Reaction of 3,4,5,6-Tetrahydro-2*H*-azepin-7-ol Hydrogen Sulfate with Nucleophilic Reagents

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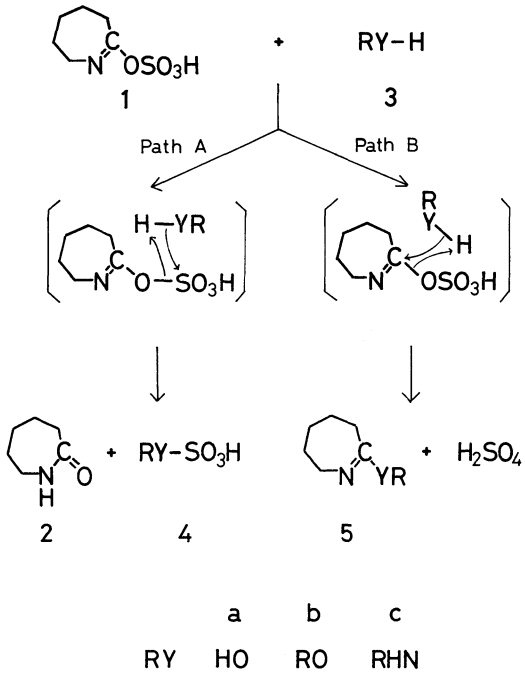
(Received May 11, 1973)

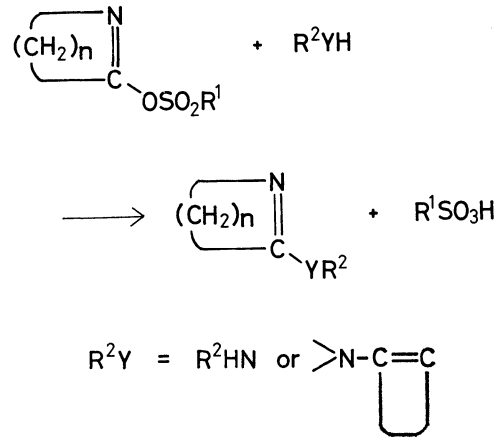
The reaction of 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate with nucleophilic reagents was studied. The tetrahydroazepin-7-ol hydrogen sulfate reacted with alcohols and oximes to give respectively ε-caprolactam and the corresponding hydrogen sulfate of the reagents in good yields. Treatment with cyclohexylamine or benzylamine afforded ε-caprolactam, the amine salt of the corresponding sulfamic acid, and the corresponding amine salt of the tetrahydroazepin-7-ol hydrogen sulfate, while anilinium phenylsulfamate was formed exclusively in the reaction with aniline. From these results, the tetrahydroazepin-7-ol hydrogen sulfate was confirmed to undergo exclusively a cleavage of the oxygen-sulfur bond by an attack of nucleophiles on the sulfur atom.

3,4,5,6-Tetrahydro-2*H*-azepin-7-ol hydrogen sulfate (**1**) is known as an isolatable intermediate in a Beckmann rearrangement of cyclohexanone oxime to ε-caprolactam (**2**), when sulfuric acid and/or sulfur trioxide is used as the rearranging agent.[1,2] However, the reactivity of **1** has not been studied except for hydrolysis,[2] which gave ε-caprolactam (**2**) and sulfuric acid. The hydrolytic reaction can be envisaged to take place through two pathways (Scheme 1); A which involves a nucleophilic attack by water (**3a**) on the sulfur atom of **1**, resulting in the tetrahydroazepinyl substituted oxygen-sulfur bond fission, and B which involves a nucleophilic attack by water (**3a**) on the carbon atom, resulting in the carbon-oxygen bond fission. No report has referred to the mechanism of the hydrolysis, presumably because both pathways give rise to identical products.

When nucleophilic reagents other than water such as alcohol or amine are used with **1**, a reaction along path A would give ε-caprolactam (**2**) and the corresponding sulfonated derivatives of reagent (**4**), while path B would give rise to the formation of sulfuric acid and 7-substituted 3,4,5,6-tetrahydro-2*H*-azepine derivatives (**5**), such as 7-alkoxy (**5b**) or 7-amino compound (**5c**). Reactions of 2-aza-1-cycloalkenyl benzenesulfonates with amine[3,4] or enamine[5] have been reported to yield α-substituted cyclic imino compounds resulting from the cleavage of the carbon-oxygen bond (Scheme 2). Thermal rearrangement of cycloalkanone oxime benzenesulfonates in the presence of alcohols or amines is also known to give α-substituted cyclic imino compounds.[6] The reaction of the oxime benzenesulfonates with acetic acid or methanol afforded lactam as a main product.[7]



Scheme 1.



