BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 3168—3173 (1973)

Formation and Reaction of Cyclohexanone Oxime Hydrogen Sulfate[1)]

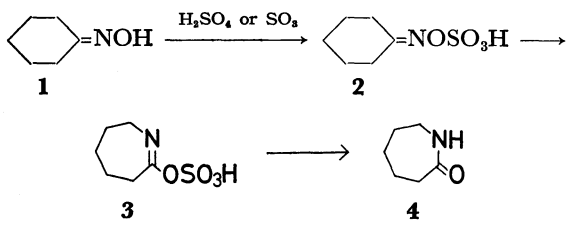
Kiyoshi FUKUI, Masaru UCHIDA, and Mitsuo MASAKI

Polymer Research Laboratory, Ube Industries, Ltd., Goi, Minamikaigan, Ichihara, Chiba 290

(Received May 11, 1973)

Cyclohexanone oxime hydrogen sulfate, prepared by the reaction of cyclohexanone oxime with sulfur trioxide–1,4-dioxane complex under mild conditions, was isolated as stable salts with various Lewis bases. It was found that a Beckmann rearrangement of the oxime hydrogen sulfate to 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate was retarded by the weak Lewis base 1,4-dioxane and prevented by a stronger Lewis base aniline. The rearrangement of the oxime hydrogen sulfate was also found to be promoted by Lewis acids such as sulfur trioxide, tin tetrachloride or zinc chloride. Hydrogen chloride retarded the rearrangement. Alcoholysis of the oxime hydrogen sulfate gave cyclohexanone oxime and monoalkyl sulfate quantitatively, while hydrolysis of the oxime hydrogen sulfate gave cyclohexanone, cyclohexanone oxime and ε-caprolactam.

It has been suggested that the Beckmann rearrangement of cyclohexanone oxime (**1**) by sulfuric acid and/or sulfur trioxide involves cyclohexanone oxime hydrogen sulfate (**2**) and 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate (**3**) as intermediates.[2,3)] Ogata *et al.*[3)] obtained **2** as an unstable solid in the reaction of **1** with chlorosulfonic acid. Csuros *et al.*[4)] reported that the reaction of cyclohexanone with hydroxylamine-*O*-sulfonic acid in the presence of potassium bicarbonate led to the formation of potassium salt of **2** (**5a**), which was hydrolyzed to ε-caprolactam (**4**) in aqueous acidic or basic solution. **3** was isolated in the reaction of **1** with the sulfur trioxide–1,4-dioxane complex by Turbak,[5)] who postulated that **2** was an intermediate in the reaction. However, very little is known about the reactivity of these intermediates. This paper deals with the formation and reactions of **2**.



Formation of **2** by the reaction of **1** with sulfur trioxide has not been reported, presumably because the reactivity of free sulfur trioxide is too great to permit

1) A Japanese patent has been applied for a part of this work: M. Masaki and M. Uchida (to Ube Ind., Ltd.), Japanese Patent Application, S. 44-67955 (1969).

2) D. E. Pearson and F. Ball, *J. Org. Chem.*, **14**, 118 (1949).

3) Y. Ogata, M. Okano, and K. Matsumoto, *J. Amer. Chem. Soc.*, **77**, 4643 (1955).

4) Z. Csuros, K. Zech, S. Zech, and G. Binder, *Acta Chim. Hung.*, **1**, 83 (1951).

5) A. F. Turbak, *Ind. Eng. Chem., Prod. Res. Develop.*, **7**, 189 (1968).

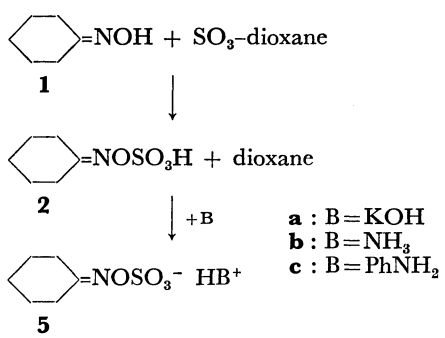
Table 1. Salt of cyclohexanone oxime hydrogen sulfate (**2**) with Lewis bases

