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.

N^1-(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.

N^1-(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, N^1-alkylphenyl-4-acetylaminonaphthalenesulfonamide was obtained, which was hydrolyzed to N^1-aklylphenyl-4-aminonaphthalenesulfonamide.

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

3) N^1-(2'- and 4'-Methylphenyl)-4-acetylaminonaphthalenesulfonamide and N^1-(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 N^1-Acyl-4-acetylaminonaphthalenesulfonamides and N^1-Acyl-4-aminonaphthalenesulfonamides.

(*Pharmaceutical Institute, Keio-Gijuku University***)

As described in the preceding papers, it was shown by the present authors that among the compounds of the 4-aminonaphthalenesulfonamide series, N^1-(*p*-azobenzene)-, N^1-(*o*-azotoluene)-[2], N^1-(*p*-tolyl)-, and N^1-(*o*-tolyl)-4-aminonaphthalenesulfonamides[3] and their N^1-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, N^1-acyl-4-acetylamino- and N^1-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 N^1-acyl-4-acetylamino- and N^1-acyl-4-aminonaphthalenesulfonamides.

Synthesis of N^1-Acyl-4-acetylaminonaphthalenesulfonamide N^1-Acyl-4-aminonaph-

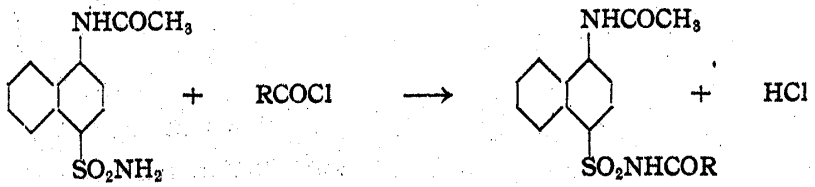
* Takeo Ueda and Shigeshi Toyoshima : Researches on Chemotherapeutic Drugs against Viruses. XXI.

** Shinano-machi, Shinjuku-ku, Tokyo (和智恒雄，和田多嘉子).

1) Part XX : This Bulletin, **2**, 419(1954).
2) T. Wachi : *Ibid.* **2**, 415(1954).
3) T. Wachi : *Ibid.* **2**, 419(1945).
4) T. Ito, *et al.* : *Ibid.*, **1**, 278(1953).

thalenesulfonamides and their N^4-acyl derivatives have not been described by either Northey[5] 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:



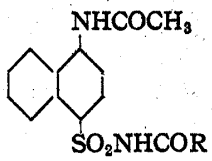
(R=alkyl, alkylenyl, aralkyl, aralkylenyl, or aryl group)

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.

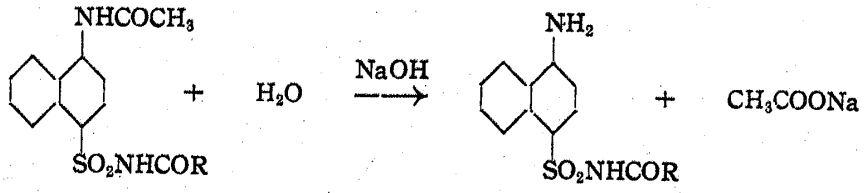
TABLE I.



