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Reaction of 3,4,5,6,-Tetrahydro-2*H*-azepin-7-ol Hydrogen Sulfate with Cyclohexanone Oxime–Tin Tetrachloride Complex

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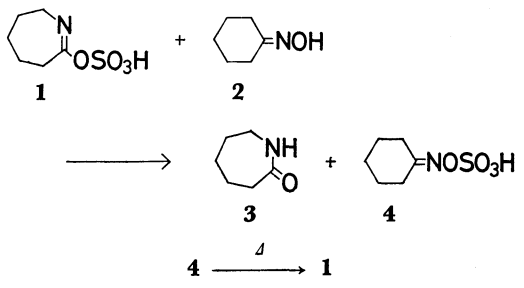
Cyclohexanone oxime hydrogen sulfate was found to undergo facile rearrangement to 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate in the presence of ε-caprolactam–tin tetrachloride complex, while the oxime hydrogen sulfate decomposed in the presence of ε-caprolactam. Other metal halides were studied to see if the oxime hydrogen sulfate undergoes rearrangement in the presence of the lactam. Cyclohexanone oxime–tin tetrachloride complex was synthesized. Its reaction with the tetrahydroazepin-7-ol hydrogen sulfate was found to give the lactam–tin tetrachloride complex and the oxime hydrogen sulfate which regenerated the tetrahydroazepin-7-ol hydrogen sulfate in the reaction system. Tin tetrachloride complex was prepared with several oximes.

Tetrahydroazepin-7-ol hydrogen sulfate undergoes an oxygen-sulfur bond fission exclusively on treatment with nucleophilic reagents.[1] The reaction of 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate (**1**) with cyclohexanone oxime (**2**) afforded ε-caprolactam (**3**) and cyclohexanone oxime hydrogen sulfate (**4**) in good yields. The reaction indicates a possible regeneration of **1** in the reaction system, since the compound has been known to be produced by a thermal rearrangement of **4**.[2] It is of interest to examine the possibility, because a Beckmann rearrangement using sulfuric acid and/or sulfur trioxide as a rearranging agent has been known to require at least one equiv. of the agent.[3] Preliminary experiments revealed, however, that **4** decomposed in the presence of **3** and did not undergo rearrangement. Though the decomposition products



1) M. Masaki, M. Uchida, and K. Fukui, This Bulletin, **46**, 3174 (1973).

2) K. Fukui, M. Uchida, and M. Masaki, *ibid.*, **46**, 3168 (1973).

3) a) L. G. Donaruma and W. Z. Heldt, "Organic Reactions," Vol. 11, ed. by A. C. Cope *et al.*, John Wiley & Sons, Inc., New York, N. Y., (1960) p. 57; b) N. Tokura, R. Asami, and R. Tada, *Sci. Repts. Research Inst., Tohoku Univ., Ser.* **A8**, 151 (1956).

and mechanism are not clear,[4] the decomposition seems to be ascribable to an interaction between the oxime hydrogen sulfate (strong acid) and the lactam function (weak base). Thus **4** might be expected to undergo rearrangement normally, when the lactam function is protected by converting the lactam into a complex with Lewis acid.

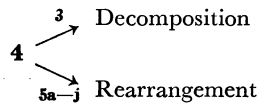
This paper describes a Beckmann rearrangement of oxime hydrogen sulfate (**4**) in the presence of lactam–Lewis acid complex and a conversion of cyclohexanone oxime–tin tetrachloride complex into ε-caprolactam-tin tetrachloride complex by means of a circulatory use of sulfur trioxide moiety in **4** or tetrahydroazepin-7-ol hydrogen sulfate (**1**).

Results and Discussion

When a mixture of cyclohexanone oxime hydrogen sulfate (**4**) and 1 equiv. of ε-caprolactam–zinc chloride complex (2: 1 in molar ratio, **5a**) in ethylene dichloride was heated to 64 °C, no exothermic phenomenon nor any remarkable coloration of the reaction mixture was observed, in contrast to the fact that **4** decomposes with a remarkable coloration of the mixture in the presence of ε-caprolactam (**3**) under similar conditions, and when alone, undergoes rearrangement exothermally under milder conditions.[2] After hydrolysis and neutralization of the reaction product, **3** was obtained in 152% yield based upon the lactam complex (**5a**). The results showed that more than 52% of **4** underwent rearrangement to **1** and less than 48% decomposed, competitively. The partial decomposition might be due to a partial dissociation of **5a** into **3** and zinc chloride.

