

The Use of Lewis Base-Sulfur Trioxide Complexes as Reagents for the Beckmann Rearrangement of Ketoximes

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Complexes of sulfur trioxide with various Lewis bases have been studied as reagents for the Beckmann rearrangement of ketoximes. All the complexes studied yield isolable Beckmann intermediates, some of which have been identified. Only some of these intermediates could be hydrolyzed to the corresponding amides, but all of them yield their amides on pyrolysis. The intermediates most commonly found included the sulfonic acid derivative of the ketoxime which contained the Lewis base as an integral part of the intermediate. However, when the dimethylformamide-sulfur trioxide complex and the dioxane (di)-sulfur trioxide complex were used, two and three intermediates for the respective complexes were found.

While sulfur trioxide has been reported to promote the Beckmann rearrangement, in all but a few special cases¹ the reactivity of free sulfur trioxide is too great to permit a controlled reaction. In the cases where this reaction was apparently possible,² no mention or observation was made to substantiate any formation of the corresponding *N*-substituted amide. The reaction between a ketoxime and several sulfur trioxide complexes has been reported^{3,4} in limited studies in the past.

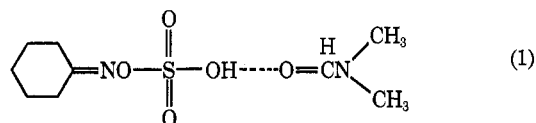
Results and Discussion

The Lewis bases studied as complexing agents for sulfur trioxide were *N,N*-dimethylformamide (DMF), *N,N*-diethylformamide, *N*-methylacetamide, *N,N*-dimethylacetamide, *N,N*-diethylacetamide, *N*-methylpropionamide, *N,N*-dimethylpropionamide, *N,N*-diethylpropionamide, *N,N*-dimethylbutyramide, *N,N*-diethylbutyramide, caprolactam, pyrrolidone, and *N,N*-dimethylbenzamide. It should be noted that any amide employed must be at least *N*-monoalkyl substituted to avoid dehydration to the nitrile. In addition to the above amides, various amines, cyclic ethers, nitriles, and nitro compounds were employed for this purpose. These were pyridine, 1,4-dioxane, tetrahydrofuran, benzonitrile, and nitrobenzene. Sulfur trioxide complexes of various polymers were also evaluated and include Carbowax 20M, polyvinyl pyrrolidone, trioxane, 2-vinylpyridine, nylon-6, and nylon-66.

The yields of caprolactam using the above complexes of sulfur trioxide were all in the range of 95–100%, with the exception of the amine complexes which were 0–30%. It was observed that in the case of the amine complexes the yield is inversely proportional to the basic strength of the amine employed.

To avoid the complexities associated with the rearrangement of a mixture of *cis* and *trans* oxime isomers, cyclohexanone oxime was chosen to evaluate the various sulfur trioxide complexes. During the course of the rearrangement of cyclohexanone oxime with these complexes, it was possible in all cases to isolate the corresponding intermediate. With the exception of three solid intermediates isolated while employing the

dioxane complex, all other intermediates were oils of varying viscosity and stability. The dimethylformamide-sulfur trioxide is capable of forming two intermediates with cyclohexanone oxime on a one-to-one and two-to-one molar ratio of oxime to complex. This is the only complex examined that was capable of rearranging an oxime on greater than a one-to-one molar basis. Both intermediates were examined by nuclear magnetic resonance and infrared spectroscopy. However, the structural difference was difficult to elucidate because of their limited solubility. It was determined that the intermediate resulting from the one-to-one molar reaction is a hydrogen-bonded species of the sulfonic acid derivative of cyclohexanone oxime and dimethylformamide as shown in (1). The nuclear magnetic



resonance data also suggest that a rapid equilibrium exists between the sulfonic acid and oxime portions of the intermediate.

