Studies on New Derivatives of ε-Caprolactam

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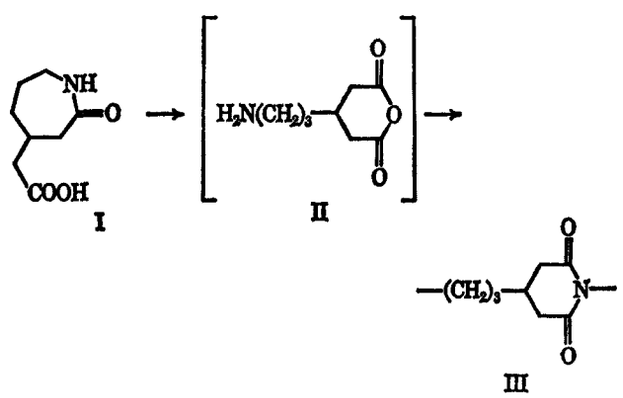
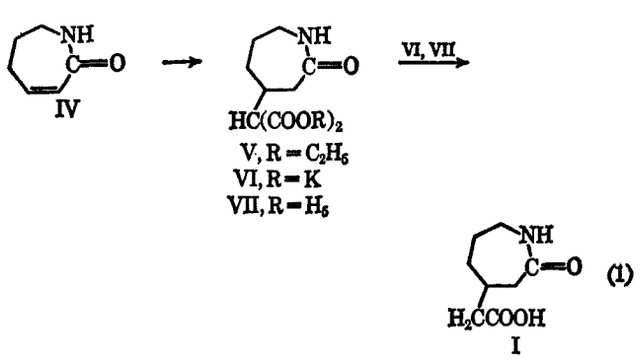
β-Carboxymethylcaprolactam has been synthesized by a sequence of reactions that comprised dehydrobromination of α-bromocaprolactam, Michael reaction with diethyl malonate with the product of this dehydrobromination, hydrolysis of the resulting β-(dicarbethoxymethyl)caprolactam, and decarboxylation of the β-(dicarboxymethyl)caprolactam. The dehydrobromination yielded a mixture of 1,3,6,7-tetrahydro-2H-azepin-2-one and 1,5,6,7-tetrahydro-2H-azepin-2-one. The structures of these compounds were investigated and verified by spectral studies. Both isomers participated as an acceptor in typical 1,4 additions that resulted in identical reaction products. These results have been explained by a shift of the double bond from the β,γ to the α,β position under the employed reaction conditions. A mechanism for the formation of the two isomers has been suggested.

Recent communications from this laboratory have been concerned with a novel polyimide, poly[(2,6-dioxo-1,4-piperidinediyl)trimethylene] (III), which resulted from the thermal polymerization of β-carboxymethylcaprolactam (I) by a mechanism that consists of an initial isomerization of I to 3-(3-aminopropyl)glutaric anhydride (II), and subsequent polymerization of the latter by condensation.[1-3]



In this paper we shall deal with the preparative procedures employed in the synthesis of I, and shall discuss the discovery, identification and behavior of a hitherto unknown tetrahydro-2H-azepin-2-one.

The approach that was considered most suitable for the synthesis of I is illustrated by eq 1 and consists of



the Michael reaction on 1,5,6,7-tetrahydro-2H-azepin-2-one (IV), hydrolysis of the resulting β-(dicarbethoxymethyl)caprolactam V, and decarboxylation of the β-(dicarboxymethyl)caprolactam VII. As it will be shown in the Experimental Section, I could indeed be obtained in good yields by this sequence of reactions.

The unsaturated caprolactam IV had been synthesized by Donat and Nelson,[4] who reported it to be a colorless oil. Their synthesis involved preparation, isolation, and Beckmann rearrangement of *syn*-2-cyclohexenone oxime. Bara[5] observed the formation of an "α,β unsaturated caprolactam" in oil form as a by-product in attempts to synthesize α-cyanocaprolactam by treating α-bromocaprolactam with potassium cyanide.

Results

The dehydrobromination of α-bromocaprolactam by treatment of the latter with bases such as lutidine or sodium alkoxides appeared to be a convenient method and we therefore chose it for the preparation of IV.

Work-up of respective reaction mixtures showed that in every case two different unsaturated caprolactams had been formed. One was a solid (IVa) that melted at 79° and the other was an oil (IVb) having a refractive index of $n^{25}D$ 1.5267.