When a mixture of **4** and 1 equiv. of ε-caprolactam–tin tetrachloride complex (2: 1 in molar ratio, **5b**) in ethylene dichloride was gradually heated to 48 °C, exothermic rearrangement of **4** occurred to afford **3** in 190% yield, after hydrolysis and neutralization. It is apparent that at least 90% of **4** rearranged in the presence of **5b**.

Various metal halides were similarly examined to see whether **4** underwent rearrangement in their presence with ε-caprolactam (**5**). The results are summarized in Table 1. Tin tetrachloride was found to be most effective among the metal halides examined.



5a—j = $\left(\text{NH}\right)_m MX_n$

	a	**b**	**c**	**d**	**e**
MX_n	$ZnCl_2$	$SnCl_4$	BF_3	$CdCl_2$	$HgCl_2$
m	2	2	1	1	1
	f	**g**	**h**	**i**	**j**
MX_n	$FeCl_3$	$ZrCl_4$	$SbCl_5$	$SbCl_5$	$SnBr_4$
m	2	2	1	2	2

4) The oxime hydrogen sulfate decomposed when heated in the presence of 1 equiv. of ε-caprolactam, giving an intractable mixture consisting of more than at least three components. A similar decomposition also took place when substances having amide function were used in place of ε-caprolactam.

Table 1. Rearrangement of cyclohexanone oxime hydrogen sulfate (**4**) in the presence of ε-caprolactam–metal halide complex (**5**)

Metal halide	Reaction temp °C	Risen temp °C	Color of reaction mixture	ε-Caprolactam yield: Based on **5**, %	ε-Caprolactam yield: Based on **4**, %
$ZnCl_2$	64	0	colorless	152	52
$SnCl_4$	48	17	colorless	190	90
BF_3	55	10.5	colorless	188	88
$CdCl_2$	55	0	pale yellow	122	22
$HgCl_2$	55	0	pale yellow	124	24
$FeCl_3$	25	few	yellowish brown	148	48
$ZrCl_4$	25	16	colorless	180	80
$SbCl_5$	55	0	yellowish brown	178	78
$SnBr_4$	50	0	orange	157	57

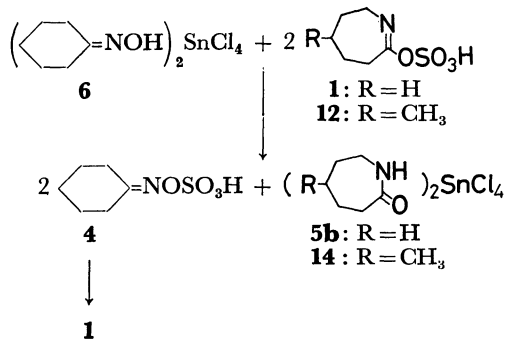
It might be concluded that a regeneration of **1** in the reaction system is possible, when tin tetrachloride is added subsequently to the formation of **4** and **3** in the reaction of **1** with **2**. It might be expected that a reaction of **1** with cyclohexanone oxime–tin tetrachloride complex (**6**) affords **5b** and **1**.

Treatment of **2** with 1/2 equiv. of tin tetrachloride in ethylene dichloride gave cyclohexanone oxime–tin tetrachloride complex (2: 1 in molar ratio, **6**), which was confirmed by elemental analysis and infrared spectrum. Since this was the first example of complexes of oximes with tin tetrachloride, several other oximes were treated in a similar way with tin tetrachloride. The results are summarized in Table 2. All complexes (**7**—**11**) synthesized consist of two oximes and one tin tetrachloride in molar ratio.

