. Yield, 44%. *Anal.* Calcd. for C₂₁H₂₈O₃N₂S: N, 7.21. Found: N, 7.41.

N¹-Cinnamoyl-4-aminonaphthalenesulfonamide—Recrystd. twice from MeOH to light yellow needles, m.p. 193~194°. Yield, 67%. *Anal.* Calcd. for C₁₉H₁₆O₃N₂S: N, 7.95. Found: N, 7.95.

N¹-Benzoyl-4-aminonaphthalenesulfonamide—Recrystd. twice from 70% EtOH to prisms, m.p. 186~187°. Yield, 68%. *Anal.* Calcd. for C₁₇H₁₄O₃N₂S: N, 8.58. Found: N, 8.54.

N¹-Phenylacetyl-4-aminonaphthalenesulfonamide—Recrystd. twice from dil. EtOH to plates, m.p. 184~185°. Yield, 56%. *Anal.* Calcd. for C₁₈H₁₆O₃N₂S: N, 8.24. Found: N, 8.12.

Summary

1) Condensation of 4-acetylaminonaphthalenesulfonamide with acyl chloride afforded N¹-acyl-4-acetylaminonaphthalenesulfonamide, which was hydrolyzed to N¹-acyl-4-aminonaphthalenesulfonamide. The available conditions for accomplishing these reactions were also studied.

2) The antiviral effects of these compounds were tested against the Nakayama strain of the Japanese encephalitis virus and the Lansing strain of poliomyelitis virus.

3) Several substances in these series were found to be effective against the neurotropic virus, and N¹-dodecanoyl-4-acetylaminonaphthalenesulfonamide (PANS-No. 610) was especially of promise for chemotherapeutic use on diseases caused by neurotropic virus.

(Received June 19, 1954)