Reactions of 1-Halo-1-nitroso- and 1-Halo-1-nitrocycloalkanes with Triphenylphosphine. A New Synthesis of Lactam[1]

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Reactions of 1-halo-1-nitroso- and 1-halo-1-nitrocycloalkanes with triphenylphosphine have been carried out. The Perkov reaction and Beckmann rearrangement occurred successively with the formation of lactams in high yields. The reaction of cycloalkanone oxime with halogen in the presence of triphenylphosphine also gave lactams in one step.

Many works have been carried out on the Perkov reaction since 1955.[2] However, little is known about the reaction of halonitroso- and halonitroalkanes with trivalent organophosphorus compounds. The reactions of 2-chloro-1-nitrosopropane with 1 mol of triethyl phosphite and 2-chloro-2-nitropropane with 2 mol of triethyl phosphite afforded diethyl isopropylideneamino phosphate, but no Beckmann rearrangement product was obtained by its pyrolysis.[3] The reaction of bromonitromethane and triphenylphosphine smoothly forms a phosphonium salt that gives triphenylphosphine oxide and fulminic acid[4] with aqueous alkali at 0 °C. Treatment of 1-bromo-1-nitroalkanes with triphenylphosphine generally gives nitriles.[5] However, no investigation has been carried out on the Perkov type reaction of 1-halo-1-nitroso- and 1-halo-1-nitrocycloalkanes with trivalent organophosphorus compounds.[2]

We wish to report the first successful Beckmann rearrangement of 1-halo-1-nitroso- and 1-halo-1-nitrocycloalkanes (2 and 6) with triphenylphosphine.

All 1-halo-1-nitrosocycloalkanes (2) were prepared by the reaction of cycloalkanone oximes (1) with halogens according to the method of Piloty and Stork.[6] 1-Chloro-1-nitrocyclohexane was prepared by the reaction of sodium salt of nitrocyclohexane and chlorine according to the method of Robertson.[7] 1-Chloro-1-nitrocycloalkanes of 8- and 12-membered rings were prepared by the oxidation of the corresponding compound 2 with nitric acid according to the method of Iffland et al.[8]

Reaction of 1-Halo-1-nitrosocycloalkanes. 1-Chloro-1-nitrosocycloalkanes (2) were dissolved in nonpolar solvents such as benzene, toluene, ether, or tetrahydrofuran, and treated with 1 mol equivalent of triphenylphosphine at room temperature. The reaction was exothermic, the deep blue color characteristic of the nitroso group disappearing gradually. The reaction temperature reached 40—70 °C. After 30—60 min, the reaction mixture was hydrolyzed, the corresponding lactams (5) being obtained in moderate to excellent yields. When the temperature was kept at 0—10 °C, a very hygroscopic precipitate (the IR spectrum shows an absorption at 1655 cm⁻¹, characteristic of C=N group) was formed, which was then

heated in dry benzene at 60 °C. The reaction mixtures were worked up in the same way as described above. Lactam (5) and triphenylphosphine oxide were obtained in high yields. The results of reactions of compound 2 with triphenylphosphine are summarized in Table 1.
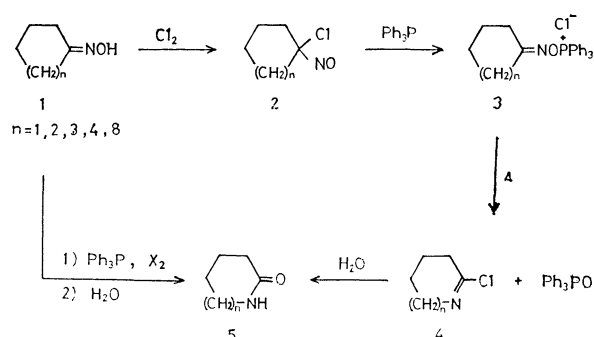
Scheme 1.

In order to simplify the reaction, compounds 1 were directly treated with halogens in the presence of equivalent amount of triphenylphosphine. The corresponding lactams 5 were obtained in good yields in the case of chlorine and bromine, and in fair yields in the case of iodine. The results are also summarized in Table 1.

