nickel,[16] 250 ml. of 70% ethanol and 5.8 g. (0.02 mole) of compound VII. The mixture was refluxed for five hours, centrifuged and decanted while still hot. The Raney nickel was washed with 500 ml. of boiling 95% ethanol, centrifuged and the supernatant liquid decanted. The ethanolic solutions were combined and evaporated to dryness to yield 3.2 g. (94%) of N-butylsuccinamide, m.p. 184–185°. Recrystallization from water raised the melting point to 190–190.5°. The infrared spectrum showed strong characteristic amide bands at 6.10, 6.02 and 6.42 μ.

Anal. Calcd. for $C_8H_{16}O_2N_2$: C, 55.79; H, 9.36; N, 16.27. Found: C, 55.83; H, 9.32; N, 16.42.

N-Butylsuccinamide from Compound VIII.—The procedure was similar to that employed in the reduction of compound VII. The reaction afforded 2.8 g. (82%) of **N-butylsuccinamide**, m.p. 183–184°. Recrystallization from water raised the melting point to 190–190.5°.

Anal. Calcd. for $C_8H_{16}O_2N_2$: C, 55.79; H, 9.36; N, 16.27. Found: C, 55.96; H, 9.50; N, 16.30.

N-Butylsuccinamide (IX) from N-Butylsuccinimide (XI).—N-Butylsuccinimide (XI, 15.5 g., 0.1 mole) and 60 ml. of 95% ethanol were placed in a combustion tube and ammonia was bubbled into the mixture until the solution was saturated. The tube was sealed and heated for 6 hours at 100°. After evaporation of the solvent, 1.0 g. (6% conversion) of N-butylsuccinamide, m.p. 180–185°, was removed by filtration from unreacted XI. The product was recrystallized from a methanol–water mixture, m.p. 140–141°. A mixed melting point with the compound obtained in this reaction with those obtained in the Raney nickel reduction of compounds VII and VIII gave no depression. The infrared spectra of all three compounds were superimposable.

N-Butylsuccinimide (XI).—In a one-liter three-necked flask equipped with a condenser, drying tube and stirrer were placed 600 ml. of dry chloroform, 79 g. (1.0 mole) of pyridine and 73 g. (1.0 mole) of *n*-butylamine. To this solution 151 g. (1.0 mole) of methylsuccinoyl chloride was added dropwise with stirring. After complete addition, the mixture was refluxed for 20 minutes and then transferred to a separatory funnel where it was first washed with 150 ml. of water and then with 50 ml. of a saturated aqueous solution of sodium bicarbonate.

(16) R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, THIS JOURNAL, **65**, 1013 (1943).

The water layers were combined and extracted with 150 ml. of chloroform. The chloroform fractions were combined, dried over magnesium sulfate and subsequently distilled at atmospheric pressure to remove the chloroform. Vacuum distillation of the residue yielded 130 g. (70%) of impure methyl N-butyl succinamate, b.p. 128–135° (0.5 mm.), $n^{20}D$ 1.4560. Fractionation through a 1.5-foot spiral column at 1–7 mm. (pressure did not remain constant) yielded nearly quantitatively, N-butylsuccinimide boiling at 100–117°; b.p. 75° (0.5 mm.), b.p. 139° (12 mm.), $n^{20}D$ 1.4749 (lit. value[11,12] b.p. 80–82° (0.5 mm.), b.p. 137–139°, (12 mm.), $n^{25}D$ 1.4720.

Silver Salt of Maleic Hydrazide.—An aqueous solution of the ammonium salt of maleic hydrazide was added to an aqueous solution of excess silver nitrate and heated on a steam-cone for several hours. The gelatinous precipitate was filtered with the aid of large quantities of water, and washed with ethanol and ether to give a quantitative yield of silver maleic hydrazide.

Anal. Calcd. for $C_4H_3N_2O_2Ag$: Ag, 49.23. Found: Ag, 49.30.

6-Butoxy-3(2H)-pyridazinone (XII).—In a 500-ml. round-bottom flask were placed 21.9 g. (0.1 mole) of the silver salt of I, 22.1 g. (0.12 mole) of butyl iodide and 300 ml. of xylene. The mixture was refluxed for 120 hours and then filtered. Evaporation of the filtrate afforded an oil which was dissolved in boiling hexane. Upon cooling 5.1 g. of XII, m.p. 99–100°, was obtained. Recrystallization from hexane raised the melting point to 102–103°. The precipitate obtained upon filtration of the reaction mixture was treated with 35 ml. of 4 *N* hydrochloric acid, heated to boiling and filtered. Upon cooling, 5.0 g. of maleic hydrazide was recovered. Thus the total yield of XII was 60%. The infrared spectrum showed a strong band at 5.98 μ for the ring carbonyl.

Anal. Calcd. for $C_8H_{12}O_2N_2$: C, 57.13; H, 7.14; N, 16.66. Found: C, 57.37; H, 7.10; N, 16.94.

Ultraviolet Spectral Measurements.—All ultraviolet spectral measurements were made with a Cary model 10–11 spectrophotometer. The solvent employed was commercial 95% ethanol.

LAFAYETTE, IND.

[CONTRIBUTION FROM EASTERN LABORATORY OF THE EXPLOSIVES DEPARTMENT, E. I. DU PONT DE NEMOURS & CO.]

Beckmann Rearrangement. I. Syntheses of Oxime *p*-Toluenesulfonates and Beckmann Rearrangement in Acetic Acid, Methyl Alcohol and Chloroform

BY WALTER Z. HELDT

RECEIVED JANUARY 8, 1958

Oxime *p*-toluenesulfonates were synthesized in high conversions from the sodium salt of the oxime and *p*-toluenesulfonyl chloride in benzene. Acetolysis of cycloalkanone oxime *p*-toluenesulfonates yielded mainly the corresponding lactams; methanolysis yielded O-methyl lactim ethers and degradation products; rearrangement in chloroform yielded as final product N-substituted lactams.