Since the elemental composition was found to be the same for both the solid and the oil, an isomeric relation between the two materials was presumed and then confirmed by the catalytic hydrogenation which yielded in either case ε-caprolactam. The different physical properties and differences in both the nmr and infrared spectra appeared to be indicative of different positions of the double bond. On the other hand, however, bromination yielded identical dibromocaprolactam VIII, and Michael reaction with malonic ester on both the solid and the oil resulted in either case in the same (dicarbethoxymethyl)caprolactam (V). For further identification this compound was then converted *via* I into the β-(carbethoxymethyl)caprolactam (IX). The material derived from the oil was identical with the one derived from the solid. The structure of IX has been confirmed by both the infrared and nmr spectra. The infrared spectrum exhibited the following characteristic absorptions: 1655 (amide I), 3210 (NH stretching), 1735 (ester carbonyl), and 1205 cm^{-1} (CO stretching). The nmr spectrum, obtained with an external TMS reference standard, showed a triplet at δ 1.25 ppm (relative intensity = 3) and a quartet at 4.10 ppm (relative intensity = 2); both were due to

(1) H. K. Reimschuessel, *Polym. Lett.*, **4**, 953 (1966).
(2) H. K. Reimschuessel, L. G. Roldan, and J. P. Sibilia, *J. Polym. Sci., Part A-2*, **6**, 559 (1968).
(3) H. K. Reimschuessel, 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, L80.
(4) F. J. Donat and A. L. Nelson, *J. Org. Chem.*, **22**, 1107 (1957).
(5) H. Bara, *Faserforsch. Textiltechnik*, **14** (9), 368 (1963).

the ethoxy group of the ester moiety. There was coupling of about 7.2 Hz. A broad multiplet centered at δ 1.74 ppm integrated to a relative intensity of 4 and was assigned to the methylene groups in the γ and δ positions. A doublet at δ 2.30 ppm (relative intensity = 4) was assigned to the two methylene groups adjacent to the two carbonyl groups; coupling was about 2.5 Hz. A broad multiplet centered at δ 3.18 ppm (relative intensity = 2) was due to the methylene group adjacent to the nitrogen, while the downfield absorption at about δ 8.0 ppm (relative intensity = 1) was assigned to the absorption of the amide proton.

These results may be explained by assuming $\beta\gamma$-$\alpha\beta$ isomerization during the course of both bromination and Michael reaction. While this type of isomerization has been observed in other instances there is a report[6] where it could not be detected in similar structures.

In the present case, therefore, a more detailed spectroscopical analysis was conducted in order to elucidate the structures of the two isomeric tetrahydroazepins.

The 100-MHz nmr spectrum of the solid isomer (IVa) consisted of five major groups, the integrals of which correspond to the proportional relation of 1:2:2:2:2.

A broad "singlet" at 8.3 ppm from TMS has been attributed to the proton of the amide group. The aggregation of absorptions centered at 5.6 ppm had the general appearance of an AB quartet and has been assigned to isolated olefinic *cis* protons belonging to a group such as $-CH_2CH^*{=}CH^*CH_2-$.

A narrow multiplet centered at about 3.05 ppm has been attributed to protons belonging to a methylene group located between a carbonyl group and a vinyl-type group.

The absorptions of the protons belonging to the methylene group adjacent to the amide nitrogen appeared as a "quartet" centered at about 3.35 ppm. A multiplet at 2.25 ppm has been assigned to the $-CH_2^*-$ unit in the $-CH_2CH_2^*CH{=}CH_2-$ moiety. Thus in the case of the solid isomer the double bond must be in the β,γ position, and this isomer has therefore been identified as 1,3,6,7-tetrahydro-2H-azepin-2-one (IVa).

The infrared spectrum (KBr) of IVa showed the amide I band as a barely resolved doublet (1660, 1670 cm^{-1}). A weak shoulder which appeared at about 1650 cm^{-1} has been attributed to the stretching vibration of the isolated *cis* double bond.[7]

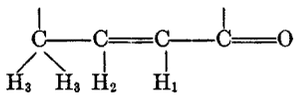
Other frequencies characteristic for this isomer are the 3030-cm^{-1} band (due to olefinic C–H stretching vibrations) and the 1410-cm^{-1} band (due to deformation vibrations of a methylene group adjacent to a carbonyl group).

The isolated oil which was expected to be 1,5,6,7-tetrahydro-2H-azepin-2-one (IVb) was found to contain appreciable quantities (about 40%) of the 1,3,6,7-tetrahydro-2H-azepin-2-one (IVa). A 100-MHz nmr spectrum of this mixture was obtained.

The amide proton absorptions were indicated by two broad triplets at about 8.1 and 8.3 ppm.

A well-resolved doublet of triplets in the 6–6.5-ppm region resulted from the downfield lines of the AB quartet (arising from the olefinic protons in IVb) being split by an adjacent methylene group. Spin coupling observed in one of the upfield lines of the AB quartet (~5.8 ppm) was relatively small (about 1 Hz) and has been attributed to four bond coupling between the protons of the methylene group adjacent to the double bond and the proton in the α position. The line furthest upfield (~5.7 ppm) in the AB quartet was partly overlapped by the absorptions of the olefinic protons of the solid isomer. These data were consistent with the expected structure of the second isomer.