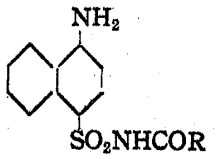
R	Mol. formula	m.p. °C. (decomp.)	Appearance	N% Calcd.	N% Found
$-COCH_3$	$C_{14}H_{14}O_4N_2S$	(269~271)	Prisms	9.15	9.21
$-COCH_2CH_3$	$C_{15}H_{16}O_4N_2S$	(241~242)	〃	8.76	8.89
$-CO(CH_2)_2CH_3$	$C_{16}H_{18}O_4N_2S$	209~211	〃	8.39	8.47
$-CO(CH_2)_4CH_3$	$C_{18}H_{22}O_4N_2S$	214.5~216	Needles	7.74	7.69
$-CO(CH_2)_6CH_3$	$C_{20}H_{26}O_4N_2S$	161~162	〃	7.18	7.02
$-CO(CH_2)_8CH_3$	$C_{22}H_{30}O_4N_2S$	163~166.5	Prisms	6.70	6.73
$-CO(CH_2)_{10}CH_3$	$C_{24}H_{34}O_4N_2S$	192~195	Plates	6.28	6.54
$-CO(CH_2)_{12}CH_3$	$C_{26}H_{38}O_4N_2S$	152~156.6	〃	5.94	5.78
$-CO(CH_2)_{14}CH_3$	$C_{28}H_{42}O_4N_2S$	169~170.5	〃	5.58	5.72
$-CO(CH_2)_{16}CH_3$	$C_{30}H_{46}O_4N_2S$	169.5~170.5	〃	5.28	5.39
$-COCH_2CH(CH_3)_2$	$C_{17}H_{20}O_4N_2S$	218.5~219	Prisms	8.05	8.12
$-CO(CH_2)_8CH=CH_2$	$C_{28}H_{30}O_4N_2S$	167~173	Plates	6.52	6.53
$-CO(CH_2)_7CH=CH(CH_2)_7CH_3$	$C_{30}H_{44}O_4N_2S$	159.5~161	Amorphous	5.30	5.32
$-COCH=CH-C_6H_5$	$C_{21}H_{18}O_4N_2S$	(248~249)	Light yellow prisms	7.12	7.21
$-CO-C_6H_5$	$C_{19}H_{16}O_4N_2S$	(232~233)	Plates	7.62	7.58
$-COCH_2-C_6H_5$	$C_{20}H_{18}O_4N_2S$	(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.	N% Found
$-COCH_3$	$C_{12}H_{12}O_3N_2S$	(238~239)	Needles	10.60	10.51
$-COCH_2CH_3$	$C_{13}H_{14}O_3N_2S$	180.5~181.5	Plates	10.09	10.07
$-CO(CH_2)_2CH_2$	$C_{14}H_{16}O_3N_2S$	155.6~156.5	Prisms	9.57	9.71
$-CO(CH_2)_4CH_3$	$C_{16}H_{20}O_3N_2S$	172~173	〃	8.75	8.74
$-CO(CH_2)_6CH_3$	$C_{18}H_{24}O_3N_2S$	103~106	Needles	8.05	8.01
$-CO(CO_2)_8CH_3$	$C_{20}H_{28}O_3N_2S$	120~121	Plates	7.45	7.51
$-CO(CH_2)_{10}CH_3$	$C_{22}H_{32}O_3N_2S$	125~127	Needles	6.93	6.81
$-CO(CH_2)_{12}CH_3$	$C_{24}H_{36}O_3N_2S$	98~101	Plates	6.47	6.50
$-CO(CH_2)_{14}CH_3$	$C_{26}H_{40}O_3N_2S$	87~89	Amorphous	6.07	6.11
$-CO(CH_2)_{16}CH_3$	$C_{28}H_{44}O_3N_2S$	105~108	Plates	5.73	5.75
$-COCH_2CH(CH_3)_2$	$C_{15}H_{18}O_3N_2S$	—	Oil	9.15	
$-CO(CH_2)_8CH=CH_2$	$C_{21}H_{28}O_3N_2S$	120~124	Needles	7.21	7.41
$-CO(CH_2)_7CH=CH(CH_2)_7CH_3$	$C_{28}H_{42}O_3N_2S$	—	Oil	5.76	
$-COCH=CH-C_6H_5$	$C_{19}H_{16}O_3N_2S$	193~194	Light yellow needles	7.95	7.95
$-CO-C_6H_5$	$C_{17}H_{14}O_3N_2S$	186~187	Prisms	8.58	8.54
$-COCH_2-C_6H_5$	$C_{18}H_{16}O_3N_2S$	184~185	Plates	8.24	8.12

Most of N¹-acyl-4-acetylamino- 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-acetylamino compounds were more organic in character than N¹-acylamino 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 V[8] 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
p-(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.

N^1-octanoyl, N^1-decanoyl, N^1-dodecanoyl, N^1-tetradecanoyl, N^1-hexadecanoyl, and N^1-octadecanoyl derivatives in the series of N^1-acyl-4-acetylaminonaphthalenesulfonamides, and N^1-decanoyl, N^1-dodecanoyl, and N^1-tetradecanoyl derivatives in the series of N^1-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 XVI[9]: 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 N^1-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 N^1-acyl-4-acetylaminonaphthalenesulfonamide series exerted stronger activitiy than those of the N^1-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 N^1-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 N^1-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 N^1-substituted 4-aminonaphthalenesulfonamides and screening the resulting surfactant compounds by *in vitro* and *in vivo* tests.