A convenient way to rearrange an oxime to the corresponding lactam is to prepare "*in situ*" the oxime benzenesulfonate which rearranges in aqueous solution to the lactam in high yields.[1] If water is replaced by a solvent which can act as a nucleophile the rearrangement is arrested at the imine stage. In such a way numerous O-alkyl-[2] and O-aryl-imine[2] ethers, amidines,[2] sulfamidines,[2] O-imidylphosphates[3] and tetrazoles[4] have been prepared in good yields. If a strong nucleophile such as potassium ethoxide is added, the so-called Neber rearrangement takes place.[5]

(1) (a) R. F. Brown, N. M. van Gulick and G. H. Schmidt, THIS JOURNAL, **77**, 1094 (1955); (b) J. S. Buck and W. S. Ide, *ibid.*, **53**, 1536 (1931); (c) H. M. Kissman and J. Williams, *ibid.*, **72**, 5323 (1950); (d) G. Rosenkranz, O. Mancera, F. Sondheimer and C. Djerassi, *J. Org. Chem.*, **21**, 520 (1956); (e) L. G. Donaruma and W. Z. Heldt, "Organic Reactions," Vol. XI to be published.

(2) (a) P. Oxley and W. F. Short, *J. Chem. Soc.*, 1514 (1948); (b) G. Schroeter, R. Gluschke, S. Götzky, J. Huang, G. Irmisch, E. Laves, O. Schrater and G. Stier, *Ber.*, **63**, 1308 (1930).

(3) R. F. Atherton, A. L. Morrison, R. J. W. Cremlyn, G. W. Kenner, A. Todd and R. F. Webb, *Chemistry & Industry*, 1183 (1955).

(4) (a) E. K. Harrvill, C. W. Roberts and R. M. Herbst, *J. Org. Chem.*, **15**, 58 (1950); (b) Boehringer und Sohn, German Patent 540,409; (c) Knoll, A. G., German Patent 574,943.

(5) (a) P. W. Neber and A. von Friedolsheim, *Ann.*, **449**, 109 (1926); (b) P. W. Neber and A. Uber, *ibid.*, **467**, 52 (1928); (c) P. W. Neber and A. Burgard, *ibid.*, **493**, 281 (1932); (d) P. W. Neber and G. Huk, *ibid.*, **515**, 283 (1935); (e) P. W. Neber, A. Burgard and W. Thier, *ibid.*, **526**, 277 (1936); (f) M. J. Hatch and D. J. Cram, THIS JOURNAL, **75**, 38 (1953).

TABLE I

OXIME *p*-TOLUENESULFONATES

Oxime *p*-toluenesulfonates	Oxime m.p. or b.p., °C.	Infrared oxime *p*-toluene-sulfonate >C=N— in cm.$^{-1}$	Yield, % Crude	Yield, % Purified	M.p., °C., (uncor.)	M.p., °C., reported	Ref.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
Acetoxime	62	1660	100	95	83–85	..	..	52.85	53.21	5.77	5.98	6.16	6.15
Acetophenone oxime	59–60	1640	88	80	73–74.5	..	2a	62.27	62.02	5.23	5.21	4.83	4.99
Benzophenone oxime	144	1645(?)	~90	60	82–83	88	2a	68.35	68.20	4.87	4.86	3.98	3.87
Cyclopentanone oxime	56.9	1660	95	~70	74.6–76.0	..	..	56.80	56.55	5.96	6.01	5.53	5.07
Cyclohexanone oxime	88.69	1640	90	40	56.9–58.0	60	8	58.40	58.63	6.41	6.53	5.24	4.96
Cycloheptanone oxime	93–94[a]	1625	~90	55	59.3–60.2	..	..	59.76	59.83	6.81	6.94	4.98	4.90
Cyclooctanone oxime	96–98[b]	1625	~85	35	56.8–57.8	..	..	60.96	60.82	7.20	7.00	4.74	4.57

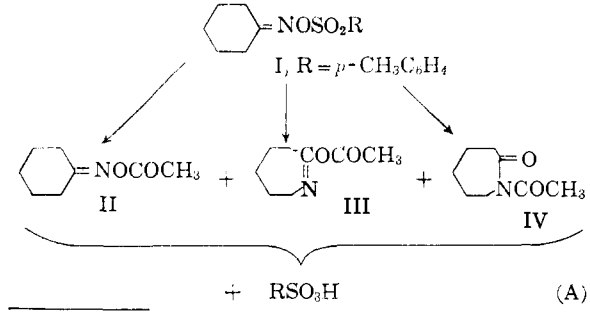
[a] B.p. at 3.5 mm.; $n^{25}D$ 1.4992. [b] B.p. at 4.0 mm.; $n^{25}D$ 1.4538.

Several methods[2a,5a,5c,6,7] are known for the preparation of oxime *p*-toluenesulfonates but only one method[8] gave reportedly good yields of cycloalkanone oxime *p*-toluenesulfonates. The purpose of this work was to develop a convenient synthesis for cycloalkanone oxime *p*-toluenesulfonates and to determine quantitatively the products of their rearrangement in acetic acid, methanol and chloroform.

Results and Discussion of Results

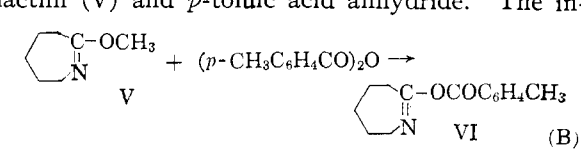
Synthesis of Oxime *p*-Toluenesulfonates.—Several oxime *p*-toluenesulfonates previously were prepared from the corresponding oxime, sodium hydroxide and *p*-toluenesulfonyl chloride in acetone as the solvent.[5f] In our hands satisfactory conversions were obtained by this method; however, the esters thus prepared decomposed after several days (frequently with vigor). A better method for the preparation of oxime *p*-toluenesulfonates is a modification of the method of Csuros.[8] The oxime was treated with sodium amide in benzene to form the sodium salt; the toluenesulfonyl chloride was then added to an excess of the salt suspended in dry benzene at 20–30°. The conversion to the oxime *p*-toluenesulfonates was 85–100% if sufficiently pure sodium amide was employed in the preparation. Data for eight oxime *p*-toluenesulfonates which were prepared are summarized in Table I.