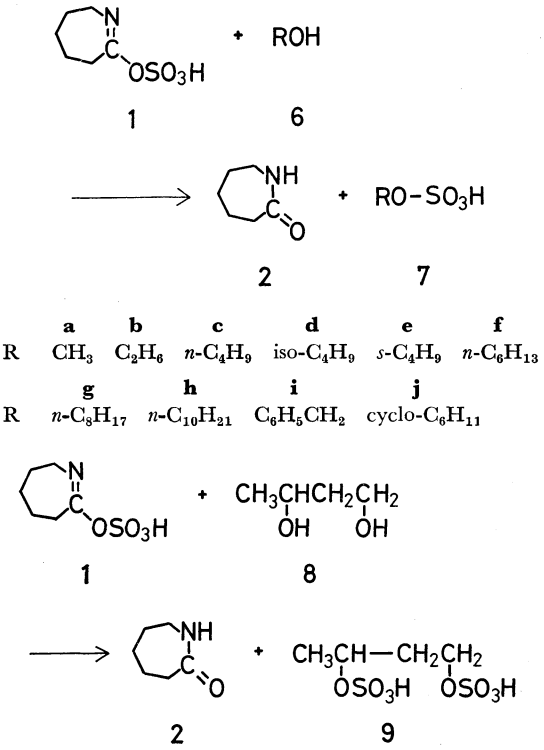
Scheme 2.

We have found that nucleophilic reagents caused an exclusive cleavage of the oxygen-sulfur bond of tetrahydroazepin-7-ol hydrogen sulfate (**1**, path A). This paper describes the reaction of **1** with alcohols, amines, and oximes.

1) L. Giuffre, G. Sioli, and E. Losio, *Chim. Ind. (Milan.)*, **50**, 983 (1968).
2) A. F. Turbak, *Ind. Eng. Chem., Prod. Res. Develop.*, **7**, 190 (1968).
3) P. Oxley, D. A. Peak, and W. F. Short, *J. Chem. Soc.*, **1948**, 1618.
4) R. Huisgen, D. Vossius, and M. Appl, *Chem. Ber.*, **91**, 1 (1958).
5) S. Hünig, W. Lücke, V. Meuer, and W. Grässmann, *Angew. Chem.*, **75**, 295 (1963).
6) P. Oxley and W. F. Short, *J. Chem. Soc.*, **1948**, 1514.
7) W. Z. Heldt, *J. Amer. Chem. Soc.*, **80**, 5880 (1958).

Results and Discussion

Reaction of 3,4,5,6-Tetrahydro-2H-azepin-7-ol Hydrogen Sulfate (1) with Alcohols. When **1** was treated with methanol (**6a**) in ethylene dichloride at 50 °C, ε-caprolactam (**2**) and monomethyl sulfate (**7a**) were obtained in 99 and 85% yields, respectively. The latter was isolated as a sodium salt. A similar treatment of **1**



with a half equiv. of 1,3-butanediol (**8**) yielded ε-caprolactam and 1,3-butanediol bis(hydrogen sulfate) (**9**) in 96 and 90% yields, respectively. **9** was isolated as a barium salt. Similarly, reactions of **1** with various alcohols (**6**) gave ε-caprolactam and the corresponding monoalkyl sulfates (**7**) in good yields. Monoalkyl sulfates (**7**) were isolated as stable salts with *S*-benzylthioformamidine. The results are summarized in Tables 1 and 2.

Table 1. Reaction of 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate (**1**) with alcohols

	Alcohol	Products, yields %	
		Lactam	Monoalkyl sulfate
6a	Methanol	99	85[a]
6b	Ethyl alcohol	90	51[b]
6c	Butyl alcohol	98	95[b]
6d	Isobutyl alcohol	97	89[b]
6e	*sec*-Butyl alcohol	94	86[b]
6f	Hexyl alcohol	77	78[b]
6g	Octyl alcohol	83	80[b]
6h	Decyl alcohol	72	86[b]
6i	Benzyl alcohol	65	89[b]
6j	Cyclohexanol	98	83[b]
8	1,3-Butanediol	96	90[c]

a) Based on conversion into the sodium salt.
b) Based on conversion into the *S*-Benzylthioformamidinium salt.
c) Based on conversion into the barium salt.