Under normal conditions, the acidic rearranging reagent is neutralized and/or the intermediate is hydrolyzed prior to work-up of the reaction mixture. However, the hydrolysis of these intermediates under basic conditions can proceed in one of two directions, depending in part on the sulfur trioxide complex used. The hydrolysis reaction can produce caprolactam or the intermediate may simply revert to the free oxime, sulfate salt, and the Lewis base used in the complex. Cyclohexanone oxime intermediates can be hydrolyzed to caprolactam if the following Lewis bases are employed in the complex: 1,4-dioxane, tetrahydrofuran, caprolactam, *N,N*-diethylacetamide, *N,N*-diethylpropionamide, *N,N*-dimethylbutyramide, *N,N*-diethylbutyramide, and *N,N*-dimethylbenzamide. The rest of the intermediates listed previously revert to cyclohexanone oxime on hydrolysis.

An examination of the amides in Table I indicates that the degree of substitution on the nitrogen affects the route taken during hydrolysis when cyclohexanone oxime is used.

This is observed on comparing group Ia, Ib, and Ic, and group Id, Ie, and If. However, the results obtained using *N,N*-diethylformamide (Ig), and compared to those found for Ic and If, indicate that the degree of nitrogen substitution is not the only factor affecting the

(1) Potts (to Henkel and Cie GmbH), British Patent 732,899 (1955); N. Tokura, R. Asami, and R. Tado, *Sci. Rep. Res. Inst. Tohoku Univ., Ser. A*, **8**, 149 (1956).

(2) S. I. Burmestrov and A. G. Taranenko, *Ukr. Khim. Zh.*, **22**, 620 (1956); A. P. Terent'ev and N. B. Kupletskaya, *Zh. Obshch. Khim.*, **26**, 451 (1956).

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

(4) F. R. Atherton, A. L. Morrison, R. J. W. Cremlyer, G. W. Kenner, A. Todd, and R. F. Webb, *Chem. Ind. (London)*, 1183 (1955).

TABLE I

Lewis base used	No.	Hydrolysis product
CH ₃ CONHCH ₃	Ia	Oxime
CH ₃ CON(CH ₃) ₂	Ib	Oxime
CH ₃ CON(CH ₂ CH ₃) ₂	Ic	Lactam
CH ₃ CH ₂ CONHCH ₃	Id	Oxime
CH ₃ CH ₂ CON(CH ₃) ₂	Ie	Oxime
CH ₃ CH ₂ CON(CH ₂ CH ₃) ₂	If	Lactam
HCON(CH ₂ CH ₃) ₂	Ig	Oxime
CH ₃ (CH ₂) ₂ CON(CH ₃) ₂	Ih	Lactam
CH ₂ (CH ₂) ₂ CONH	Ii	Oxime
CH ₂ (CH ₂) ₃ CONH	Ij	Lactam

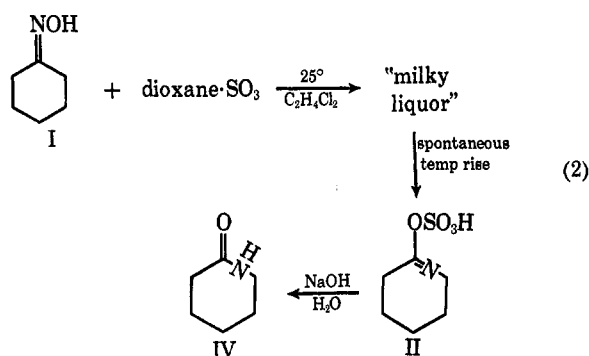
hydrolysis route. Therefore, it appears that the carbon number (and/or molecular weight) of the amide is the major factor influencing the hydrolysis route taken. This is substantiated by comparing Ie with Ih and Ii with Ij. This last sample in particular serves to indicate that the carbon number and not the parent chain length is responsible for the preferred route taken during hydrolysis. Therefore, it can be generalized that the cyclohexanone oxime intermediates formed from amide complexes containing five carbons or less will revert back to the oxime, while those intermediates formed from amide complexes containing six carbons or more will proceed on to the lactam upon hydrolysis. This generalization may not hold true when other oximes are used.