Lewis Base	Yield %	Mp °C	Formula	Anal, %	
				Calcd	Found
Diethylamine	91	136—138[a]	$C_{10}H_{22}N_2O_4S$	C, 45.09	45.20
				H, 8.33	8.05
				N, 10.52	10.79
				S, 12.04	12.03
Triethylamine	87	—[b]	$C_{12}H_{26}N_2O_4S$	N, 9.51	9.13
				S, 10.89	11.52
n-Propylamine	96	125—128	$C_9H_{20}N_2O_4S$	C, 42.84	42.87
				H, 7.99	7.84
				N, 11.10	10.45
				S, 12.71	12.90
Isopropylamine	94	107—110	$C_9H_{20}N_2O_4S$	N, 11.10	11.26
				S, 12.71	12.98
t-Butylamine	99	160—163[a]	$C_{10}H_{22}N_2O_4S$	N, 10.52	10.14
				S, 12.04	11.91
Cyclohexylamine	95	156—158[a]	$C_{12}H_{24}N_2O_4S$	N, 9.58	9.29
				S, 10.96	10.78
Aniline	92	170—175[c]	$C_{12}H_{18}N_2O_4S$	C, 50.33	50.19
				H, 6.34	6.53
				N, 9.78	10.01
Imidazole	100	114—116[d]	$C_9H_{15}N_3O_4S$	C, 41.37	41.54
				H, 5.79	5.78
				N, 16.08	16.18

a) Recrystallized from methanol–ether.
b) Attempts to determine the melting point of the salt were unsuccessful as the salt was extremely hygroscopic.
c) Recrystallized from ethanol.
d) Recrystallized from methanol–acetone.

a controlled reaction. Recently, Kelly and Matthews[6] reported the reaction of **1** with the complexes of sulfur trioxide with various Lewis bases, which resulted in the formation of **2**. Independently of this, we found that the reaction of **1** with the sulfur trioxide–1,4-dioxane complex afforded **2** under mild conditions.[1]

When the complex was treated with **1** in ethylene dichloride below 20 °C, **2** was formed as a crystalline precipitate. Since it is extremely hygroscopic and decomposes explosively, **2** was confirmed by treatment of the reaction mixture with ammonia or aniline under cooling, giving the corresponding ammonium (**5b**) or anilinium salt (**5c**). In a similar way salts with various organic bases such as diethylamine, triethylamine, *n*-propylamine, isopropylamine, *t*-butylamine, cyclohexylamine or imidazole were obtained.



Attempts to rearrange **5c** were unsuccessful. When **5c** suspended in ethylene dichloride was heated at refluxing temperature for 20 min, the statring material was recovered in a high yield. Treatment of **5b** with potassium hydroxide and **5c** with potassium bicarbonate in aqueous solution led to the formation of **5a**, which was identical with the specimen prepared according to the method described by Csuros.[4] When **5c** was treated with 2,4-dinitrophenylhydrazine under acidic conditions, 2,4-dinitrophenylhydrazone of cyclohexanone was formed.

When **2** was heated at 50 °C for about 15 min in the presence of 1/2 equiv. of 1,4-dioxane in ethylene dichloride, it was exothermically transformed into **3**, which was confirmed by treatment of the reaction mixture with aniline, giving anilinium phenylsulfamate and **4**.[7] In the presence of 1 equiv. of 1,4-dioxane, however, the exothermic rearrangement of **2** to **3** occurred after heating for 20—30 min at the same temperature. Apparently 1,4-dioxane retarded the rearrangement of **2** to **3**, which is probably due to the formation of the salt-like compound between 1,4-dioxane and **2**. The retarding effect by 1,4-dioxane as a Lewis base is also supported by the fact that the rearrangement of the salt of **2** with a stronger base,

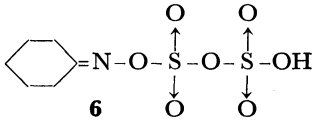
6) K. K. Kelly and J. S. Matthews, *J. Org. Chem.*, **36**, 2159 (1971).

7) It was found that the reaction of 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate with 2 equiv. of aniline in refluxing ethylene dichloride led to exclusive formation of anilinium phenylsulfamate and ε-caprolactam: M. Masaki, M. Uchida and K. Fukui, This Bulletin, **46**, 3174 (1973).

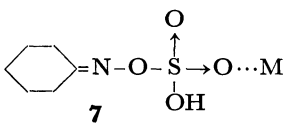
5c, did not occur even when it was heated at 82 °C for 20 min under anhydrous conditions. The retarding effect of bases for the rearrangement suggests that **2** would be formed if sulfur trioxide was gradually added to **1** under mild conditions, since **2** formed initially would be stabilized by the unreacted oxime, a Lewis base.