Table 2. *S*-Benzylthioformamidinium monoalkyl sulfates

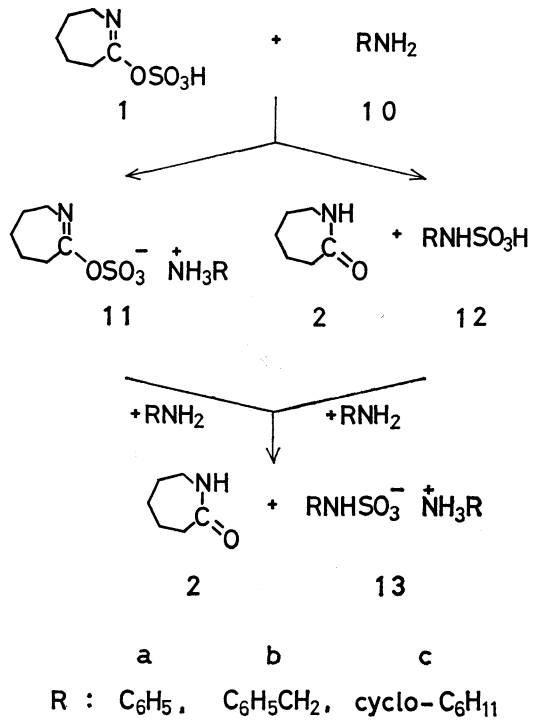
$R\text{-}OSO_3^-\ \ H_2N^+=C(NH_2)\text{—}S\text{—}CH_2C_6H_5$

R	Mp, °C	Formula		Anal % Calcd	Anal % Found
C_2H_5	112—114	$C_{10}H_{16}N_2O_4S_2$	C	41.10	41.11
			H	5.52	5.38
			N	9.59	9.61
			S	21.90	21.56
C_4H_9	99—100	$C_{12}H_{20}N_2O_4S_2$	N	8.74	8.66
			S	20.01	19.82
iso-C_4H_9	134—137	$C_{12}H_{20}N_2O_4S_2$	N	8.74	8.85
			S	20.01	20.31
sec-C_4H_9	124—126	$C_{12}H_{20}N_2O_4S_2$	N	8.74	8.92
			S	20.01	20.10
C_6H_{13}	83—84.5	$C_{14}H_{24}N_2O_4S_2$	C	42.27	42.49
			H	6.94	6.78
			N	8.04	8.16
			S	18.37	18.57
C_8H_{17}	69—70.5	$C_{16}H_{28}N_2O_4S_2$	C	51.05	50.96
			H	7.50	7.27
			N	7.44	7.80
			S	17.00	17.22
$C_{10}H_{21}$	63—66	$C_{18}H_{33}N_2O_4S_2$	C	53.45	53.83
			H	7.98	7.95
			N	6.92	6.53
			S	15.85	15.65
$C_6H_5CH_2$	145—147	$C_{15}H_{18}N_2O_4S_2$	C	50.83	50.69
			H	5.12	5.09
			N	7.90	7.79
			S	18.09	18.41
cyclo-C_6H_{11}	170—173	$C_{14}H_{22}N_2O_4S_2$	C	48.53	48.67
			H	6.40	6.17
			N	8.09	8.31

In these reactions, formation of 7-alkoxy-3,4,5,6-tetrahydro-2*H*-azepine (**5b**, path B) was not detected. In a reaction of **1** with *tert*-butyl alcohol, ε-caprolactam (**2**) and sulfuric acid were isolated. Formation of sulfuric acid could be explained by the decomposition[8] of mono-*tert*-butyl sulfate formed initially, along path A.

Reaction of 3,4,5,6-Tetrahydro-2H-azepin-7-ol Hydrogen Sulfate (1) with Amines. Treatment of **1** with 2 equiv. of aniline (**10a**) in ethylene dichloride at refluxing temperature afforded **2** and anilinium phenylsulfamate (**13a**) in 93 and 87% yields, respectively. However, reaction of **1** with 2 equiv. of benzylamine (**10b**) afforded not only **2** and benzylammonium benzylsulfamate (**13b**), but also benzylamine salt of **1** (**11b**). A considerable amount of the latter was obtained even when the reaction was carried out at 80 °C for 7 hr. Similarly, reaction of **1** with 2 equiv. of cyclohexylamine (**10c**) afforded **2**, cyclohexylammonium cyclohexanesulfamate (**13c**), and cyclohexylamine salt of **1**

8) C. M. Suter and J. D. Malkemus, *ibid.*, **63**, 978 (1941).