Reaction of 1-Halo-1-nitrocycloalkanes. On the basis of the reaction of compound 2 with triphenylphosphine, reactions of 1-chloro-1-nitrocycloalkane (6) with triphenylphosphine were studied. 1-Chloro-1-nitrocyclohexane was treated with 2 mol of triphenylphosphine in benzene under reflux for 5 h. After the reaction mixture had been treated with 2 M hydrochloric acid, the benzene solution afforded triphenylphosphine oxide in 86% yield and the aqueous solution afforded ε-caprolactam in 55—60% yield. Treatment with 1 mol and 3 mol of triphenylphosphine gave ε-caprolactam in 34 and 77% yields, respectively. It seems reasonable to assume that 2 mol of triphenylphosphine are required to remove two oxygen atoms of the nitro group. The same reaction of 1-chloro-1-nitrocyclooctane and 1-chloro-1-nitrocyclododecane with 2 mol of triphenylphosphine afforded perhydroazonin-2-one in 43% yield and azacyclotridecan-2-one in 32% yield, respectively.

Mechanisms. The reactions of 1-chloro-1-nitroso- and 1-chloro-1-nitrocycloalkanes with triphenylphosphine provide a new synthetic method of lactams. The mechanisms of the new reactions are explained in Schemes 1 and 2.

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Table 1. Reactions of 1-halo-1-nitroso- and 1-halo-1-nitrocycloalkanes with triphenylphosphine

Starting material	Reagent	Product[a]	Yield/%
1-Chloro-1-nitrosocyclopentane	$(C_6H_5)_3P$	δ-Valerolactam	57
1-Chloro-1-nitrosocyclohexane	$(C_6H_5)_3P$	ε-Caprolactam	96
1-Chloro-1-nitrosocycloheptane	$(C_6H_5)_3P$	Perhydroazonin-2-one	76
1-Chloro-1-nitrosocyclooctane	$(C_6H_5)_3P$	Perhydroazonin-2-one	83
1-Chloro-1-nitrosocyclododecane	$(C_6H_5)_3P$	Azacyclotridecan-2-one	78
Cyclopentanone oxime	$(C_6H_5)_3P,Cl_2$	δ-Valerolactam	76
Cyclohexanone oxime	$(C_6H_5)_3P,Cl_2$	ε-Caprolactam	86
Cyclohexanone oxime	$(C_6H_5)_3P,Br_2$	ε-Caprolactam	74
Cyclohexanone oxime	$(C_6H_5)_3P,I_2$	ε-Caprolactam	39
Cyclooctanone oxime	$(C_6H_5)_3P,Br_2$	Perhydroazonin-2-one	74
Cyclooctanone oxime	$(C_6H_5)_3P,I_2$	Perhydroazonin-2-one	60
Cyclododecanone oxime	$(C_6H_5)_3P,Br_2$	Azacyclotridecan-2-one	81
Cyclododecanone oxime	$(C_6H_5)_3P,I_2$	Azacyclotridecan-2-one	48
1-Chloro-1-nitrocyclohexane	$(C_6H_5)_3P$	ε-Caprolactam	77
1-Chloro-1-nitrocyclooctane	$(C_6H_5)_3P$	Perhydroazonin-2-one	42
1-Chloro-1-nitrocyclododecane	$(C_6H_5)_3P$	Azacyclotridecan-2-one	32

a) All lactams were confirmed to be identical with authentic samples prepared by the usual Beckmann rearrangement.
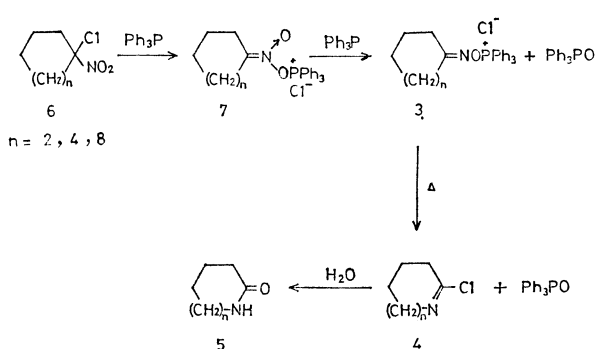
Scheme 2.