The structure of the oxime also plays an important role in the hydrolysis. The intermediate from the reaction of cyclohexanone oxime and the dimethylformamide-sulfur trioxide complex reverts to free oxime upon hydrolysis while 2-*n*-butylcyclohexanone oxime and 2-methylcyclohexanone oxime react with the same complex to form intermediates which hydrolyze to their respective lactams, the latter being a mixture.

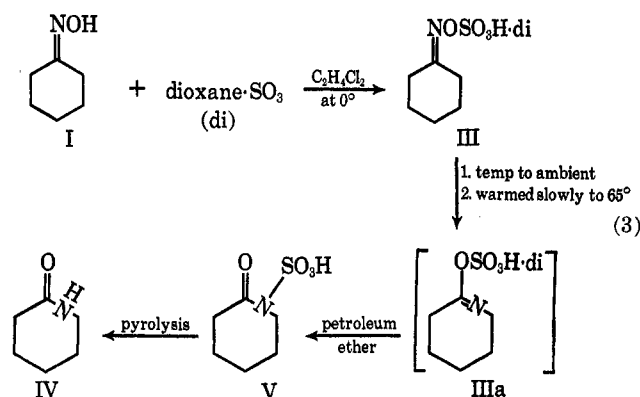
A number of solvent types can be employed to prepare these Beckmann intermediates. They include alcohols, ethers, esters, amines, ketones, amides, paraffins, and halogenated hydrocarbons. Although specific members of each broad classification have served with varying degrees of success, it was found that the halogenated hydrocarbons are the most suitable for this purpose. The reaction between any oxime and sulfur trioxide is nearly instantaneous and complete in these solvents. An exception to this was observed with the amine complexes. The amines form a very stable complex with sulfur trioxide due to their relatively high basic strength. This results in a very low reactivity and produces low yields of amides.

Although only approximately one-half of the cyclohexanone oxime intermediates studied could be hydrolyzed to the amide, it was possible to pyrolyze all of them to the amide. The pyrolysis is highly exothermic. It can be initiated by rapidly raising the temperature of the intermediate to its decomposition point after which the heat of reaction allows it to continue. Once initiated, this reaction is essentially spontaneous so that it becomes necessary to provide sufficient cooling to keep the reaction under control. The pyrolysis can be conducted in the gas phase in the presence of the solvent or in a small batch-type reaction after the solvent has been removed. The pyrolysis of these intermediates will not produce good yields of

amide if initiated under super- or subatmospheric pressures. Although a decomposition does occur under these conditions, the reaction product contains neither caprolactam, cyclohexanone oxime, nor any Beckmann intermediate. The products from such a decomposition have not been identified. The reaction of cyclohexanone oxime with the dioxane-sulfur trioxide (di-SO₃) complex yields solid intermediates which more readily lend themselves to structural analysis. This reaction has been reported³ and a mechanism was formulated according to eq 2.



However, by slightly varying the reaction conditions, a more complete picture of the reaction sequence was observed. On lowering the temperature at which the reaction was run by only a few degrees, a series of different intermediates was found as shown in eq 3.



The first intermediate (III) has a melting point of 26° dec⁵ and remains as a white solid in the reaction solvent below 10°. Allowing the reaction mixture to come to ambient temperature results in the solution of III, but the "milky liquor" or a spontaneous temperature rise was not observed as reported by Turbak.³ This indicates that the intermediates initially formed in eq 2 and 3 are not the same. When III is warmed to 65°, it is spontaneously transformed to a second intermediate (V) exothermically. Possibly this intermediate is derived by the Chapman rearrangement of IIIa with the loss of dioxane.

Experimental Section

Gas chromatographic analyses of the reaction products were performed on an F & M Model 720 dual column chromatograph equipped with thermal conductivity detectors. The column used was 0.25 in. × 4 ft stainless steel packed with 25% SE-31, with

(5) Although it is possible to isolate this intermediate, extreme care should be taken since experience has shown that it can decompose explosively.

a helium flow of 50 ml/min. Analyses were made at 135° isothermally with a bridge current of 150 mA.