(**11c**) in 22, 27, and 69% yields, respectively.

Thus, the reaction of **1** with an amine could be explained to consist of two competitive reactions, a simple salt formation between **1** and the amine, and a nucleophilic attack of the amine on sulfur atom of **1** to give **2** and the corresponding sulfamic acid (**12**) which afforded the corresponding ammonium salt (**13**). Exclusive formation of **13a** in the reaction with aniline was rationalized by the fact that **11a** could undergo a further nucleophilic attack by another molecule of aniline to give **2** and **13a**.

When **1** was treated with 1 equiv. of aniline below −8 °C, aniline salt of **1** (**11a**) was produced in 75% yield. A reaction of **11a** with aniline at 80 °C resulted in the formation of **13a** in 67% yield. The cyclohexylamine salt (**11c**) was obtained by a treatment of **1** with 1 equiv. of cyclohexylamine (**10c**) in 76% yield. Reaction of **11c** with aniline was carried out at 80 °C for 1 hr, the starting materials being recovered.

The difference in reactivity of **11a** and **11c** could be ascribed to the basicity of the parent amines (**10**). The anionic character of sulfate moiety of the salt (**11**) would increase with increasing basicity of **10**. The electron density on the sulfur atom of sulfate (**11c**) would be larger than that of sulfate (**11a**), and it would become difficult for the former to undergo a nucleophilic attack by an amine on the sulfur atom as compared with the case of aniline salt (**11a**). Analogous phenomena have been observed in the Beckmann rearrangement of cyclohexanone oxime hydrogen sulfate (**15a**), its rearrangement being retarded by the Lewis base.[9] Salt formation with the base would increase the electron density on the sulfur atom of **15a** and make the heterolytic fission of nitrogen-oxygen bond more difficult, which is a rate-determining step in the rearrangement.[10]

Table 3. Reaction of 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate (**1**) with oximes

	Oxime	Products, yield %	
		Lactam	Oxime hydrogen sulfate
14a	Cyclohexanone oxime	82	90[a]
14b	Acetoxime	100	85[b]
14c	Acetophenone oxime	66	50[b]
14d	Cyclopentanone oxime	96	63[b]
14e	Cyclododecanone oxime	100	68[b]

a) Based on conversion into the anilinium salt.
b) Based on conversion into the imidazolium salt.

Table 4. Imidazolium salts of oxime hydrogen sulfates (**15**)

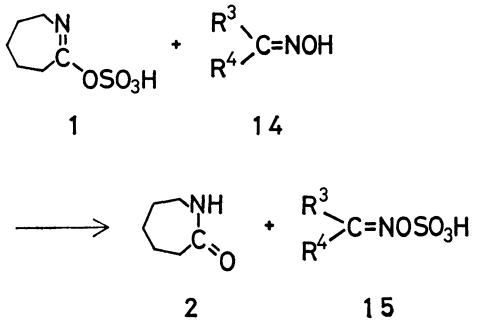
$$\begin{matrix} R_3 \\ R_4 \end{matrix}\!\!>\!CNOSO_3H\cdot\text{Imidazole}$$

R^3	R^4	Mp, °C	Formula		Anal % Calcd	Found
CH_3	CH_3	102—105[a]	$C_6H_{11}N_3O_4S$	N	18.99	18.84
				S	14.49	14.37
CH_3	C_6H_5	92—95[b]	$C_{11}H_{13}N_3O_4S$	N	14.87	14.86
				S	11.32	11.08
$-(CH_2)_4-$		79—84[b]	$C_8H_{13}N_3O_4S$	N	16.99	16.90
				S	12.97	12.13
$-(CH_2)_{11}-$		157—159[c]	$C_{15}H_{27}N_3O_4S$	N	12.16	12.56
				S	9.28	9.67

a) Recrystallized from methanol–acetone.
b) Recrystallized from methanol–ether.
c) Recrystallized from methanol.

In every reaction of **1** with amines, no formation of 7-amino derivatives of 3,4,5,6-tetrahydro-2*H*-azepine (**5c**) could be observed which might be formed according to path B.

*Reaction of 3,4,5,6-Tetrahydro-2*H*-azepin-7-ol Hydrogen Sulfate (1) with Oximes.* **1** was treated with cyclohexanone oxime (**14a**) in ethylene dichloride to give cyclohexanone oxime hydrogen sulfate (**15a**) and **2** in



a $-(CH_2)_5-$
b CH_3 CH_3
c CH_3 C_6Ht
d $-(CH_2)_4-$
e $-(CH_2)_{11}-$

9) K. Fukui, M. Uchida, and M. Masaki, This Bulletin, **46**, 3168 (1973).