The Acetolysis of Cycloalkanone Oxime *p*-Toluenesulfonates in Glacial Acetic Acid.—The acetolysis of cyclohexanone oxime *p*-toluenesulfonate (I) conceivably could yield three different products if the reaction in glacial acetic acid proceeds with partial ionization of the N–O bond of the parent oxime.



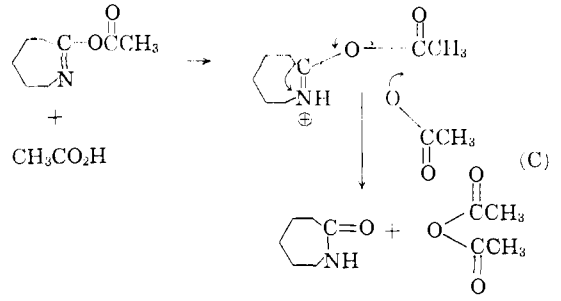
(A)

For this reason attempts were made to synthesize cyclohexanone oxime acetate (II), O-acetylcaprolactim (III) and N-acetyl-ε-caprolactam (IV). Compound II was synthesized according to a known procedure[8] from cyclohexanone oxime and acetyl chloride in pyridine and IV was obtained according to the procedure of Hudlicky from caprolactam and acetyl chloride in pyridine.[9] Attempts to synthesize III were unsuccessful. A model compound, O-toluylcaprolactim (VI) could be prepared, however, by heating O-methylcaprolactim (V) and *p*-toluic acid anhydride. The infrared spectra of II, V and VI differed considerably (see Experimental) so that an identification of all three compounds was possible by this method. The acetolysis of I in acetic acid to which a slight excess of acetic anhydride was added was 99% complete in one hour at 35° as indicated by titration of the reaction mixture with standard sodium acetate using brom phenol blue as indicator.[10] However, the only product isolated from the reaction mixture after careful processing was ε-caprolactam in quantitative conversion. No II or IV could be detected by infrared analysis of a chloroform solution of the reaction product when this sample was run against a solution of pure caprolactam in the reference cell.



(B)

The acetolysis of I appears, therefore, to proceed with the formation of III, which reacts rapidly with acetic acid to form probably acetic anhydride and ε-caprolactam.



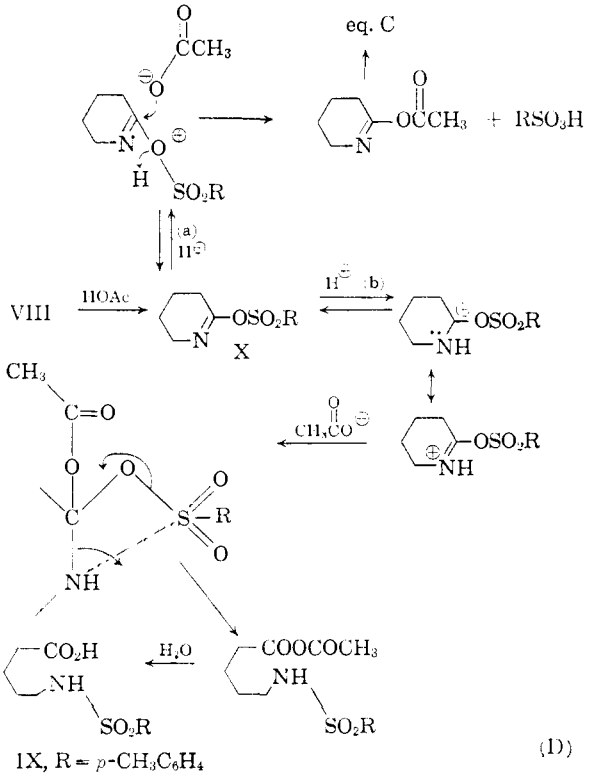
(C)

(6) T. A. Geissman and A. Armen, THIS JOURNAL, **77**, 1623 (1955).
(7) D. J. Cram and M. J. Hatch, *ibid.*, **75**, 33 (1953).
(8) Z. Csuros, K. Zech, G. Dely and E. Zaly, *Acta Chim. Acad. Sci. Hung.*, **1**, 66 (1951).
(9) M. Hudlicky, *Chem. Listy*, **37**, 208 (1943).
(10) J. D. Roberts, W. G. Young and S. Winstein, THIS JOURNAL, **64**, 2157 (1942).

A similar nucleophilic substitution by acetic acid on imido esters has been described by Cramer and Pawelzik.[11]

Solvolysis of cycloheptanone oxime *p*-toluenesulfonate (VII) in acetic acid was complete in two hours at room temperature. The product of the reaction was a mixture of enantholactam and a trace of O-acetylenantholactim. The lactim was tentatively identified by the 1740 cm.$^{-1}$ [12] band, characteristic of an ester (also present in VI), and by the very strong band at 1645 cm.$^{-1}$, characteristic of animine band >C=N—[13] (see Experimental).

When cyclopentanone oxime *p*-toluenesulfonate (VIII) was solvolyzed in 100% acetic acid at 35° for two hours, the reaction mixture yielded a solid precipitate (IX); 90% of the theoretically possible *p*-toluenesulfonic acid was generated in the reaction. The solid (IX) after purification, proved to be identical (on the basis of infrared spectra and mixed melting point) with δ-(*p*-toluenesulfonamido)-valeric acid, prepared by the Schotten–Baumann reaction of δ-aminovaleric acid and *p*-toluenesulfonyl chloride. The total conversion of IX from VIII was 8% after recrystallization from water. The infrared spectrum of the solid obtained in the filtrate from IX indicated that it was a mixture containing δ-valerolactam, and a small amount of O-acetylvalerolactim (ester band at 1742 cm.$^{-1}$ appearing as a shoulder, lactim band at 1645 cm.$^{-1}$ appearing as a shoulder). The total conversion to this reaction mixture accounted for 90% of the theoretically possible δ-valerolactam.