When **6** was treated with 1 equiv. of 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate (**1**) in ethylene dichloride at room temperature, a slight exothermic reaction occurred, **5b** being obtained as a crystalline

Table 2. Oxime–tin tetrachloride complexes

Complex	Yield %	Mp °C	Formula	Anal %:	Calcd	Found
6	97	170(dec.)	$(C_6H_{11}NO)_2SnCl_4$	C	29.57	29.60
				H	4.52	4.47
				N	5.75	5.93
7	89	169—170	$(C_5H_9NO)_2SnCl_4$	C	26.16	26.23
				H	3.92	3.97
				N	6.10	6.02
8	96	217—219	$(C_3H_7NO)_2SnCl_4$	C	17.70	17.83
				H	3.44	3.40
				N	6.88	6.76
9	96	139.5—140	$(C_8H_9NO)_2SnCl_4$	C	36.16	35.08
				H	3.39	3.38
				N	5.27	5.21
10	85	161—163	$(C_7H_{13}NO)_2SnCl_4$	C	32.68	32.81
				H	5.06	4.93
				N	5.45	5.46
11	72	144.5—145.5	$(C_{12}H_{23}NO)_2SnCl_4$	C	43.71	44.00
				H	7.03	6.99
				N	4.28	4.29



Scheme 1

precipitate in 65% yield. Hydrolysis and neutralization of products in the solution afforded **3** in 113% yield based on **1**, showing the presence of more than 13% yield of **5b** in the solution. The reaction can be summarized as in Scheme 1.

Although oximes are known to be transformed into amides or lactams by means of Lewis acid,[5] such a rearrangement requires more drastic conditions. Control experiments showed that the starting material was recovered when the oxime complex was heated under reflux in ethylene dichloride alone or in the presence of excess tin tetrachloride. We were able to isolate a reaction intermediate, the oxime hydrogen sulfate derived from the oxime complex.

When a reaction of 4-methyl-3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate (**12**) with cyclohexanone oxime-tin tetrachloride complex (**6**) in ethylene dichloride below 5 °C was followed by treatment with imidazole, 4-methyl-ε-caprolactam (**13**) and imidazole salt of cyclohexanone oxime hydrogen sulfate were obtained in 87 and 62% yields, respectively.

When the reaction mixture resulting from the reaction of **1** and 1 equiv. of **6** (Scheme 1) was further treated with 1 equiv. of **6**, a slight exothermic reaction occurred and **5a** was obtained as a crystalline precipitate in 85% yield based upon **6**. The regeneration of **1** in the reaction mixture was thus confirmed.

Experimental

Concentration and evaporation were carried out with a rotary evaporator under reduced pressure. All melting points were determined in a liquid bath, and are uncorrected unless otherwise stated. Solvents were used after drying and distillation.

Materials. Complexes of ε-caprolactam with zinc chloride (**5a**),[6] tin tetrachloride (**5b**),[6] boron trifluoride (**5c**),[7] cadmium chloride (**5d**),[8] mercuric chloride (**5e**),[8] ferric chloride (**5f**),[8] and zirconium tetrachloride (**5g**)[8] were prepared by known methods. The suspension of cyclohexanone oxime hydrogen sulfate (**4**) in ethylene dichloride was prepared by a reaction of cyclohexanone oxime with sulfur trioxide–1,4-dioxane complex.[2] The solution of 3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate (**1**) in ethylene dichloride was prepared by two methods.[1]

ε-Caprolactam–Antimony Pentachloride Complex. The reaction of **3** with antimony pentachloride in methylene chloride has been reported by Rothe *et al.*[7a] to give ε-caprolactam–antimony pentachloride complex (3:2 in molar ratio). However, we obtained two complexes (2:1 and 1:1).

Complex (1:1, 5h): A solution of **3** (2.71 g, 24 mmol) in ethylene dichloride (30 ml) was added dropwise to a solution of antimony pentachloride (7.18 g, 24 mmol) in ethylene dichloride (20 ml) with stirring below 0 °C. Crystals formed were collected by filtration. Yield 2.81 g (28%). Mp 135—145 °C (on a hot plate). Found: Cl, 42.72%. Calcd for $C_6H_{11}NO \cdot SbCl_5$: Cl, 43.01%.