10) L. G. Donaruma and W. Z. Heldt, "Organic Reactions," Vol. 11, ed. by A. C. Cope, Wiley, New York, N. Y. (1960), p. 1.

good yields. Formation of **15a** was confirmed by treatment of the reaction mixture with aniline, giving aniline salt of cyclohexanone oxime hydrogen sulfate in 90% yield. Similar reactions of **1** with acetoxime (**14b**), acetophenone oxime (**14c**), cyclopentanone oxime (**14d**), and cyclododecanone oxime (**14e**) resulted in the formation of the corresponding oxime hydrogen sulfate (**15**) and **2** in good yields. Most of the oxime hydrogen sulfate (**15**) were isolated as stable salts with imidazole. The results are summarized in Tables 3 and 4.

Experimental

Concentration and evaporation were performed with a rotary evaporator under reduced pressure. Melting points were determined in a liquid bath and are uncorrected. Reagents and organic solvents for reactions were used as anhydrous states.

3,4,5,6-Tetrahydro-2H-azepin-7-ol Hydrogen Sulfate (1). A solution of **1** in ethylene dichloride was prepared by two methods. *a*) A modification of the method of Giuffre *et al*:[1] A solution of sulfur trioxide (2 ml, 48 mmol) in ethylene dichloride (40 ml) was added dropwise to a solution of ε-caprolactam (5.42 g, 48 mmol) in an appropriate amount of ethylene dichloride with stirring under ice cooling; *b*) A modification of the method of Turbak:[2] A suspension of cyclohexanone oxime hydrogen sulfate was heated to 40—50 °C until exothermic rearrangement took place.

Reaction of 1 with Methanol. Methanol (3.8 g, 120 mmol) was added dropwise with stirring at room temperature to a solution of **1** (120 mmol) in ethylene dichloride (250 ml). The mixture was then stirred at room temperature for 30 min, heated to 50 °C and further stirred for 30 min. The reaction mixture was concentrated. The syrup-like residue was dissolved in ice water (50 ml) and treated with a solution of sodium hydroxide (4.8 g, 120 mmol) under cooling. The solution was then extracted with chloroform (50 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **2**. Yield 13.5 g (99%).

The aqueous solution remaining after chloroform extraction was concentrated to 10 ml, and ethyl alcohol (50 ml) was added to the concentrate. The crystalline precipitate was collected by filtration and found to be identical with authentic sodium monomethyl sulfate monohydrate by infrared spectrum. Yield 15.5 g (85%).

Reaction of 1 with 1,3-Butanediol. A solution of 1,3-butanediol (5.4 g, 60 mmol) in ethylene dichloride (20 ml) was added dropwise to a solution of **1** (120 mmol) in ethylene dichloride (250 ml) with stirring at room temperature. The mixture was thereafter stirred for 30 min at room temperature, heated to 50 °C and stirred for 30 min. The reaction mixture was concentrated. The syrup-like residue was dissolved in ice water (50 ml) and neutralized with an aqueous barium hydroxide. The aqueous solution was extracted with chloroform (50 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **2**. Yield 13 g (96%).

The aqueous solution remaining after chloroform extraction was treated with activated carbon and concentrated to 20 ml. Ethyl alcohol was added to the concentrate to cause precipitation of barium 1,3-butanediol bis(hydrogen sulfate) dihydrate, which was collected by filtration and confirmed by an infrared spectroscopic comparison with that of an authentic sample. Yield 19.2 g (90%).

Reaction of 1 with Ethyl Alcohol. To a solution of **1** (48 mmol) in ethylene dichloride (85 ml) was added dropwise at room temperature a solution of ethyl alcohol (2.2 g, 48 mmol) in ethylene dichloride (15 ml). The mixture was stirred for 1 hr at room temperature, heated to 50 °C, and further stirred for 30 min. The reaction mixture was concentrated. The syrup-like residue was dissolved in water (25 ml) and neutralized with sodium bicarbonate. The aqueous solution was then extracted with chloroform (30 ml× 5). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **2**. Yield 4.85 g (89%).

The aqueous solution remaining after chloroform extraction was treated with activated carbon. A solution of *S*-benzylthioformamidine hydrochloride (9.72 g, 48 mmol) in water (15 ml) was then added to the aqueous solution. The resulting solution was concentrated and ethyl alcohol was added to the residue. An insoluble matter was removed by filtration and the filtrate was treated with water (30 ml) to give *S*-benzylthioformamidinium monoethyl sulfate as pale yellow needles. Yield 1.05 g (7%). The mp and analytical results are shown in Table 2.