As expected, cyclohexanone oxime hydrogen sulfate (**2**) was obtained as a colorless crystalline precipitate by the gradual addition of sulfur trioxide to **1** in ethylene dichloride below −6 °C. The suspension of **2** in ethylene dichloride was then heated in order to examine the rearrangement of **2** in the absence of the Lewis base. As soon as the temperature of the suspension reached 44 °C, a vigorous exothermic reaction occurred, **2** being transformed into **3**. The conditions under which **2** began to rearrange were apparently milder than those needed in the presence of 1,4-dioxane. However, when the addition of sulfur trioxide was attempted at room temperature, the reaction accompanied decomposition.[8]

On the other hand, an inverse addition method did not lead to the formation of **2**. When **1** was added to sulfur trioxide in ethylene dichloride below −2 °C, a vigorous exothermic reaction occurred, no formation of **2** being observed. However, after hydrolysis of the reaction product **4** was obtained in 85% yield. This indicates that sulfur trioxide promotes the rearrangement of **2**. The rearrangement of **2** took place even below −3 °C, when sulfur trioxide was added to a suspension of **2** in ethylene dichloride. Kuhara and Todo[9] demonstrated that the rates of rearrangement of a series of ester of benzophenone oxime were proportional to the acid strength of the esterifying acid. The rate-determining step in a Beckmann rearrangement is known to be the partial ionization of the nitrogen-oxygen bond of the oxime.[10] The promoting effect by sulfur trioxide might be explained by a formation of cyclohexanone oxime hydrogen pyrosulfate (**6**), or by a simple coordination (**7**) of sulfur trioxide to the oxygen atom of **2**.



6

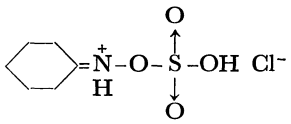


7

M: SO_3, $SnCl_4$, $ZnCl_2$

Thus, we examined whether other Lewis acids promote the rearrangement of **2**. When tin tetrachloride was added to the suspension of **2** in ethylene dichloride, the exothermic rearrangement began to occur below 15 °C, as expected. An analogous effect was observed by using zinc chloride.

The effect of hydrogen chloride on rearrangement of **2** was also studied, a retarding effect being observed. Treatment of cyclohexanone oxime monohydrochloride with sulfur trioxide below −2 °C, and heating of the reaction mixture at 50 °C for 30 min followed by hydrolysis of the product yielded only 52% of **4**. This might be rationalized by the fact that hydrogen chloride protonated on the nitrogen atom[11] of **2** to give **8**, contrary to the case of a Lewis acid, and the nitrogen-oxygen bond became difficult to be cleaved.



8

Hydrolysis of **2** under refluxing conditions gave **4** in 64% yield and a mixture of cyclohexanone and **1** in 17% yield. In a similar way, the hydrolysis of **2** in the presence of Lewis bases such as 1,4-dioxane, **4** and aniline yielded three products. These results are in contrast to those of Kelly and Matthews,[6] who reported the hydrolysis of **2** in the presence of 1,4-dioxane or **4** resulting exclusively in the formation of **4**.

In contrast, methanolysis of **2** gave rise to the formation of **1** and monomethyl sulfate, which was confirmed by treatment of the reaction mixture with aniline, giving the corresponding anilinium salt in 96% yield. Analogous alcoholysis of **2** with *n*-butanol gave **1** in 81% and mono-*n*-butyl sulfate in 76% yield.

Experimental

Concentration and evaporation were carried out under reduced pressure with a rotary evaporator. All melting points were determined in a liquid bath and are uncorrected.

Reaction of Cyclohexanone Oxime (1) with Sulfur Trioxide–1,4-Dioxane Complex. A solution of 1,4-dioxane (2.3 g, 26 mmol) in ethylene dichloride (10 ml) was added dropwise below 10 °C, with stirring, to a solution of sulfur trioxide (2 ml, 48 mmol) in ethylene dichloride (40 ml). To the resulting suspension of sulfur trioxide–1,4-dioxane complex was added dropwise a solution of **1** (5.43 g, 48 mmol) in ethylene dichloride (30 ml) with stirring below 20 °C. The complex dissolved and then colorless crystals separated gradually. The crystals was confirmed to be cyclohexanone oxime hydrogen sulfate (**2**).