In the case of compound **2**, the mechanism includes initial attack of phosphorus on oxygen to give phosphonium salts (**3**) directly followed by thermal rearrangement to chloro imine (**4**) which could not be isolated, and in line with the present understanding of the reactions of α-bromo ketone with triphenylphosphine.[9]

The reaction of compound **6** with triphenylphosphine differs a great deal from that of compound **2**. The former is endothermic, requiring drastic conditions, but the latter is exothermic and can be carried out smoothly at room temperature. The evidences combined with the fact that no blue coloration takes places during the course of reaction suggest that the reaction mechanism is not by way of compound **2**, but by the formation of Perkov type intermediate (**7**) followed by transformation into a phosphonium salt (**3**) and then the Beckmann rearrangement.

Experimental

Melting points and boiling points are uncorrected. IR spectra were taken on a Hitachi EPI-S2 spectrometer.

1-Chloro-1-nitrosocyclohexane. In a 1-litre three-necked, round-bottomed flask, equipped with a gas inlet tube and a mechanical stirrer, were placed 500 ml of cyclohexane and 56.5 g of cyclohexanone oxime. The flask was covered

with a black cloth so as to prevent exposure to sun-light. Chlorine gas was passed into the solution with stirring at room temperature in the course of about 2 h. A solution of a deep blue color was obtained. The excess chlorine remaining in the flask was removed under reduced pressure. The solution was washed successively with water, 1 M sodium hydroxide, and water; dried over anhydrous sodium sulfate. Cyclohexane was removed by distillation, and the residue was distilled under reduced pressure. The yield of **2** was 63.5 g (86%) of dark blue liquid, bp 75 °C/41 mmHg. IR (liquid film): 1570 cm⁻¹ (NO).

Of 1-chloro-1-nitrosocycloalkanes prepared by the same procedure, 5-, 6-, 7-, and 8-membered ring compounds are dark blue liquids. Only 1-chloro-1-nitrosocyclododecane is a blue crystalline material which melts at 53—55 °C after recrystallization from ethanol.

Their infrared spectra show an absorption at 1570—1580 cm⁻¹, characteristic of monomeric nitroso group.

Reaction of 1-Chloro-1-nitrosocyclohexane with Triphenylphosphine. In a 300 ml three-necked, round-bottomed flask fitted with a condenser, a dropping funnel, and a mechanical stirrer were placed 10 g (0.068 mol) of 1-chloro-1-nitrosocyclohexane and 100 ml of benzene. A solution of 17.8 g (0.068 mol) of triphenylphosphine in 100 ml of benzene was slowly added from the dropping funnel, with stirring for 30 min at room temperature. The deep blue color of the solution disappeared within 15 min and the temperature rose as high as 70 °C. After 30 min, the reaction mixture was treated with 100 ml of 1 M hydrochloric acid. Triphenylphosphine oxide was obtained in 95% yield (18.5 g) from the organic layer. The aqueous fraction was evaporated to dryness under reduced pressure on a water bath. The residue was neutralized with 2 M sodium hydroxide, and extracted with three 100 ml portions of dichloromethane–ether (1 : 1). The extract was dried with anhydrous sodium sulfate and evaporated to dryness under reduced pressure on a water bath. The residual solid was 7.6 g (99%) of crude ε-caprolactam and was distilled under reduced pressure. The main fraction was distilled at 165—167 °C/33 mmHg. Its infrared spectrum and mp were identical with those of an authentic sample.

Other 1-halo-1-nitrosocycloalkanes were treated with triphenylphosphine in a similar way. Lactams of 6- to 8-membered ring showed a single characteristic absorption (1650—1660 cm⁻¹). Those of 9- and 13-membered ring

showed two characteristic absorptions (1635—1655 cm^{-1} and 1535—1550 cm^{-1}).