These results can be rationalized if one assumes that O-(*p*-toluenesulfonyl)-δ-valerolactim (X) is formed as a distinct compound which reacts further with acetic acid in several different ways eq. C — D. In D(a) it is assumed that O-acetylvalerolactim is formed as a reaction intermediate which reacts with acetic acid to yield δ-valerolactam and acetic anhydride. Some evidence that weak nucleophiles such as nitromethane or nitroethane may displace a lactim ether (or ester) according to D(a) was found by Schlack and Peterson[14] who treated V with nitromethane and obtained 1-caprolactimino-O-1-nitromethane. In a separate experiment, N-*p*-toluenesulfonyl-δ-valerolactam (XI) was recovered unchanged from boiling acetic acid after 3 hours. The breakage of the C–N linkage must, therefore, precede the formation of XI.

Methanolysis of Oxime *p*-Toluenesulfonates in 99.9% Methanol.—Cyclohexanone oxime *p*-toluenesulfonate (I), when solvolyzed in absolute methanol, could probably yield cyclohexanone oxime methyl ether (XII), O-methylcaprolactim (V) or N-methylcaprolactam (XIII). Compound XII was synthesized from sodium cyclohexanone oxime and methyl bromide according to the method of Hudlicky[15]; V and XIII were synthesized by alkylating ε-caprolactam with dimethyl sulfate according to the method of Benson.[16] When compound I was solvolyzed in 99.98% methanol at 20° overnight and a sample of the solution was titrated potentiometrically with standard sodium hydroxide in water, the formation of *p*-toluenesulfonic acid was quantitative. The products isolated were 22% of V, 48% of ε-caprolactam and 20% tar. The infrared spectrum of the tar indicated that it contained an amide linkage (3400, 1665 and 1412 cm.$^{-1}$), and probably consisted of poly-ε-caprolactam. There also was a distinct band at 2250 cm.$^{-1}$ indicating the presence of a nitrile[17] in the tar in about 2–3% by weight.

In a similar manner cycloheptanone oxime *p*-toluenesulfonate (VII) solvolyzed completely in 99.98% methanol overnight at 25° to *p*-toluenesulfonic acid and derivatives of enantholactam. O-Methylenantholactim was isolated in 62% conversion. The infrared spectrum of the tarry residue in chloroform exhibited a –CONH– band at 1665 cm.$^{-1}$ and a N–H band at 3440 cm.$^{-1}$ but no nitrile band. Again no oxime methyl ether or N-methylenantholactam could be detected by means of the infrared spectrum.

Cyclopentanone oxime *p*-toluenesulfonate (VIII) was solvolyzed in absolute methanol considerably more slowly than were I and VII. When a sample of VIII was refluxed in absolute methanol for three hours with rapid stirring, in a vessel closed by a Dry Ice trap, the solution became quite dark brown. A sample withdrawn after this time and titrated potentiometrically with standard base indicated that only 88% of the theoretically pos-

(11) F. Cramer and K. Pawelzik, *Angew. Chem.*, **68**, 649 (1956).
(12) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley & Sons, Inc., New York, N. Y., 1956, p. 153.
(13) Reference 12, p. 227.
(14) (a) P. Schlack, U. S. Patent 2,356,622; (b) S. Peterson, *Angew. Chem.*, **64**, 602 (1952).
(15) M. Hudlicky and H. Hokr, *Collection Czechoslov. Chem. Communs.*, **14**, 561 (1949).
(16) R. E. Benson and T. L. Cairns, THIS JOURNAL, **70**, 2115 (1948).
(17) Reference 12, p. 223.

sible *p*-toluenesulfonic acid was accounted for. Again no oxime and methyl ether or N-methylvalerolactam could be detected. O-Methylvalerolactim was isolated in 40% conversion and δ-valerolactam in 30% conversion. A brown high boiling residue remained. The infrared spectrum of this residue indicated the presence of an amide band at 1678 cm.$^{-1}$ (polyvalerolactam), but there was no band in the nitrile region at 2150–2300 cm.$^{-1}$.

Rearrangement of Cyclohexanone Oxime *p*-Toluenesulfonate in Chloroform.—The rearrangement of benzophenone oxime *p*-benzenesulfonate in chloroform was a classic work of Kuhara and coworkers[18] who, for the first time, determined the intermediates occurring in the Beckmann rearrangement. The purpose of the present investigation was to isolate and prepare the intermediates occurring in the Beckmann rearrangement of I in chloroform. As described by Kuhara the first intermediate in the rearrangement of I in chloroform is O-(*p*-toluenesulfonyl)-ε-caprolactim (XIV), which was identified from the infrared spectrum by its characteristic bands at 1660 and 1490 cm.$^{-1}$; XIV rearranges gradually to the N-*p*-toluenesulfonylcaprolactam (XV) which has strong bands at 1710, 1640 and 1400 cm.$^{-1}$; XIV appears to be extremely unstable and numerous attempts to isolate or synthesize it failed.

The final product of rearrangement of I in chloroform was a material, m.p. 124.6–125°, apparently N-*p*-toluenesulfonylcaprolactam (XV), but no correct analysis for this compound was obtained. After numerous attempts, XV was synthesized by pyrolysis of N-*p*-toluenesulfonyl-ε-aminocaproic acid (XVI) at 0.3 mm. in very small conversions. The structure of XVI was proved by its hydrolysis to XV in boiling concentrated hydrochloric acid.

Experimental

Synthesis of Oximes.—Oximes were prepared according to the method of Ruzicka[19] from the corresponding ketone, hydroxylamine hydrochloride and sodium bicarbonate in absolute methanol. The yields of the oximes after purification were between 60 and 90%.