Oxime hydrogen sulfate (**2**) is hygroscopic and becomes like honey when allowed to stand in an atmosphere after filtration. When dried over phosphorus pentoxide in a vacuum desiccator it decomposed within a few hour.

Aniline Salt of Cyclohexanone Oxime Hydrogen Sulfate (5c). To a suspension of **2** prepared from sulfur trioxide (5 ml, 120 mmol), 1,4-dioxane (10.5 g, 120 mmol) and **1** (13.6 g, 120 mmol) in ethylene dichloride (150 ml) was added dropwise aniline (33.5 g, 360 mmol) with stirring below 10 °C. The resulting mixture was stirred at room temperature for 1 hr. A crystalline substance, aniline salt of cyclohexanone

8) It has been shown that when cyclohexanone oxime hydrogen sulfate was heated in the presence of cyclohexanone oxime or ε-caprolactam, the oxime hydrogen sulfate decomposed to give an intractable substance: M. Masaki, K. Fukui, M. Uchida, K. Yamamoto, and I. Uchida, This Bulletin, **46**, 3179 (1973).

9) M. Kuhara and Y. Todo, *Memoirs Coll. Sci., Kyoto*, **2**, 387 (1910).

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

11) a) H. Saito, K. Nukada, and M. Ohno, *Tetrahedron Lett.*, **1964**, 2124; b) H. Saito, *Nippon Kagaku Zasshi*, **85**, 724 (1964).

oxime hydrogen sulfate (**5c**), was collected by filtration (35.2 g). Recrystallization from ethanol gave colorless needles. Yield 31.5 g. Mp and analytical results are shown in Table 1.

A solution of **5c** (0.5 g, 0.17 mmol) in water (40 ml) and methanol (40 ml) was treated with a solution of 2,4-dinitrophenylhydrazine[12] to give 2,4-dinitrophenylhydrazone of cyclohexanone (0.48 g, 99%). Recrystallization from ethanol gave orange leaves, mp 159 °C (lit,[13] 160 °C).

A suspension of **5c** (13.13 g, 46 mmol) in ethylene dichloride (100 ml) was heated under reflux for 20 min and then stirred at room temperature for 41 hr. The crystalline substance collected by filtration was identified as the starting material. Yield 10.6 g (81%).

*Ammonia Salt of Cyclohexanone Oxime Hydrogen Sulfate (**5b**).* To a suspension of **2** prepared from sulfur trioxide (5 ml, 120 mmol), 1,4-dioxane (10.5 g, 120 mmol) and **1** (13.6 g, 120 mmol) in ethylene dichloride (150 ml) was added gaseous ammonia below 0 °C. The resulting mixture was stirred at room temperature for 1 hr and allowed to stand overnight. A crystalline substance, ammonia salt of cyclohexanone oxime hydrogen sulfate (**5b**), was collected by filtration. Yield 22.8 g (91%). Mp 140—145 °C decomp.

*Diethylamine Salt of Cyclohexanone Oxime Hydrogen Sulfate (**5d**).* A suspension of **2** (48 mmol) in ethylene dichloride prepared in a similar way to that for **5b** was treated with a solution of diethylamine (3.5 g, 49 mmol) in ethylene dichloride (10 ml) with stirring below 0 °C. The resulting mixture was stirred at room temperature for 1 hr and concentrated, the residue being treated with ether. A crystalline substance, diethylamine salt of cyclohexanone oxime hydrogen sulfate (**5d**) was collected by filtration. Yield 11.7 g. Mp and analytical results are given in Table 1.

*Triethylamine, n-Propylamine, Isopropylamine, and t-Butylamine Salts of Cyclohexanone Oxime Hydrogen Sulfate (**5e**, **5f**, **5g**, and **5h**).* These ammonium salts were prepared by treating **2** with the corresponding amines in a similar way to that for **5d**. The results are given in Table 1.

*Cyclohexylamine and Imidazole Salts of Cyclohexanone Oxime Hydrogen Sulfate (**5i** and **5j**).* These salts were prepared by treating **2** with cyclohexylamine and imidazole, respectively, in a similar way to that for **5c**. The results are shown in Table 1.