The filtrate was concentrated and the residue was treated with methanol (90 ml) to afford more *S*-benzylthioformamidinium monoethyl sulfate. Yield 5.8 g (41%).

Reaction of 1 with Butyl Alcohol, Isobutyl Alcohol, sec-Butyl Alcohol, Hexyl Alcohol, Octyl Alcohol, Decyl Alcohol, Benzyl Alcohol, or Cyclohexanol. In a similar way to that for the reaction of **1** with ethyl alcohol, a solution of **1** (48 mmol) in ethylene dichloride (85 ml) was treated with a solution of the alcohol (48 mmol) in ethylene dichloride (15 ml). The results are summarized in Tables 1 and 2.

Reaction of 1 with tert-Butyl Alcohol. To a solution of **1** (48 mmol) in ethylene dichloride (70 ml) was added dropwise with stirring below 0 °C a solution of *tert*-butyl alcohol (3.6 g, 48 mmol) in ethylene dichloride (10 ml). The mixture was stirred at room temperature for 2 hr and at 40 °C for 1 hr, and then treated with aniline (4.5 g, 48 mmol) under 0 °C. The resulting mixture was allowed to stand overnight. The crystalline substance collected by filtration was confirmed as anilinium sulfate by comparison of its infrared spectrum with that of the authentic sample. Yield 6.76 g (48% based upon **1**). The filtrate was concentrated to half, and treated with aniline (4.5 g, 48 mmol) under ice cooling to afford more anilinium sulfate. Yield 5.56 g (39%).

The ethylene dichloride solution separated from the above crystalline substance by filtration was concentrated. The residue was dissolved in water (40 ml) and hydrochloric aicd (1N, 10 ml) and extracted with chloroform (50 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **2**. Yield 4.93 g (91%).

Reaction of 1 with Two Equiv. of Aniline. To a solution of **1** (48 mmol) in ethylene dichloride (80 ml) was added dropwise below −5 °C with stirring a solution of aniline (8.93 g, 96 mmol) in ethylene dichloride (20 ml). Stirring was continued for 30 min. The mixture was heated under reflux for 1 hr, and then allowed to stand at room temperature to cool down. The precipitated crystals were collected by filtration and identified as anilinium phenylsulfamate (**13a**) by comparison of its infrared spectrum with that of the authentic sample.[9]

The mother liquor separated from the crystals was concentrated. Water (50 ml) was added to the residue, and the aqueous solution was washed with ether (50 ml) and extracted with chloroform (50 ml×5). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **2**. Yield 5 g (93%).

Reaction of 1 with One Equiv. of Aniline. A solution of aniline (4.47 g, 48 mmol) in ethylene dichloride (30 ml) was added dropwise to a solution of **1** (48 mmol) in ethylene dichloride (100 ml) with stirring below −8 °C, taking about 15 min. Stirring was continued for 2 hr below −5 °C and overnight at room temperature. The mixture was filtered to give 11.94 g of colorless powder, which was identified by elemental analysis and infrared spectrum as a homogeneous mixture of aniline salt of 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate and anilinium hydrogen sulfate (4:1 in molar ratio). Mp 124—146 °C. Found: C, 48.43; H, 6.06; N, 9.43; S, 12.24%. Calcd for $(C_{12}H_{18}N_2O_4S)_4 \cdot C_6H_9NO_4S$: C, 48.53; H, 6.07; N, 9.44; S, 11.99%. The infrared spectrum exhibited characteristic absorption bands at 1650 cm^{-1} (C=N), and 1270 and 1200 cm^{-1} (SO_2). The yield of **11a** was 10.23 g (75%).

The filtrate was concentrated, and the residue was dissolved in water (12 ml) and extracted with chloroform (20 ml×5). The combined extracts were dried over anhydrous sodium sulfate and concentrated to dryness, yielding 1.13 g (21%) of **2**.

Reaction of Aniline Salt of 1 (11a) with Aniline. A solution of aniline (2.81 g, 30 mmol) in ethylene dichloride (20 ml) was added with stirring below 0 °C to a suspension of a mixture of **11a** (6.5 g, 22.8 mmol) and anilinium hydrogen sulfate (1.1 g, 5.7 mmol) in ethylene dichloride (40 ml). The mixture was stirred at room temperature for 1 hr and then at the refluxing temperature for 1 hr. Filtration afforded 7 g of colorless powder which was identified by infrared spectrum as a mixture consisting of anilinium phenylsulfamate (**13a**) and a small amount of anilinium sulfate.