Preparation of Sulfur Trioxide Complexes.—The method of preparation of all the complexes employed in this study is essentially identical. In general, the Lewis base is dissolved (suspended if an insoluble polymer) in dichloromethane, cooled to ice bath temperature, and 1 molar equiv of sulfur trioxide was added. The white crystalline complex precipitates, is filtered, and washed with dichloromethane. The melting point of these complexes is difficult to determine because of their rapid uptake of water. Two examples illustrate this preparation.

Dimethylformamide-Sulfur Trioxide Complex.—Dimethylformamide (100 g, 1.37 mol) in 75 ml of dichloromethane was placed in a 500-ml three-necked round-bottom flask equipped with a magnetic stirrer, cold finger condenser, and drying tube. This solution was cooled to 0° in an ice water bath and 1.37 mol (109 g, 56 ml) of stabilized liquid sulfur trioxide (at room temperature) was added dropwise from a pressure equalizing dropping funnel over a period of 45 min. Upon completion of addition, the white crystalline complex was removed by vacuum filtration and washed several times with dichloromethane. During filtration and washing, the filtering funnel was covered with a rubber membrane to prevent exposure of the complex to atmospheric moisture. A theoretical quantity (209 g) of the complex was obtained.

Polyvinyl Pyrrolidone.—Liquid sulfur trioxide (0.5 g) was added dropwise to a previously cooled solution of 1 g of polyvinyl pyrrolidone in 30 ml of 1,2-dichloroethane. The white crystalline complex began to precipitate from solution soon after the initial addition of the sulfur trioxide. After the required volume of sulfur trioxide had been added, the solid was removed by vacuum filtration, washed with 1,2-dichloroethane, and vacuum dried at room temperature to give a 98% yield (1.5 g) of the complex. Titration of a small quantity of this complex showed the available sulfur trioxide concentration to be 0.0046 mol/g of complex.

Beckmann Rearrangement Studies. Rearrangement of Cyclohexanone Oxime Using Flow-through Reactor.—A 1 × 14 cm condenser was clamped in a vertical position and packed with 2.7 g (0.018 mol) of the dimethylformamide-sulfur trioxide complex supported on a glass wool plug. Water at 40° was circulated through the condenser jacket. Cyclohexanone oxime (2.0 g, 0.018 mol) was dissolved in 5.0 ml of dichloromethane contained in a small pressure-regulating dropping funnel. This solution was then allowed to flow through the reagent bed under a slight pressure to prevent the solvent from boiling. As the reaction proceeded, the reagent was consumed and the effluent from the column was collected in a two-necked 50-ml round-bottom flask. The condenser was washed with 2.0 ml of dichloromethane and the washings were added to the reaction mixture. The solvent was removed by evacuating the flask on a rotatory evaporator at 3 mm at room temperature over a 0.5-hr period. The clear viscous oil remaining in the flask is the Beckmann intermediate. An electric resistance heater was immersed in the oily intermediate. With the material previously cooled to 0°, the resistance heater was activated momentarily to initiate the decomposition, after which the reaction proceeded on its own due to the exothermicity of the reaction. Immediately after the onset of the pyrolytic reaction, the pressure was rapidly lowered to 3 mm to remove liberated sulfur trioxide. The pyrolysis product (greenish brown oil) was taken up in methanol. A thin layer chromatogram (2% methanol in benzene on silica gel) confirmed the presence of free caprolactam. Examination of this solution by glc showed a 96% yield of caprolactam based on molar response.