*Potassium Salt of Cyclohexanone Oxime Hydrogen Sulfate (**5a**).* *a) From Aniline Salt of Cyclohexanone Oxime Hydrogen Sulfate (**5c**)*: A saturated aqueous solution of potassium bicarbonate was added to an aqueous solution of **5c** (2.86 g, 10 mmol) until gas evolution ceased. The resulting mixture was washed with benzene and concentrated. The residue was treated with an aqueous ethanol. The crystalline precipitate was collected by filtration and identified with authentic potassium salt of cyclohexanone oxime hydrogen sulfate (**5a**)[4] by infrared spectrum. Yield 1.6 g (69%). Extraction with ethanol by means of Soxhlet extractor gave colorless needles as an extract, mp 172—180 °C (lit,[4] 155—180 °C decomp.).

*b) From Ammonia Salt of Cyclohexanone Oxime Hydrogen Sulfate (**5b**)*: An aqueous solution of potassium hydroxide (0.56 g, 10 mmol) was added under ice cooling to an aqueous solution of **5b** (2.1 g, 10 mmol). The resulting solution was concentrated. Treatment of the residue with an aqueous ethanol afforded the potassium salt of cyclohexanone oxime hydrogen sulfate (**5a**), the infrared spectrum of which was superimposable on that of the authentic sample.[4] Yield 1.3 g (56%).

*Addition of Sulfur Trioxide to Cyclohexanone Oxime (**1**).* *a) Addition under Ice-Salt Cooling*: A solution of sulfur trioxide (2 ml, 48 mmol) in ethylene dichloride (40 ml) was added dropwise with stirring below −6.5 °C to a solution of **1** (5.4 g, 48 mmol) in ethylene dichloride (40 ml). The resulting solution was stirred under ice-salt cooling for 1 hr and then treated with a solution of aniline (4.46 g, 48 mmol) in ethylene dichloride (20 ml) below −5 °C. The mixture was stirred at room temperature for 3 hr and filtered to give aniline salt of cyclohexanone oxime hydrogen sulfate (**5c**) as a crystalline substance. Yield 11.23 g (82%).

b) Addition at Room Temperature: A solution of sulfur trioxide (5 ml, 120 mmol) in ethylene dichloride (40 ml) was added dropwise at room temperature to a solution of **1** (13.5 g, 120 mmol) in ethylene dichloride (60 ml). The temperature of the mixture rose to a refluxing temperature. The reaction mixture was treated under ice-salt cooling with water (20 ml) and aqueous ammonium hydroxide (20 ml of a 28% solution) and concentrated. The residue was dissolved in water (40 ml) and extracted with chloroform (40 ml×4). Evaporation of chloroform from the combined extracts afforded a brown crystalline residue, the solution of which in benzene (50 ml) was extracted with water (50 ml×4). The combined aqueous layers were concentrated to about 40 ml and extracted with chloroform (40 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **4**. Yield 6.4 g (47%).

*Addition of Cyclohexanone Oxime (**1**) to Sulfur Trioxide.* A solution of **1** (5.4 g, 48 mmol) in ethylene dichloride (60 ml) was gradually added dropwise below −2 °C, with stirring, to a solution of sulfur trioxide (2 ml, 48 mmol) in ethylene dichloride (40 ml). The mixture was stirred under cooling for 1 hr and at room temperature for 3 hr, treated under ice-salt cooling with water (20 ml) and aqueous ammonium hydroxide (20 ml of a 28% solution) and concentrated. The residue was dissolved in water (40 ml) and extracted with chloroform (40 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **4**. Yield 4.6 g (85%).

Reaction of Cyclohexanone Oxime Monohydrochloride with Sulfur Trioxide. A solution of sulfur trioxide (2 ml, 48 mmol) in ethylene dichloride (40 ml) was added dropwise, with stirring, below −2.5 °C to a solution of cyclohexanone oxime monohydrochloride (7.2 g, 48 mmol), prepared according to the method of Saito,[11b] in ethylene dichloride (60 ml). The resulting mixture was heated at 50 °C for 30 min, stirred at room temperature for 1.5 hr, treated with water (20 ml) and aqueous ammonium hydroxide (20 ml of a 28% solution) under ice-salt cooling, and concentrated. The residue was dissolved in water (40 ml) and extracted with chloroform (40 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give a mixture of **1** and **4** (4 g), which was confirmed by vapor-phase chromatographic analysis. The mixture (0.5 g) was treated with a solution of 2,4-dinitrophenylhydrazine[12] to afford 2,4-dinitrophenylhydrazone of cyclohexanone (0.38 g), the amount of **1** being 1.2 g and that of **4** 2.8 g (52%).