Synthesis of Oxime *p*-Toluenesulfonates.—The following example illustrates the preparation of oxime *p*-toluenesulfonates. Cycloöctanone oxime (19.5 g., 0.138 mole), b.p. 96–98° (4.0 mm.), n^{25}D 1.4538, was dissolved in 70 ml. of dry benzene (distilled over sodium). To this rapidly stirred solution sodium amide (5.5 g., 0.14 mole) was added in such a way that the temperature did not exceed 35°. The reaction mixture was then stirred for 16 hours at room temperature. Thereafter the reaction mixture was filtered, and the precipitate was washed several times with dry benzene and dried on the filter paper under dry nitrogen. The yield was quantitative, 22.5 g. (The yield of the sodium cycloalkanone oxime was quantitative only if a very pure grade of sodium amide was employed. If the sodium amide was less than 90% pure, the salt had to be washed very thoroughly with dry benzene whereby much smaller conversions to the oxime *p*-toluenesulfonates were obtained.) To a rapidly stirring slurry of sodium cycloöctanone oxime (22.5 g., 0.138 mole) in 100 ml. of dry benzene *p*-toluenesulfonyl chloride (20 g., 0.105 mole) in 70 ml. of dry benzene was added dropwise and the reaction temperature during the addition was maintained between 25 and 35°. After the addition was completed the reaction mixture was stirred for two hours at room temperature. The benzene-insoluble material was filtered off and the benzene solution was freeze-dried. The residue of freeze-drying was dissolved in a minimum amount of carbon tetrachloride, and petroleum ether (b.p. 30–60°) was added to the carbon tetrachloride solution until it became cloudy. Upon standing in the refrigerator overnight 32 g. of cycloöctanone oxime *p*-toluenesulfonate crystallized out of the solution (about 85% conversion). The sulfonate ester was redissolved in carbon tetrachloride and treated with charcoal (if impure sodium amide was employed). Petroleum ether was added until the solution became cloudy. The first fraction separated was rejected. Upon standing in the refrigerator overnight 15 g. of cycloöctanone oxime *p*-toluenesulfonate crystallized out of the solution. Evaporation of the mother liquors increased the total amount of sulfonate ester isolated to 29 g. The ester was then dried at 25° (1 mm.) in a clean drying pistol without a drying agent. (Traces of impurities appeared to accelerate the decomposition of the sulfonate. A sample of cyclohexanone oxime *p*-toluenesulfonate exploded in a drying pistol which was not previously cleaned.) The melting points and analytical data on this and other oxime *p*-toluenesulfonates prepared by this method are summarized in Table I.

Acetolysis of Cyclohexanone Oxime *p*-Toluenesulfonate (I).—Cyclohexanone oxime *p*-toluenesulfonate (10 g., 0.037 mole) was added to 100 ml. of 99.7% acetic acid and 1 ml. of acetic anhydride and the solution was thermostated at 35° for one hour. Titration of an aliquot of the sample with 0.699 *N* sodium acetate with brom phenol blue as the indicator indicated the formation of 0.0365 mole of *p*-toluenesulfonic acid. The reaction mixture was neutralized with 3.3 g. of sodium acetate (0.04 mole) and freeze-dried. The residue was extracted with petroleum ether (b.p. 30–60°) and was vacuum distilled. Only one fraction, 4.731 g., was obtained, b.p. 76° (0.4 mm.). The material solidified and had a m.p. of 63–65°. The infrared spectrum of this material was identical with the spectrum of ε-caprolactam.

Cyclohexanone oxime *p*-toluenesulfonate (10 g., 0.037 mole) was added to 100 ml. of 99.7% acetic acid and the reaction mixture was thermostated at 35° for one hour in a closed vessel. When the reaction mixture was processed in the same manner as described above, only ε-caprolactam was isolated in quantitative conversion, 4.735 g.

Cyclohexanone oxime acetate (II) was prepared from cyclohexanone oxime and a slight excess of acetyl chloride and pyridine in chloroform as the solvent.[9] The yield was quantitative, b.p. 68–69° (0.3 mm.); infrared spectrum (cm.$^{-1}$): 3000 (m), 2860 (w), 1755 (vs), 1648 (s), 1450 (s), 1369 (s), 1280 (m), 1248 (s), 1194 (vs), 1102 (vs), 989 (s), 860 (s), 840 (m).

Anal. Calcd. for $C_8H_{13}O_2N$: C, 61.91; H, 8.44; N, 9.02. Found: C, 61.8; H, 8.6; N, 8.8.

N-Acetyl-ε-caprolactam (IV).—N-Acetyl-ε-caprolactam was prepared in 80% conversion from ε-caprolactam and acetyl chloride.[9] The product, after fractional distillation, boiled at 134–135° (26 mm.), n^{25}D 1.4880; infrared spectrum (cm.$^{-1}$): 2910 (vs), 2840 (m), 1700 (vs), 1670 (vs), 1460 (w), 1435 (w), 1384 (s), 1370 (s), 1350 (s), 1335 (s), 1260 (vs), 1210 (vs), 1185 (vs), 1156 (w), 1125 (w), 965 (s).

Attempted Preparation of O-Acetylcaprolactim (III).—Acetic anhydride (12 g., 0.12 mole) and O-methylcaprolactim (6.25 g., 0.05 mole) were refluxed for 16 hours. Distillation yielded a material, b.p. 96–148° (3.5 mm.). Attempts to purify this reaction mixture by further fractional distillation failed.

Preparation of *O*-*p*-Toluylcaprolactim (VI). *p*-Toluic acid anhydride was prepared in 70% conversion from *p*-toluic acid and acetic acid anhydride according to the method of Autenrieth,[20] m.p. 95–96°. O-Methylcaprolactim (25 g., 0.2 mole) and *p*-toluic acid anhydride (26 g., 0.1 mole) were refluxed for one hour. The reaction mixture then was washed with an aqueous solution of 3% sodium bicarbonate; the organic layer was dried with magnesium sulfate and was distilled. A material (18 g.), b.p. 80–85° (9.5 mm.), was isolated. Fractional distillation of this material through a column of about 20 plates yielded a fraction of 13 g. or 56% conversion, b.p. 85° (6.5 mm.), n^{27}D 1.5180; infrared spectrum (cm.$^{-1}$): 2910 (vs), 2820 (w), 1722 (vs), 1642 (vs), 1483 (vs), 1440 (s), 1430 (s), 1392 (s),

(18) M. Kuhara, A monograph edited by S. Komatsu incorporating the complete work of Kuhara and entitled: "M. Kuhara on the Beckmann Rearrangement" published by Imperial University, Tokyo, 1926 (in English).