Vapor Phase Pyrolysis of Beckmann Intermediate.—A one-to-one molar ratio intermediate was prepared using the flow-

through reactor technique. The total reaction mixture was drawn into a 10-ml glass syringe equipped with a 5.5 in. filling needle. The syringe was mounted horizontally in an adjustable rate infusion pump. The needle was completely inserted through a rubber septum into the horizontal pyrolysis tube (1 × 47 cm), containing a helium flow of 100 ml/min and equipped with a cold trap, so that the tip of the needle just touched the edge of a glass wool packing 5 cm in length. The tube packing was centered in a micro combustion furnace 20 cm in length. With the furnace preheated to 230 ± 2°, the intermediate reaction mixture was injected at the rate of 0.2 ml/min. After complete injection, the furnace was rapidly cooled using compressed air and the syringe needle withdrawn. The residual material in the heated zone was eluted using methanol and combined with the condensate in the cold trap. This mixture was neutralized with ammonia and filtered, and the filtrate made up to 250.0 ml with methanol. Examination of this solution by glc showed a 67.5% yield of caprolactam based on molar response.

Dioxane-Sulfur Trioxide Intermediates.—The dioxane-sulfur trioxide complex (3.0 g, 0.018 mol) was slurried in 10 ml of 1,2-dichloroethane using a magnetic stirrer and cooled to 0° using an ice water bath. An equimolar quantity of cyclohexanone oxime (2.0 g) was placed in a pressure-equalizing dropping funnel and dissolved in 10 ml of dichloroethane. This solution was added slowly to the slurry of the complex over a 15-min period in order to maintain the reaction temperature at 0°. After the addition was complete, the white crystalline intermediate III was removed by vacuum filtration under anhydrous conditions. Examination of this intermediate by ir showed a sulfate group (1240 cm⁻¹) present with no carbonyl evident (1669 cm⁻¹). Nmr showed that a seven-membered lactam ring was not present by the absence of the δ 3.4 peak (CH₂NCO) and that dioxane was present in a one-to-one molar ratio to the cyclohexane portion of the intermediate. The experimentally determined molecular weight and elemental analysis also support the proposed structure. The molecular weight was determined by a vapor pressure osmometer method to give 290 vs. 281 calculated. *Anal.* Calcd for C₁₀H₁₉O₄NS: C, 42.7; H, 6.8; N, 5.0; O, 34.1; S, 11.4. Found: C, 42.8; H, 6.7; N, 4.9; O, 34.3; S, 11.4.

When this intermediate, as formed in the reaction solvent, was slowly warmed to 65° using a water bath, it was spontaneously transformed to a second intermediate (V, eq 3) exothermally. Examination of this intermediate by ir showed a lactam carbonyl (1669 cm⁻¹). The nmr spectrum exhibited peaks (acetone-*d*₆ vs. TMS) at δ 13.8 (acid H), 3.4 (CH₂NCO), 2.3 (CH₂CON). No dioxane was evident and an electronegative group was present on the nitrogen. *Anal.* Calcd for C₈H₁₁O₄NS: C, 37.3; H, 5.7; N, 7.3; O, 33.1; S, 16.6; mol wt, 193. Found: C, 37.4; H, 5.8; N, 7.2; O, 33.2; S, 16.6; mol wt, 188.

Registry No.—DMF-SO₃ complex, 29584-42-7; *N,N*-diethylformamide-SO₃ complex, 29584-43-8; *N*-methylacetamide-SO₃ complex, 29584-44-9; *N,N*-dimethylacetamide-SO₃ complex, 29641-83-6; *N,N*-diethylacetamide-SO₃ complex, 29584-45-0; *N*-methylpropionamide-SO₃ complex, 29584-46-1; *N,N*-dimethylpropionamide-SO₃ complex, 29641-84-7; *N,N*-diethylpropionamide-SO₃ complex, 29584-47-2; *N,N*-dimethylbutyramide-SO₃ complex, 29584-48-3; *N,N*-diethylbutyramide-SO₃ complex, 29584-49-4; caprolactam-SO₃ complex, 29641-85-8; pyrrolidone-SO₃ complex, 29584-50-7; *N,N*-dimethylbenzamide-SO₃ complex, 29584-51-8.