*Rearrangement of Cyclohexanone Oxime Hydrogen Sulfate (**2**).* *a)* A solution of sulfur trioxide (2 ml, 48 mmol) in ethylene dichloride (40 ml) was added dropwise, with stirring, below −1.5 °C to a solution of **1** (5.4 g, 48 mmol) in ethylene dichloride (60 ml). When the resulting suspension of **2** was heated to 44 °C, the suspended **2** disappeared and the temperature of the mixture rose to 49.5 °C. The resulting solu-

12) The solution of 2,4-dinitrophenylhydrazine used was prepared from 2,4-dinitrophenylhydrazine (3 g), conc. sulfuric acid (15 ml), methanol (70 ml), and water (20 ml): R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compound," Wiley, New York (1956), p. 111.

13) C. F. H. Allen, *J. Amer. Chem. Soc.*, **52**, 2955 (1930).

tion was stirred at room temperature, treated with water (20 ml) and aqueous ammonium hydroxide (20 ml of a 28% solution) under ice-salt cooling, and then concentrated. The residue was dissolved in water (40 ml) and extracted with chloroform (40 ml×5). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **4**. Yield 4.3 g (80%).

b) In the Presence of 1/2 Equiv. of 1,4-Dioxane: To a suspension of sulfur trioxide–1,4-dioxane complex, prepared from sulfur trioxide (2 ml, 48 mmol) and 1,4-dioxane (2.3 g, 26 mmol) in ethylene dichloride (50 ml) was added dropwise a solution of **1** (5.42 g, 48 mmol) in ethylene dichloride (30 ml) below −5 °C with stirring. When the resulting suspension was heated at 50 °C for 15 min, the suspended **2** disappeared and the temperature of the mixture rose rapidly to 58 °C. The resulting solution was stirred at room temperature for 3 hr and then treated with a solution of aniline (8.93 g, 96 mmol) in ethylene dichloride (20 ml) under ice-salt cooling. The mixture was stirred at room temperature for 20 min, heated at refluxing temperature for 1 hr, and then allowed to stand at room temperature overnight. The crystalline substance, anilinium phenylsulfamate, was collected by filtration. Yield 11.15 g (87%). Mp 185—195 °C. Found: C, 54.01; H, 5.26; N, 10.85; S, 12.24%. Calcd for $C_{12}H_{14}N_2O_3S$: C, 54.12; H, 5.30; N, 10.52; S, 12.04%.

The filtrate was concentrated. The residue was dissolved in water (30 ml) and aqueous hydrochloric acid (10 ml of 1 N solution) and extracted with chloroform (40 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **4**. Yield 4.59 g (85%).

c) In the Presence of 1 Equiv. of 1,4-Dioxane: When a suspension of **2** in the presence of 1 equiv. of 1,4-dioxane, prepared from sulfur trioxide (2 ml, 48 mmol), 1,4-dioxane (4.4 g, 50 mmol) and **1** (5.4 g, 48 mmol) in ethylene dichloride (100 ml) was heated at 50 °C for 26 min, the suspended **2** disappeared and the temperature of the mixture rose rapidly to 60 °C. The mixture was treated with water (20 ml) and aqueous ammonium hydroxide (20 ml of a 28% solution) under ice-salt cooling and concentrated. The residue was dissolved in water (40 ml) and extracted with chloroform (40 ml×4). The combined extracts were evaporated to give **4**. Yield 4.7 g (87%).

d) In the Presence of Sulfur Trioxide: To a suspension of **2** prepared by the addition of sulfur trioxide (2 ml, 48 mmol) in ethylene dichloride (40 ml) to **1** (5.4 g, 48 mmol) in ethylene dichloride (60 ml) was added a solution of sulfur trioxide (12 mmol) in ethylene dichloride (10 ml) dropwise below −5 °C with stirring. The suspension turned solution, the temperature of the mixture rising to 10 °C. The mixture was stirred at room temperature for 1.5 hr and heated at 50 °C for 30 min, no exothermic phenomenon being observed. The mixture was then treated with water (20 ml) and aqueous ammonium hydroxide (20 ml of a 28% solution) under ice-salt cooling and concentrated. The residue was dissolved in water (40 ml) and extracted with chloroform (40 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **4**. Yield 4.7 g (87%).