Reaction of Cyclohexanone Oxime with Chlorine in the Presence of Triphenylphosphine. In a 300 ml three-necked, round-bottomed flask, fitted with a gas inlet tube, a mechanical stirrer, and a condenser, were placed a solution of 5.7 g (0.05 mol) of cyclohexanone oxime and 13.1 g (0.05 mol) of triphenylphosphine in 100 ml of benzene. Chlorine gas was passed into the solution with stirring at room temperature, the reaction temperature rising as high as 50—60 °C. After the temperature had fallen to room temperature, bubbling of chlorine was stopped. The reaction mixture was worked up in a similar way to that above. ε-Caprolactam was obtained in 86% yield (4.9 g) from the aqueous layer and triphenylphosphine oxide being obtained quantitatively from the benzene layer. A solution of bromine or iodine in benzene could also be used instead of chlorine gas.

1-Chloro-1-nitrocyclohexane. In a 100 ml Erlenmeyer flask provided with a magnetic stirrer was placed 10 g (0.08 mol) of nitrocyclohexane. A solution of 5 g (0.123 mol) of sodium hydroxide in 60 ml of water was added dropwise with stirring at room temperature. After being stirred for 3 h, the reaction mixture became homogeneous. Chlorine gas was then passed into the solution which had been cooled to −5—0 °C in an ice–salt bath. Pale blue oil separated out after 1.5 h. The reaction mixture was extracted three times with 60 ml portions of dichloromethane–ether (1 : 1). The extract was dried with anhydrous sodium sulfate and evaporated to dryness. The oily residue (12.3 g) was distilled under reduced pressure. The principal fraction was 10 g of 1-chloro-1-nitrocyclohexane, a colorless oil boiling at 53.5 °C/1 mmHg.

1-Chloro-1-nitrocyclododecane. In a 200 ml separatory funnel was placed a solution of 5.00 g (0.022 mol) of 1-chloro-1-nitrosocyclododecane in 50 ml of cyclohexane, and 12.5 ml of concentrated nitric acid was added. The funnel was then shaken until the blue color of the solution disappeared. The reaction mixture was washed successively with 50 ml of water, 50 ml of 5% aqueous sodium hydroxide, and 50 ml of water. After being dried over anhydrous sodium sulfate, the cyclohexane was removed under atmospheric pressure, and 5.44 g of the oily residue was distilled under reduced pressure. The product of 1-chloro-1-nitrocyclododecane was 3.62 g (68%) of colorless crystal boiling

at 118—119 °C/0.2 mmHg and melting at 49.5—50.5 °C after recrystallization from acetone. IR (KBr): 1556, 1348 cm^{-1} (NO$_2$). 1-Chloro-1-nitrocyclooctane was also prepared in a similar way. The product was 5.52 g (44.2%) of colorless liquid boiling at 74 °C/0.6 mmHg. IR (liquid film): 1563, 1333 cm^{-1} (NO$_2$).

Reaction of 1-Chloro-1-nitrocyclohexane with Triphenylphosphine. In a 100 ml flask fitted with a reflux condenser was placed a solution of 4.8 g (0.0294 mol) of 1-chloro-1-nitrocyclohexane in 40 ml of benzene and a solution of 16.2 g (0.0618 mol) of triphenylphosphine in 20 ml of benzene. The mixture was refluxed for 4 h on a steam bath. The reddish reaction mixture was washed three times with 180 ml portions of 2 M hydrochloric acid. The yellow organic layer was dried with anhydrous sodium sulfate and evaporated. Triphenylphosphine oxide was obtained in 86% yield (14.0 g). The aqueous layer was evaporated. The oily residue was made basic to litmus with 2 M sodium hydroxide and was extracted with dichloromethane–ether (1 : 1). After the extract had been dried over anhydrous sodium sulfate, the dichloromethane and ether were removed by distillation. ε-Caprolactam was obtained in 58% yield (1.93 g).

Reactions of 1-chloro-1-nitrocyclooctane and 1-chloro-1-nitrocyclododecane with triphenylphosphine were also carried out in a similar way.

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