Chemotherapeutic effect[9] of N^1-dodecanoyl-4-acetylaminonaphthalenesulfonamide, named PANS-No. 610, has already been examind 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.

Experimantal

General Method of Synthesis of N^1-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 filterd, and washed well with water. The crude N^1-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 N^1-acyl-4-acetylaminonaphthalenesulfonamide.

General Method of Synthesis of N^1-Acyl-4-aminonaphthalenesulfonamides—1 mole of the N^1-acyl-4-acetylamino 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 N^4-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 N^1-acyl-4-aminonaphthalenesulfonamide was obtained.

N^1-Acetyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 70% EtOH to prisms, m.p. 269~271°(decomp.). Yield, 77%. *Anal.* Calcd. for $C_{14}H_{14}O_4N_2S$: N, 9.15. Found: N, 9.21.

N^1-Propionoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 30% EtOH to prisms, m.p. 241~242°(decomp.). Yield, 55%. *Anal.* Calcd. for $C_{15}H_{16}O_4N_2S$: N, 8.76. Found: N, 8.89.

N^1-Butanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 30% EtOH to prisms, m.p. 209~211°. Yield, 55%. *Anal.* Calcd. for $C_{16}H_{18}O_4N_2S$: N, 8.39. Found: N, 8.47.

N^1-Hexanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 60% EtOH to needles, m.p. 214.5~216°. Yield, 66%. *Anal.* Calcd. for $C_{18}H_{22}O_4N_2S$: N, 7.74. Found: N, 7.69.

N^1-Octanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 60% EtOH to needles, m.p. 161~162°. Yield, 68%. *Anal.* Calcd. for $C_{20}H_{26}O_4N_2S$: N, 7.18. Found: N, 7.02.

N^1-Decanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 70% EtOH to prisms, m.p. 163~166.5°. Yield, 85%. *Anal.* Calcd. for $C_{22}H_{30}O_4N_2S$: N, 6.70. Found: N, 6.73.

N^1-Dodecanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 80% EtOH to plates, m.p. 192~195°. Yield, 80%. *Anal.* Calcd. for $C_{24}H_{34}O_4N_2S$: N, 6.28. Found: N, 6.54.

N^1-Tetradecanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 80% EtOH to plates, m.p. 152~156.5°. Yield, 90%. *Anal.* Calcd. for $C_{26}H_{33}O_4N_2S$: N, 5.94. Found: N, 5.78.

N^1-Hexadecanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 80% EtOH to plates, m.p. 169~170.5°. Yield, 70%. *Anal.* Calcd. for $C_{23}H_{42}O_4N_2S$: N, 5.58. Found: N, 5.72.

N^1-Octadecanoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 80% EtOH to plates, m.p. 169.5~170.5°. Yield, 90%. *Anal.* Calcd. for $C_{30}H_{46}O_4N_2S$: N, 5.28. Found: N, 5.39.

N^1-Isovaleroyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 50% EtOH to prisms, m.p. 218.5~219°. Yield, 60%. *Anal.* Calcd. for $C_{17}H_{20}O_4N_2S$: N, 8.05. Found: N, 8.12.

N^1-Undecylenoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 70% EtOH to plates, m.p. 167~173°. Yield, 95%. *Anal.* Calcd. for $C_{28}H_{30}O_4N_2S$: N, 6.52. Found: N, 6.53.

N^1-Oleinoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 85% EtOH to amorphous powder, m.p. 159.5~161°. *Anal.* Calcd. for $C_{30}H_{44}O_4N_2S$: N, 5.30. Found: N, 5.32.

N^1-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 $C_{21}H_{18}O_4N_2S$: N, 7.12. Found: N, 7.21.

N^1-Benzoyl-4-acetylaminonaphthalenesulfonamide—Recrystd. from 70% EtOH to plates, m.p. 232~233°(decomp.). Yield, 38%. *Anal.* Calcd. for $C_{19}H_{16}O_4N_2S$: N, 7.62. Found: N, 7.58.

N^1-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 $C_{20}H_{18}O_4N_2S$:

N, 7.33. Found: N, 7.42.

N^1-Acetyl-4-aminonaphthalenesulfonamide—Recrystd. from hot water to needles, m.p. 238~239°(decomp.). Yield, 54%. *Anal.* Calcd. for $C_{12}H_{12}O_3N_2S$: N, 10.60. Found: 10.51.