(19) L. Ruzicka, M. Kobelt, O. Haflinger and V. Prelog, *Helv. Chim. Acta*, **32**, 544 (1949).

(20) W. Autenrieth and G. Thomae, *Ber.*, **57**, 423 (1924).

1350 (w), 1276 (vs), 1198 (s), 1177 (s), 1105 (vs), 1076 (w), 1021 (vs), 840 (s).

Anal. Calcd. for $C_{14}H_{17}O_2N$: C, 72.69; H, 7.41. Found: C, 72.47; H, 7.03.

Acetolysis of Cycloheptanone Oxime *p*-Toluenesulfonate (VII).—Cycloheptanone oxime *p*-toluenesulfonate (5.7 g., 0.02 mole) was added to 99.9% acetic acid and the solution allowed to stand at room temperature for two hours. Anhydrous sodium acetate (1.64 g., 0.02 mole) was added to the solution. The acetic acid was removed by freeze-drying and the residue was dissolved in several drops of methanol; the last traces of acetic acid were neutralized with two drops of 0.1 *N* sodium methoxide. The methanol was evaporated to dryness and the residue was extracted with ether (2 × 30 ml.). The ether layer was distilled to yield 2.67 g. of product, b.p. 96–99° (0.6 mm.), m.p. 32.8–33.6°. The spectrum of this material was nearly identical with that of enantholactam. When a chloroform solution of the reaction product was run against a solution of pure enantholactam in the reference cell two bands at 1740 and 1645 cm.$^{-1}$ appeared which indicate the presence of about 2–4% of O-acetylenantholactim.

Acetolysis of Cyclopentanone Oxime *p*-Toluenesulfonate (VIII). Cyclopentanone oxime *p*-toluenesulfonate (6 g., 0.024 mole) was dissolved in 10 ml. of 100% acetic acid and the reaction mixture was kept at 35° for two hours. The solution gradually became yellow and then deep red and a solid material precipitated. The solid material, 1.73 g., was filtered off and was recrystallized from water and then from glacial acetic acid, m.p. 151–152°.

Anal. Calcd. for $C_{12}H_{17}O_4NS$: C, 53.14; H, 6.28; N, 5.16. Found: C, 53.22, 53.29; H, 6.43, 6.49; N, 4.76, 4.81.

This sample did not depress the melting point of an authentic sample of δ-(*p*-toluenesulfonamido)-valeric acid. The filtrate of the solid was diluted to 50 ml. with 100% acetic acid and 1 ml. of this solution was titrated with 0.07 *N* sodium acetate in glacial acetic acid with crystal violet as an indicator. One ml. of the solution consumed 6.1 ml. of 0.07 *N* sodium acetate, which fact indicates the presence of 21.4 meq. of strong acid in the filtrate. Sodium acetate (1.754 g., 21.4 meq.) was added to the filtrate and the acetic acid was removed by freeze-drying. The residue was extracted with ether and was distilled using a mercury diffusion pump to yield 2.02 g. of semi-solid material, b.p. 47° (0.02 mm.). The infrared spectrum of this material indicated the presence of acetic acid, 1705 and 3240 cm.$^{-1}$, δ-valerolactim O-acetate, 1740 cm.$^{-1}$ and valerolactam, 1645 cm.$^{-1}$.

Anal. Calcd. for $C_7H_{11}O_2N$: C, 59.55; H, 7.89; N, 9.92. Calcd. for C_5H_9ON: C, 60.57; H, 9.95; N, 14.12. Found: C, 55.93, 56.15; H, 8.88, 8.94; N, 10.97, 11.10.

Synthesis of δ-(*p*-Toluenesulfonamido)-valeric Acid (IX).—δ-Valerolactam (35 g., 0.35 mole) was dissolved in 60 ml. of water, and 36 g. of 95% sulfuric acid (0.35 mole) was added to the solution. The solution was refluxed for 2.5 hours and without isolating the acid, the solution was made alkaline with 40 g. (1.0 mole) of sodium hydroxide dissolved in 80 ml. of water. A solution of *p*-toluenesulfonyl chloride (50 g., 0.26 mole), was dissolved in 300 ml. of dry acetone and was dropped simultaneously into the sodium aminovalerate solution with sodium hydroxide, (12 g., 0.3 mole) dissolved in 100 ml. of water in such a way that the temperature did not exceed 40°. After the addition was complete, the solution was acidified with sulfuric acid, but no material crystallized out upon standing in the refrigerator. The water was removed by freeze-drying, the residue was extracted with 100 ml. of ethyl acetate and the ethyl acetate was removed under vacuum. The resulting black residue was recrystallized several times from water to yield 12 g. of δ-(*p*-toluenesulfonamido)-valeric acid monohydrate, m.p. 143.8–144.5°.[20] After several recrystallizations from glacial acetic acid, the water of hydration could be removed and the melting point of the sample was 151–152°.

Anal. Calcd. for $C_{12}H_{17}O_4NS \cdot H_2O$: C, 49.82; H, 6.62; N, 4.83. Found: C, 50.15; H, 6.75; N, 4.78.

Purification of Methanol.—Methanol was dried according to the procedure of Fieser[21] by refluxing a reagent grade methanol with magnesium and subsequent distillation of the methanol.