The filtrate was concentrated and the residue was treated with benzene to give 4.2 g of crystals, whose infrared spectrum was identical with that of crystals obtained above. Total yield 70%.

Complex (2:1, 5i): A solution of antimony pentachloride (7.17 g, 24 mmol) in ethylene dichloride (20 ml) was added to a solution of **3** (5.42 g, 48 mmol) in ethylene dichloride with stirring below −5 °C. The mixture was stirred at room temperature for 1 hr and filtered to give crystals. Yield 5.69 g (45%). Found: C, 27.33; H, 4.25; N, 5.21; Cl, 33.96%. Calcd for $C_{12}H_{22}N_2O_2 \cdot SbCl_5$: C, 27.43; H, 4.23; N, 5.33; Cl, 33.74%.

The filtrate was concentrated and the residue was treated with ethyl acetate to give 5.43 g of crystals, whose infrared spectrum was identical with that of crystals obtained above. Total yield 87%.

ε-Caprolactam–Tin Tetrabromide Complex (5j). A solution of tin tetrabromide (65.7 g, 0.15 mol) in ethylene dichloride (70 ml) was added dropwise to a solution of **3** (34 g, 0.3 mol) in ethylene dichloride with stirring under ice cooling. The mixture was stirred for 2 hr at room temperature and filtered to afford crystals. Yield 80.8 g (81%). Mp 145—146.5 °C. Found: C, 21.51; H, 3.16; N, 4.09; Br, 48.07%. Calcd for $C_{12}H_{22}N_2O_2 \cdot SnBr_4$: C, 21.67; H, 3.31; N, 4.21; Br, 48.11%.

Rearrangement of Cyclohexanone Oxime Hydrogen Sulfate (4). a) In the Presence of ε-Caprolactam–Zinc Chloride Complex (5a): A solution of **5a** (8.7 g, 24 mmol) in ethylene dichloride (20 ml) was added dropwise to a suspension of **4** (48 mmol) in ethylene dichloride (70 ml) with stirring below −5.5 °C. The mixture was stirred at room temperature until dissolution, and then heated gradually to 64 °C. Stirring was continued for 1 hr, during which the temperature fell gradually to room temperature. The mixture was treated with water (20 ml) and then with aqueous ammonia (28%, 20 ml) under ice cooling, and concentrated. The residue was dissolved in water (50 ml) and extracted with chloroform (50 ml × 5). The combined extracts were dried over anhydrous sodium sulfate and concentrated to dryness, giving 8.24 g of **3**. The yield was 152% based upon the lactam complex.

b) In the Presence of ε-Caprolactam–Tin Tetrachloride Complex (5b): The complex (**5b**, 11.7 g, 24 mmol) was added to a suspension of **4** (48 mmol) in ethylene dichloride (80 ml) at room temperature. When the mixture was gradually heated to 48 °C, the temperature of the mixture rose to 65 °C. The resulting mixture was stirred at room temperature overnight, and then filtered to give colorless crystals which were identified by infrared spectrum as **5b**. Yield 7.15 g (61%). The filtrate was concentrated and the residue

5) C. R. Hanser and D. S. Hoffenberg, *J. Org. Chem.*, **20**, 1482 (1955).

6) Inventa AG, Swiss 326165 (1958).

7) a) M. Rothe, G. Reinisch, W. Jaeger, and I. Schopov, *Makromol. Chem.*, **54**, 183 (1962); *b*) J. Duynstee, W. van Raayen, J. Smidt, and Th. A. Veerkamp, *Rec. Trav. Chim. Pays-Bas.*, **80**, 1323 (1961).

8) K. Sturzer, *Z. Naturforsch.*, **17b**, 197 (1962).

9) L. Giuffre, G. Sioli, and E. Losio, *Chim. Ind.* (Milan), **50**, 983 (1968).