N^1-Propionoyl-4-aminonaphthalenesulfonamide—Recrystd. twice from dil. EtOH to plates, m.p. 180.5~181.5°. Yield, 46%. *Anal.* Calcd. for $C_{13}H_{14}O_3N_2S$: N, 10.09. Found: N, 10.07.

N^1-Butanoyl-4-aminonaphthalenesulfonamide—Recrystd. twice from dil. AcOH to prisms, m.p. 155.6~156.5°. Yield, 57%. *Anal.* Calcd. for $C_{14}H_{16}O_3N_2S$: N, 9.57. Found: N, 9.71.

N^1-Hexanoyl-4-aminonaphthalenesulfonamide—Recrystd. twice from dil. EtOH to prisms, m.p. 172~173°. Yield, 62%. *Anal.* Calcd. for $C_{16}H_{20}O_3N_2S$: N, 8.75. Found: N, 8.74.

N^1-Octanoyl-4-aminonaphthalenesulfonamide—Recrystd. 4 times from toluene to needles, m.p. 103~106°. Yield, 34%. *Anal.* Calcd. for $C_{18}H_{24}O_3N_2S$: N, 8.05. Found: N, 8.01.

N^1-Decanoyl-4-aminonaphthalenesulfonamide—Recrystd. 3 times from toluene to plates, m.p. 120~121°. Yield, 28%. *Anal.* Calcd. for $C_{20}H_{28}O_3N_2S$: N, 7.45. Found: N, 7.51.

N^1-Dodecanoyl-4-aminonaphthalenesulfonamide—Recrystd. 5 times from toluene and from 80% EtOH to needles, m.p. 125~127°. Yield, 60%. *Anal.* Calcd. for $C_{22}H_{32}O_3N_2S$: N, 6.93. Found: N, 6.81.

N^1-Tetradecanoyl-4-aminonaphthalenesulfonamide—Recrystd. 3 times from 80% EtOH to plates, m.p. 98~101°. Yield, 30%. *Anal.* Calcd. for $C_{24}H_{36}O_3N_2S$: N, 6.47. Found: 6.50.

N^1-Hexadecanoyl-4-aminonaphthalenesulfonamide—Recrystd. 3 times from 80% EtOH to amorphous powder, m.p. 87~89°. Yield, 26%. *Anal.* Calcd. for $C_{23}H_{40}O_3N_2S$: N, 6.07. Found: N, 6.11.

N^1-Octadecanoyl-4-aminonaphthalenesulfonamide—Recrystd. 4 times from 80% EtOH to plates, m.p. 105~108°. Yield, 22%. *Anal.* Calcd. for $C_{23}H_{44}O_3N_2S$: N, 5.73. Found: N, 5.75.

N^1-Undecylenoyl-4-aminonaphthalenesulfonamide—Recrystd. 3 times from toluene to needles, m.p. 120~124°. Yield, 44% *Anal.* Calcd. for $C_{21}H_{28}O_3N_2S$: N, 7.21, Found: N, 7.41.

N^1-Cinnamoyl-4-aminonaphthalenesulfonamide—Recrystd. twice from MeOH to light yellow needles, m.p. 193~194°. Yield, 67%. *Anal.* Calcd. for $C_{19}H_{16}O_3N_2S$: N, 7.95. Found: N, 7.95.

N^1-Benzoyl-4-aminonaphthalenesulfonamide—Recrystd. twice from 70% EtOH to prisms, m.p. 186~187°. Yield, 68%. *Anal.* Calcd. for $C_{17}H_{14}O_3N_2S$: N, 8.58. Found: N, 8.54.

N^1-Phenylacetyl-4-aminonaphthalenesulfonamide—Recrystd. twice from dil. EtOH to plates, m.p. 184~185°. Yield, 56%. *Anal.* Calcd. for $C_{18}H_{16}O_3N_2S$: N, 8.24. Found: N, 8.12.

Summary

1) Condensation of 4-acetylaminonaphthalenesulfonamide with acyl chloride afforded N^1-acyl-4-acetylaminonaphthalenesulfonamide, which was hydrolyzed to N^1-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 N^1-dodecanoyl-4-acetylaminonaphthalenesulfonamide (PANS-No. 610) was especially of promise for chemotherapeutic use on diseases caused by neurotropic virus.

(Received June 19, 1954)