Preparation of O-Methylcaprolactim (V) and N-Methylcaprolactam (XIII).—O-Methylcaprolactim was prepared according to the method of Benson,[16] from ε-caprolactam (678 g., 6 moles) and dimethyl sulfate (570 g., 4.56 moles), in 2 liters of benzene as the solvent. After processing of the reaction mixture two fractions were obtained: fraction 1: O-Methylcaprolactim, b.p. 66–67° (24 mm.), $n^{20}D$ 1.4613, 305 g. or 46% conversion; infrared spectrum (cm.$^{-1}$): 2890 (vs), 2830 (vs), 1670 (vs), 1430 (vs), 1335 (w), 1240 (vs), 1220 (vs), 1185 (s), 1141 (s), 1083 (s), 1038 (w), 996 (s), 985 (s), 948 (w), 798 (s), 742 (s), 678 (s).

Fraction 2: A mixture of O-methylcaprolactim and N-methylcaprolactam, b.p. 67–78° (23 mm.), 99 g. or 21% conversion. Fraction 2 was redistilled and 62 g. of N-methylcaprolactam, b.p. 124–126° (26 mm.), $n^{20}D$ 1.4838 was obtained; infrared spectrum (cm.$^{-1}$): 2880 (vs), 2820 (s), 1655 (vs), 1480 (s), 1436 (s), 1387 (vs), 1346 (w), 1333 (s), 1252 (s), 1219 (w), 1195 (s), 1102 (s), 1076 (w), 1000 (s).

Cyclohexanone Oxime Methyl Ether (XII).—Cyclohexanone oxime methyl ether was prepared according to the method of Hudlicky[15] from sodium cyclohexanone oxime and methyl iodide, b.p. 50–51° (10 mm.), $n^{20}D$ 1.4661; infrared spectrum (cm.$^{-1}$): 2880 (vs.), 1630 (w), 1440 (s), 1047 (vs), 938 (w), 914 (s), 867 (s), 837 (s).

Methanolysis of Cycloheptanone Oxime *p*-Toluenesulfonate (VII).—Cycloheptanone oxime *p*-toluenesulfonate (10 g., 0.0357 mole) was added to 500 ml. of 99.98% methanol and the solution was allowed to stand for 16 hours at 25° in a glass-stoppered erlenmeyer flask. The solution was titrated potentiometrically with 107 ml. of 0.0335 *N* sodium methoxide to *p*H 8.00 (99% of reaction). The bulk of the methanol was removed under vacuum, the residue was extracted with ether and the ether-insoluble material was filtered off. The ether-soluble material was vacuum distilled, b.p. 78° (20 mm.); infrared spectrum (cm.$^{-1}$): 2900 (vs), 1668 (vs), 1478 (s), 1408 (s), 1250 (s), 1150 (vs), 1098 (s).

Anal. Calcd. for O-methylenantholactim, $C_8H_{15}ON$: C, 67.97; H, 10.77; N, 9.97. Found: C, 68.31; H, 11.03; N, 10.12.

Methanolysis of Cyclohexanone Oxime *p*-Toluenesulfonate (I).—To 166 ml. of methanol, 99.98% pure,[21] was added 66 g. (0.25 mole) of cyclohexanone oxime *p*-toluenesulfonate and the solution was allowed to stand at room temperature overnight; 5 ml. of this solution consumed 7.9 ml. of 0.101 *N* sodium hydroxide indicating this reaction was complete. The reaction mixture was added to a cold solution of 12 g. of potassium hydroxide dissolved in 150 ml. of absolute methanol. The potassium *p*-toluenesulfonate precipitated out and was filtered off (52 g. or 0.25 mole). The filtrate was evaporated under 1 mm. vacuum with slight warming. The distillate was distilled through a fractionating column, and most of the methanol was removed at 760 mm. The residue consisted of O-methylcaprolactim containing some methanol which could not be removed by vacuum distillation, b.p. 61–65° (20 mm.), $n^{23}D$ 1.4600, 3 g. The residue of I was vacuum distilled: fraction A, 3.7 g. of O-methylcaprolactim, b.p. 64–66° (20 mm.), $n^{23}D$ 1.4618; fraction B, 14.8 g. of ε-caprolactam, b.p. 98.5–100° (0.8 mm.), and fraction C, residue, 5.95 g. The infrared spectrum of the residue in chloroform showed a band characteristic of an amide linkage at 1665 cm.$^{-1}$ and a band at 2250 cm.$^{-1}$, which could be attributed to a nitrile group.

Methanolysis of Cyclopentanone Oxime *p*-Toluenesulfonate (VIII).—To 750 ml. of 99.98% methanol[21] was added 34 g. (0.135 mole) of cyclopentanone oxime *p*-toluenesulfonate and the reaction mixture was refluxed for three hours. The solution was cooled to room temperature and an aliquot of 5 ml. consumed 8 ml. of 0.101 *N* sodium hydroxide. Methanolysis was thus 88% complete. The reaction mixture was processed in a similar manner to that described for cyclohexanone oxime *p*-toluenesulfonate. The total O-methylvalerolactim isolated was 6.0 g. (40%), b.p. 50–52° (17 mm.), $n^{20}D$ 1.4553; infrared spectrum (cm.$^{-1}$): 2950 (vs), 1670 (vs), 1470 (w), 1380 (w), 1355 (w), 1265 (s), 1158 (vs), 1120 (vs), 1030 (s), 1008 (s).

Anal. Calcd. for $C_6H_{11}ON$: C, 63.68; H, 9.78. Found: C, 63.68; 63.94; H, 10.07; 10.07.

Valerolactam, 4.3 g. (30%), b.p., 96–97° (1.5 mm.), was

(21) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1941, p. 359.

isolated. There remained a residue of 3.9 g. which might contain polyvalerolactam.