10) A.F. Turbak, *Ind. Eng., Chem. Prod. Res. Develop.*, **7**, 190 (1968).

was treated with water (50 ml), neutralized with aqueous ammonia under ice cooling, and evaporated to about half in volume. Tetrahydrofuran (50 ml) was added to the residual mixture and the gelatinous precipitate was removed by filtration and washed with tetrahydrofuran. The combined filtrate and washing were concentrated and 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 concentrated to dryness, giving 7 g of **3**. Yield 129%. Total yield of **3** was 190% based upon **5b**.

c) In the Presence of Complexes of ε-Caprolactam with Boron Trifluoride, Cadmium Chloride, Mercuric Chloride, Ferric Chloride, Zirconium Tetrachloride, Antimony Pentachloride, or Tin Tetrabromide (5c—h, or 5j): Twenty four mmol of **5c**, **5d**, **5e**, **5f**, **5g** or **5j**, or 48 mmol of **5h** as crystals or a solution in ethylene dichloride was added with stirring to a suspension of **4** (48 mmol) in ethylene dichloride (80 ml) below −10 °C. The mixture was stirred for 20—60 min, during which time the temperature returned gradually to room temperature. The mixture was then slowly heated to the temperature given in Table 1, when an exothermic phenomenon was observed, the temperature of the reaction mixture being raised by degrees. After stirring for 2 hr at room temperature, the mixture was concentrated and the residue was treated with water (50 ml), neutralized with aqueous ammonia and treated with methanol (50 ml). The gelatinous precipitate was filtered and washed with methanol. The combined filtrate and washing were concentrated and the residue was dissolved in water (40 ml) and extracted with chloroform (50 ml×5). The combined extracts were dried over anhydrous sodium sulfate and concentrated to give **3**. A ratio of conversion of **4** into **1** was calculated by subtraction of the theoretical yield 5.42 g of **3** based on **5c**—**h**, or **5j** from the yield of **3** obtained from the extraction. The results are summarized in Table 1.

Cyclohexanone Oxime–Tin Tetrachloride Complex (6). To a solution of cyclohexanone oxime (**2**) (11.3 g, 100 mmol) in ethylene dichloride (50 ml) was added dropwise a solution of tin tetrachloride (13.0 g, 50 mmol) in ethylene dichloride (20 ml) with stirring below 10 °C. A colorless precipitate was soon formed. After being left to stand overnight, the mixture was filtered to give 23.7 g of colorless crystals. The results are given in Table 2.

Cyclopentanone Oxime–Tin Tetrachloride Complex (7). To a solution of cyclopentanone oxime (9.9 g, 100 mmol) in ethylene dichloride (50 ml) was added dropwise a solution of tin tetrachloride (13.0 g, 50 mmol) in ethylene dichloride (20 ml) with stirring below 10 °C. The mixture was stirred for 2 hr at room temperature and concentrated. Ethyl acetate (50 ml) was added to the sirupy residue and the resulting solution was allowed to stand at room temperature to give 20.1 g of colorless crystals. The results are given in Table 2.

Tin Tetrachloride Complex with Acetoxime (8), Acetophenone Oxime (9), and 4-Methylcyclohexanone Oxime (10). The complexes were synthesized as in the case of **6** (Table 2).

Cyclododecanone Oxime–Tin Tetrachloride Complex (11). This was synthesized as in the case of **7** (Table 2).

Reaction of 3,4,5,6-Tetrahydro-2H-azepin-7-ol Hydrogen Sulfate (1) with 1 Equiv. of Cyclohexanone Oxime–Tin Tetrachloride Complex (6). **6** (11.7 g, 24 mmol) was added to a solution of **1** (48 mmol) in ethylene dichloride (80 ml) with stirring at room temperature. The temperature of the mixture rose above *ca.* 2—3 °C, a homogeneous solution being formed within 20 min. Stirring was continued for approximately 90 min after the addition of the complex, when the temperature began to fall, the solution becoming turbid, and a precipitate formed gradually. After being allowed to stand at room temperature overnight, the mixture was filtered to give 7.6 g of colorless crystals, which were identified by infrared spectrum as ε-caprolactam–tin tetrachloride complex (**5b**). The yield based on the used oxime complex (**6**) was 65%. The filtrate was concentrated and the residue was dissolved in water, neutralized with ammonia, and extracted with chloroform to afford 6.5 g of **3**.