Reaction of 1 with Two Equiv. of Benzylamine. To a solution of **1** (48 mmol) in ethylene dichloride (80 ml) was added dropwise at room temperature with stirring a solution of benzylamine (10.27 g, 96 mmol) in ethylene dichloride (20 ml) over 17 min period. When the reaction temperature reached 40 °C at the highest, crystals were precipitated. It was then heated under reflux for 7 hr and cooled. The crystalline precipitate was collected by filtration. 7.09 g of benzylammonium benzylsulfamate (**13b**) was obtained, which was identified by comparison of its infrared spectrum with that of the sample synthesized by a reaction of sulfur trioxide–1,4-dioxane complex with 2 equiv. of benzylamine. Yield 50%.

The filtrate separated from **13b** was concentrated and the residue was treated with benzene (50 ml). The crystalline substance collected by filtration was identified by infrared spectrum as a mixture (4.33 g) of **13b** and benzylamine salt of **1** (**11b**), which exhibited characteristic absorption bands at 1630 cm^{-1} (C=N), and 1260 and 1210 cm^{-1} (SO_2). The mixture was dissolved in water (50 ml), and the resulting solution was heated under reflux for 1 hr and extracted with chloroform (50 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **2**. Yield 1.39 g (26%). The yield of **11b** was 3.74 g (26%) and that of **13b** 0.59 g (4%).

The filtrate was concentrated, and the residue was dissolved in aqueous sulfuric acid (0.5N, 40 ml) and extracted with chloroform (40 ml×5). Concentration of the combined extracts afforded a yellow oily substance (7.16 g), which was extracted with hot hexane (50 ml×4). Evaporation of hexane from the combined extracts afforded **2** as colorless crystals. Yield 2.99 g (55%).

Reaction of 1 with Two Equiv. of Cyclohexylamine. To a solution of **1** (48 mmol) in ethylene dichloride (80 ml) was added dropwise with stirring below −2 °C a solution of cyclohexylamine (9.5 g, 96 mmol) in ethylene dichloride (20 ml). The mixture was stirred at room temperature for 1.5 hr, heated under reflux for 1 hr, and allowed to stand at room temperature to cool down. The crystalline substance collected by filtration was identified by infrared spectrum as cyclohexylammonium cyclohexanesulfamate (**13c**). Yield 4.06 g (27%).

The filtrate separated from **13c** was concentrated and the residue was treated with benzene (100 ml). The crystalline precipitate was collected by filtration and identified by infrared spectrum as cyclohexylamine salt of **1** (**11c**), which exhibited characteristic absorption bands at 1630 cm^{-1} (C=N), and 1260 and 1210 cm^{-1} (SO_2). Yield 9.72 g (69%).

The filtrate was concentrated, and the residue was dissolved in water (35 ml) and extracted with chloroform (40 ml×4). Concentration of the combined extracts afforded an oily substance (2.77 g), which was extracted with hot hexane (60 ml×4). Evaporation of hexane from the combined extracts afforded **2** as colorless crystals. Yield 1.22 g (22%).

Reaction of 1 with One Equiv. of Cyclohexylamine. A solution of cyclohexylamine (4.75 g, 48 mmol) in ethylene dichloride (20 ml) was added dropwise to a solution of **1** (48 mmol) in ethylene dichloride (80 ml) with stirring below −7 °C. Stirring was continued for 30 min below −9 °C and overnight at room temperature. The mixture was filtered to give 7.42 g of colorless powder, which was identified by infrared spectrum as cyclohexylamine salt of **1** (**11c**). Yield 53%.

The filtrate separated from **11c** was evaporated and the residue was treated with benzene (100 ml) to give more **11c** as an insoluble matter. Yield 3.19 g (23%).

Reaction of Cyclohexylamine Salt of 1 (11c) with Aniline. A solution of aniline (2.79 g, 30 mmol) in ethylene dichloride (10 ml) was added with stirring at room temperature to a suspension of **11c** (8.76 g, 30 mmol) in ethylene dichloride (50 ml). The mixture was heated under reflux for 1 hr and stirred at room temperature for 2 hr. The mixture was concentrated and the residue was treated with benzene (50 ml). The crystalline substance collected by filtration was identified as the starting material, amine salt (**11c**). Yield 7.36 g (84%).