e) In the Presence of Tin Tetrachloride: To a suspension of **2**, prepared from sulfur trioxide (2 ml, 48 mmol) and **1** (5.4 g, 48 mmol) in ethylene dichloride (80 ml) was added a solution of tin tetrachloride (6.25 g, 24 mmol) in ethylene dichloride (20 ml) dropwise below −4 °C. The resulting solution was gradually warmed with stirring. After reaching 15 °C, the temperature of the mixture rose exothermically to 36.5 °C and colorless crystals separated. The suspension was stirred at room temperature for 2.5 hr, treated with water (20 ml) and aqueous ammonium hydroxide (20 ml of a 28% solution) under ice-salt cooling, and concentrated. The residue was treated with water (40 ml) and the precipitate was removed by filtration. The filtrate was extracted with chloroform (40 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **4**. Yield 4.7 g (87%).

f) In the Presence of Zinc Chloride: A solution of sulfur trioxide (2 ml, 48 mmol) in ethylene dichloride (40 ml) was added dropwise, with stirring, below −8 °C to a solution of cyclohexanone oxime–zinc chloride complex (8.7 g, 24 mmol) in ethylene dichloride (60 ml). The resulting mixture of **2** and zinc chloride was stirred at room temperature for 2 hr. The temperature of the mixture rose exothermically to 32 °C. The mixture was then treated with water (20 ml) and aqueous ammonium hydroxide (20 ml of a 28% solution) under ice-salt cooling and concentrated. The residue was dissolved in water (40 ml) and extracted with chloroform (40 ml×5). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give **4**. Yield 4.73 g (87%).

Cyclohexanone Oxime–Zinc Chloride Complex. A solution of zinc chloride (21 g, 150 mmol) in acetone (50 ml) was added dropwise with stirring at room temperature to a solution of **1** (34 g, 300 mmol) in ethyl acetate (50 ml). The mixture was stirred at room temperature for 3 hr and concentrated. The residue was treated with isopropyl ether and the crystalline cyclohexanone oxime–zinc chloride complex was collected by filtration. Yield 31 g (57%). Recrystallization from isopropyl ether gave colorless crystals, mp 90—91 °C. Found: C, 39.87; H, 6.40; Cl, 19.38%. Calcd for $C_{12}H_{22}Cl_2N_2O_2Zn$: C, 39.75; H, 6.12; Cl, 19.55%.

Hydrolysis of Cyclohexanone Oxime Hydrogen Sulfate (2). To a suspension of **2**, prepared from sulfur trioxide (2 ml, 48 mmol) and **1** (5.42 g, 48 mmol) in ethylene dichloride (80 ml), was added water (20 ml) under ice-salt cooling. The mixture was then heated under refluxing for 1 hr, and neutralized with aqueous potassium hydroxide under ice-salt cooling. The precipitate, potassium sulfate (2.95 g), was removed by filtration, and the filtrate was divided into an organic layer and an aqueous layer.

The organic layer was dried over anhydrous sodium sulfate, and evaporated to give a mixture (3.34 g) of cyclohexanone, **1** and **4**, which were identified by vapor-phase chromatographic analysis. One gram of the mixture was dissolved in aqueous methanol (100 ml of a 50% solution) and treated with 2,4-dinitrophenylhydrazine to give 2,4-dinitrophenylhydrazone of cyclohexanone (0.64 g). Thus, the amount of cyclohexanone and **1** in the mixture was 7.69 mmol (16%) and that of **4** was calculated to be 2.47 g (46%).

The aqueous layer was extracted with chloroform (60 ml×3). The combined extracts were evaporated to give a mixture (1.03 g) of cyclohexanone and **1** (0.467 mmol, 1%), and **4** (0.98 g, 18%), the amounts of which were determined by a treatment of the mixture with 2,4-dinitrophenylhydrazine.

Hydrolysis of Cyclohexanone Oxime Hydrogen Sulfate (2) in the Presence of Lewis Base. a) In the Presence of 1,4-Dioxane: A suspension of **2**, prepared from sulfur trioxide (2 ml, 48 mmol), 1,4-dioxane (4.4 g, 50 mmol) and **1** (5.42 g, 48 mmol) in ethylene dichloride (100 ml), was treated with water (20 ml) under ice-salt cooling. The mixture was heated under refluxing for 1 hr, and neutralized with aqueous potassium hydroxide under ice-salt cooling. A precipitate, potassium sulfate (4.01 g), was removed by filtration, and the filtrate was treated in a similar way to that described above.

The organic layer was confirmed to involve cyclohexanone

and **1** (11.38 mmol, 24%) and **4** (2.15 g, 40%).