Reaction of 3,4,5,6-Tetrahydro-2H-azepin-7-ol Hydrogen Sulfate (1) with 2 Equiv. of Cyclohexanone Oxime–Tin Tetrachloride Complex (6). **6** (11.7 g, 24 mmol) was added to a solution of **1** (48 mmol) in ethylene dichloride (100 ml) with stirring at room temperature. The mixture rose by 2—3 °C, and became homogeneous within *ca.* 20 min. 90 min after addition of the complex, the temperature began to fall. **6** (11.7 g, 24 mmol) was again added to the mixture and stirring was continued. The reaction mixture rose 2—3 °C above room temperature. It was stirred overnight at room temperature, and then filtered to give 20.0 g of colorless crystals, which were identified by infrared spectrum as lactam complex (**5b**). The yield based upon the added oxime complex was 85%. The filtrate was treated as in the case of the reaction described above, 5.8 g of **3** being obtained.

Reaction of 4-Methyl-3,4,5,6-tetrahydro-2H-azepin-7-ol Hydrogen Sulfate (12) with Cyclohexanone Oxime–Tin Tetrachloride Complex (6): **6** (11.7 g, 24 mmol) was added with stirring at −10 °C to a solution of **12** (48 mmol) in ethylene dichloride (80 ml), prepared by the reaction of 4-methyl-ε-caprolactam (6.10 g, 48 mmol) and sulfur trioxide (2 ml, 48 mmol). The temperature of the mixture rose to −3 °C. The resulting suspension was stirred at 5 °C for approximately 1.5 hr, when it became a clear solution. This was cooled to −10 °C, and a solution of imidazole (6.5 g, 96 mmol) in chloroform (50 ml) was added dropwise. Stirring was continued, and the mixture was allowed to gradually return to room temperature. The colorless solid formed after the imidazole addition turned into an oily matter with temperature rise. After stirring at room temperature for 30 min the mixture was concentrated to remove ethylene dichloride and chloroform. To the oily residue was added tetrahydrofuran (100 ml) and the precipitated colorless solid was collected by filtration. The precipitate was hygroscopic. It was confirmed by infrared spectrum to be a mixture of imidazole salt of **1** and imidazole–tin tetrachloride complex. The mixture was added to acetonitrile (60 ml) and stirred at room temperature, in order to dissolve the imidazole salt of **1**. The insoluble imidazole–tin tetrachloride complex was separated by filtration. The filtrated cake weighed 5.8 g. The acetonitrile filtrate was concentrated to afford 7.8 g of imidazole salt of **1**, whose infrared spectrum was identical with that of the authentic specimen.[2] The yield based upon the added oxime complex (**6**) was 62%.

The tetrahydrofuran filtrate separated from the above colorless solid was concentrated, and the residue was treated with water (50 ml) and neutralized with aqueous ammonia under ice cooling. After a gelatinous precipitate was removed by filtration and washed with tetrahydrofuran, the combined filtrate and washing were concentrated. The residue was dissolved in 50 ml of water and extracted with chloroform (50 ml×5). The combined extracts were dried and concentrated to give 5.3 g of 4-methyl-ε-caprolactam. The yield based upon the employed 4-methyl-3,4,5,6-tetrahydro-2*H*-azepin-7-ol hydrogen sulfate (**12**) was 87%.

Attempted Thermal Rearrangement of Cyclohexanone Oxime–Tin Tetrachloride Complex (6). *a)* A suspension of **6** (2 g, 4.1 mmol) in ethylene dichloride (40 ml) was heated at

reflux temperature for 1.5 hr. The starting material **6** (1.9 g) was recovered in 95% yield.

b) To a suspension of **6** (10 g, 20.5 mmol) in ethylene dichloride (100 ml) was added tin tetrachloride (5.35 g, 20.5 mmol) and the mixture was heated at reflux temperature for 7.5 hr. After the mixture returned to room temperature the precipitate was collected by filtration. 8.6 g of **6** was recovered.