Synthesis of ε-(*p*-Toluenesulfamido)-caproic Acid (XVI).—ε-Aminocaproic acid (131 g., 1.0 mole) was dissolved in 250 ml. of 4 *N* sodium hydroxide and *p*-toluenesulfonyl chloride (190 g., 1.0 mole) dissolved in 500 ml. of acetone was added to the sodium aminocaproate simultaneously with a solution of 250 ml. of 4 *N* sodium hydroxide. The temperature was maintained below 35° during the addition. After the addition was complete the reaction mixture was stirred for three hours at room temperature. Acetone was distilled off and the aqueous solution was acidified with 83 ml. of concentrated hydrochloric acid. After standing overnight in a refrigerator at 0°, 280 g. (98% conversion) of ε-(*p*-toluenesulfonamido)-caproic acid was obtained. Several recrystallizations from 50% aqueous ethanol and subsequently from methyl ethyl ketone gave a material, m.p. 108.8–110.2°, lit.[22] m.p. 104–106°.

Anal. Calcd. for $C_{13}H_{17}O_4NS$: C, 55.15; H, 6.47; N, 4.94. Found: C, 55.46; H, 6.82; N, 4.97.

Synthesis of N-*p*-Toluenesulfonylcaprolactam (XV).—ε-(*p*-Toluenesulfonamido)-caproic acid (5.7 g., 0.02 mole) was heated in a small still under a vacuum of 0.01 mm. at about 125° for two hours. The material then was washed with 5% sodium bicarbonate solution and the residue was extracted with chloroform and treated with charcoal. The chloroform was evaporated under vacuum. The residue was chromatographed on neutral alumina using chloroform as the eluent. Several of the fractions eluted yielded, after recrystallizations from water and methyl ethyl ketone, a compound (55 mg.), m.p. 124–125°. The infrared spectrum of this material was essentially identical with the material obtained by rearrangement of I in chloroform.

Rearrangement of Cyclohexanone Oxime *p*-Toluenesulfonate (I) in Dry Chloroform.—Cyclohexanone oxime *p*-toluenesulfate (89 g., 0.3 mole) dissolved in 250 ml. of dry chloroform, stood for one year at 25° in a sealed flask wrapped in aluminum foil. Thereafter the solution was evaporated to dryness under vacuum leaving 90 g. of a viscous brown material. After numerous attempts at crystallization most of the material solidified to a semi-crystalline mass after being boiled with water and the water removed by freeze-drying. After several recrystallizations from methyl ethyl ketone the material melted at 124.6–125.0°; infrared spectrum (cm.$^{-1}$): 1707 (vs), 1660 (vs), 1448 (s), 1386 (s), 1352 (s) and 1163 (s).

Anal. Calcd. for $C_{13}H_{17}O_3NS$: C, 58.40; H, 6.41; N, 5.24. Found: C, 56.43, 56.65, 57.15, 56.95; H, 7.50, 7.59, 7.55, 7.59; N, 6.62, 6.60.

Acid Hydrolysis of N-*p*-Toluenesulfonylcaprolactam (XV).—N-*p*-Toluenesulfonylcaprolactam, 5.3 g. (0.02 mole), was refluxed with 20 ml. of concentrated hydrochloric acid for five hours. The solution was diluted to about 200 ml. with water and cooled to room temperature. The 3 g. of solid material which precipitated was recrystallized from water several times, m.p. 108–110°. This material did not give a melting point depression with a synthetic sample of ε-(*p*-toluenesulfonamido)-caproic acid, and the infrared spectra of these two samples were identical.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND THE LABORATORY FOR NUCLEAR SCIENCE, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Use of Hydrogen Isotope Effects to Identify the Attacking Nucleophile in the Enolization of Ketones Catalyzed by Acetic Acid[1-3]

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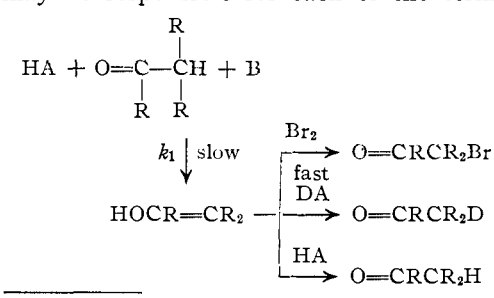
Catalysis of enolization by acetic acid is not due to an acetic acid molecule acting on the ketonic oxygen and a water molecule removing the proton from carbon, but instead to hydrogen ion acting on the ketonic oxygen and acetate ion removing the proton from carbon, in the case of α-phenylisocaprophenone (a ketone with one α-hydrogen) in aqueous solution with 8.4 *M* dioxane (72% dioxane by volume) at 100°. The magnitude of the protium/tritium isotope effect at the carbon is diagnostic of the attacking nucleophile, *increasing* as the basicity and reactivity of the nucleophile increases. For catalysis by acetic acid, it has a value (11.4) which is too high for nucleophilic attack by water, but correct for attack by acetate ion. A relation between tritium (k_H/k_T) and deuterium (k_H/k_D) isotope effects is derived and compared with experimental data.

Enolization is the rate-determining process in the bromination, iodination, deuterium exchange and racemization of ketones.[4]

The first-order rate constant for enolization of acetone in acetic acid buffers in water solution at 25° has the form[5]

$$k_1 = \frac{1}{(\text{ketone})} \times \frac{d(\text{enol})}{dt} = k_0 + k_{H^+}(H^+) + k_{HO^-}(HO^-) + k_{HOAc}(HOAc) + k_{AcO^-}(AcO^-) + k_p(HOAc)(AcO^-)$$

Table I shows possible combinations of electrophile or acid (HA) and nucleophile or base (B) that may be responsible for each of the terms.[6] The



(1) This work was supported in part by the research program of the Atomic Energy Commission under Contract No. AT(30-1-)-905.

(2) For Part II on use of hydrogen isotope effects to determine the timing of proton transfer relative to nucleophilic attack, *cf.* C. G. Swain, A. J. Di Milo and J. P. Cordner, THIS JOURNAL, **80**, Nov. 20 (1958).

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(6) Inclusion of nine terms allows for the operation of either a concerted Lowry mechanism or a stepwise Pedersen mechanism or both at once. The first six terms cannot involve protonation by the acid in a prior equilibrium step, but the last three (VII, VIII and IX) may corre-