The aqueous layer included cyclohexanone and **1** (0.647 mmol, 1.3%) and **4** (0.75 g, 14%).

b) In the Presence of ε-Caprolactam (4): To a suspension of **2**, prepared from sulfur trioxide (2 ml, 48 mmol) and **1** (5.42 g, 48 mmol) in ethylene dichloride (70 ml), was added a solution of **4** (5.42 g, 48 mmol) in ethylene dichloride (30 ml) under ice-salt cooling. The resulting solution was treated with water (20 ml) under ice-salt cooling, heated under refluxing for 1 hr, and neutralized with aqueous potassium hydroxide under ice-salt cooling. A precipitate, potassium sulfate (3.88 g), was removed by filtration, and the filtrate was treated as above.

The organic layer was confirmed to involve cyclohexanone and **1** (14.8 mmol, 31%) and **4** (60 mmol).

The aqueous layer included cyclohexanone and **1** (0.647 mmol, 1.3%) and **4** (18.5 mmol).

Hydrolysis of Aniline Salt of Cyclohexanone Oxime Hydrogen Sulfate (5c). A solution of **5c** (4.43 g, 15 mmol) in water (50 ml) 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 a mixture of cyclohexanone, **1** and **4**. Yield 1.42 g. The mixture was dissolved in aqueous methanol (100 ml of a 50% solution) and treated with a solution of 2,4-dinitrophenylhydrazine to give 2,4-dinitrophenylhydrazone of cyclohexanone (0.33 g, 1.19 mmol, 8%). Thus, the amount of **4** in the mixture was calculated to be 1.29 g (75%).

Methanolysis of Cyclohexanone Oxime Hydrogen Sulfate (2). To a suspension of **2**, prepared from sulfur trioxide (2 ml, 48 mmol), 1,4-dioxane (4.4 g, 50 mmol) and **1** (5.42 g, 48 mmol) in ethylene dichloride (90 ml), was added a solution of methanol (2 g, 63 mmol) in ethylene dichloride (10 ml) dropwise with stirring below −11.5 °C. The mixture was stirred at room temperature for 18.5 hr and treated with a solution of aniline (4.47 g, 48 mmol) in ethylene dichloride (20 ml) with stirring below −3 °C. The mixture was stirred at room temperature for 3 hr and aniline salt of monomethyl sulfate precipitated was collected by filtration. Yield 9.17 g (93%). Recrystallization from acetonitrile gave colorless needles, mp 160 °C. Found: C, 40.98; H, 5.20; N, 7.06; S, 15.45%. Calcd for $C_7H_{11}NO_4S$: C, 40.98; H, 5.37; N, 6.83; S, 15.61%.

The filtrate was concentrated and the residue was treated with benzene (100 ml) to give 0.29 g of crystals, whose infrared spectrum was identical with that of the crystals obtained above. Total yield 96%.

The filtrate was washed with water (50 ml×3), dried over anhydrous sodium sulfate and evaporated to give **1** (4.62 g, 85%). The combined washings were concentrated to about 50 ml and extracted with chloroform (50 ml×4). The combined extracts were dried over anhydrous sodium sulfate and evaporated to give further **1** (0.22 g, 4%).

n-Butanolysis of Cyclohexanone Oxime Hydrogen Sulfate (2). To a suspension of **2**, prepared from sulfur trioxide (2 ml, 48 mmol), 1,4-dioxane (4.2 g, 48 mmol), and **1** (5.4 g, 48 mmol) in ethylene dichloride (70 ml) was added a solution of *n*-butanol (3.6 g, 49 mmol) in ethylene dichloride (15 ml) dropwise with stirring at −5—0 °C. The mixture was stirred for 1 hr and then treated with a solution of aniline (4.47 g, 48 mmol) in ethylene dichloride (15 ml) under ice-salt cooling. The resulting suspension was stirred at room temperature for 2 hr and then concentrated. The residue was treated with cyclohexane (60 ml), and aniline salt of mono-*n*-butyl sulfate precipitated was collected by filtration. Yield 10 g (84%). Recrystallization from ethyl acetate gave colorless needles, mp 110—115 °C. The infrared spectrum was superimposable on that of an authentic sample (mp 111.5—112 °C).[14]

The filtrate was washed with water, dried over anhydrous sodium sulfate, and evaporated to give **1** (4.1 g, 76%).

14) F. Popelier, *Bull. Soc. Chim. Belg.*, **35**, 264 (1926).