Benzylammonium Benzylsulfamate (13b). A solution of 1,4-dioxane (4.4 g, 50 mmol) in ethylene dichloride (20 ml) was added dropwise to a solution of sulfur trioxide (2 ml, 48 mmol) in ethylene dichloride (40 ml) with stirring below 4 °C. To the resulting suspension of sulfur trioxide–1,4-dioxane complex was added dropwise with stirring below −1 °C a solution of benzylamine (10.3 g, 96 mmol) in ethylene dichloride (30 ml). The mixture was stirred at room temperature for 4 hr, and the crystalline substance, benzylammonium benzylsulfamate (**13b**), was collected by filtration. Yield 11.45 g (81%). Recrystallization from methanol gave colorless needles, mp 174—176 °C. Found: C, 57.04; H, 6.40; N, 9.71%. Calcd for $C_{14}H_{18}N_2O_3S$: C, 57.14; H, 6.12; N, 9.52%.

Cyclohexylammonium Cyclohexanesulfamate (13c). A suspension of sulfur trioxide–1,4-dioxane complex (1:1 in molar ratio, 48 mmol) in ethylene dichloride (60 ml) was treated with a solution of cyclohexylamine (9.5 g, 96 mmol) in ethylene dichloride (30 ml) in a similar way to that for **13b**. The mixture was stirred at room temperature and filtered to give 9.48 g of cyclohexylammonium cyclohexanesulfamate (**13c**). Yield 71%. Recrystallization from methanol–ether gave colorless crystals, mp 191 °C (lit,[11] 198—200 °C). Found: N, 10.18; S, 11.37%. Calcd for $C_{12}H_{26}$-

11) L. F. Audrieth and M. Sveda, *J. Org. Chem.*, **9**, 89 (1944).

N_2O_3S: N, 10.07; S, 11.51%.

*Reaction of **1** with Cyclohexanone Oxime.* A solution of cyclohexanone oxime (13.6 g, 120 mmol) in ethylene dichloride (50 ml) was added dropwise to a solution of **1** (120 mmol) in ethylene dichloride (170 ml) with stirring below 3 °C. Stirring was continued further for 30 min under cooling and for 1 hr at room temperature. The mixture was then treated with a solution of aniline (11.2 g, 120 mmol) in ethylene dichloride (30 ml) below 0 °C and stirred at room temperature for 1 hr. The crystalline precipitate was collected by filtration and identified by comparison of its infrared spectrum with that of authentic aniline salt of cyclohexanone oxime hydrogen sulfate.[9] Yield 31.3 g (90%).

Concentration of the filtrate afforded an oily substance which was dissolved in water (50 ml), washed with benzene (10 ml) and extracted with chloroform (50 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **2**. Yield 11.2 g (82%).

*Reaction of **1** with Acetoxime.* To a solution of **1** (48 mmol) in ethylene dichloride (90 ml) was added dropwise with stirring below −2 °C a solution of acetoxime (3.5 g, 48 mmol) in ethylene dichloride (20 ml). The mixture was stirred for 1 hr at room temperature, and then cooled down to −5 °C or below. A solution of imidazole (3.3 g, 48 mmol) in ethylene dichloride (50 ml) was then added dropwise to the mixture. A colorless precipitate was formed at once. Stirring was continued for further 30 min under cooling. The precipitated imidazole salt of acetoxime hydrogen sulfate was collected by filtration. Yield 8.9 g (84%). Recrystallization from methanol–acetone gave colorless prisms, mp 102—105 °C. Found: N, 18.84; S, 14.37%. Calcd for $C_6H_{11}N_3O_4S$: N, 18.99; S, 14.49%.

Concentration of the filtrate afforded a syrup-like residue which was extracted with benzene (30 ml), the extract being evaporated to give **2**. Yield 5.3 g (98%).

*Reaction of **1** with Acetophenone Oxime, Cyclopentanone Oxime, and Cyclododecanone Oxime.* In a similar way to that for the reaction of **1** with acetoxime, a solution of **1** (48 mmol) in ethylene dichloride (80 ml) was treated with a solution of acetophenone oxime (6.5 g, 48 mmol), cyclopentanone oxime (4.7 g, 48 mmol), or cyclododecanone oxime (9.5 g, 48 mmol) in an appropriate amount of ethylene dichloride. The reaction mixture was then treated with a solution of imidazole (3.8 g, 48 mmol) in chloroform (30 ml). The results are summarized in Tables 3 and 4.