Resolution of the AB pattern for the olefinic protons resulted in values of J_{12} = 12.3 Hz (δ_1 5.76 ppm, δ_2 6.23 ppm), J_{23} = 5.0 Hz, and J_{13} + 1 Hz. A value of



J = 12.3 Hz is consistent with *cis*-olefinic coupling. The complex multiplet at about 1.9 ppm has been attributed to the δ methylene protons. The absorptions at 2.3 and 3.2 ppm have been attributed respectively to the δ and ϵ protons. Both were overlapped partly by corresponding absorptions due to the presence of IVa. Both a 60-MHz nmr spectrum and an infrared spectrum (KBr pellet) of IVb were obtained from pure samples that were isolated by trapping from a gas chromatograph.

In comparison with the respective absorption of IVa, the amide I band had shifted very slightly toward lower frequencies and occurred at 1662 cm^{-1}. This relatively small effect on the amide I band due to α,β unsaturation had been noted previously.[8] The olefinic stretching absorption occurred at 1615 cm^{-1} with considerably increased intensity. Both the shift of the olefinic stretching vibration to lower frequencies and the increased intensity of this band were due to the conjugation of the double bond with the carbonyl group.

Based upon the results of the spectroscopical analysis, the successful conversion of IVa into β (carboxymethyl)-caprolactam and its derivatives by Michael addition of diethyl malonate may now be explained by the occurrence of isomerization of IVa to IVb under the conditions employed. When IVa was heated to 135°, isomerization of the considered type was indicated by the appearance of bands in the nmr spectrum in the 5.9- and 6.2-ppm regions. A detailed investigation of the process of the considered isomerization will be the subject of a separate study.

Heating IVa produced another phenomenon which has been attributed to the dissociation of the NH proton at elevated temperatures and was characterized by the collapse of the methylene "quartet" at 3.35 ppm to a triplet when the temperature exceeded 75°. The apparent quartet observed at room temperature resulted from a superposition of two triplet absorptions which were due to coupling (J = 6 Hz) of the $-CH_2N-$ protons with the NH proton. This conclusion was confirmed when a collapse of the "quartet" to a "triplet" was observed upon exchanging the NH proton with deuterium at room temperature.

(6) L. A. Paquette, *J. Org. Chem.*, **28**, 3590 (1963).

(7) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley & Sons, Inc., New York, N. Y., 1964, p 36.

(8) O. E. Edwards and T. Singh, *Can. J. Chem.*, **32**, 683 (1954).

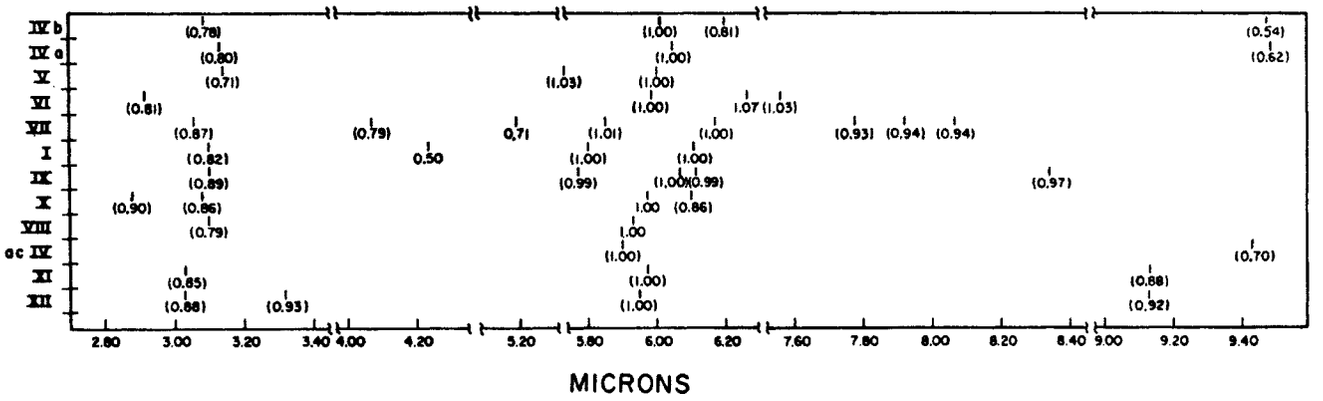
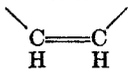
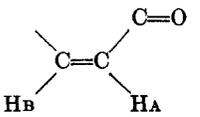
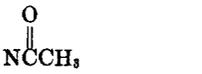


Figure 1.—Band locations (microns) and intensities of the infrared spectra of various ε-caprolactam derivatives.

A triplet-type absorption in this region was also noted in the 60-MHz nmr spectrum of a mixture of about equal concentrations of 1-acetyl-5,6,7-trihydro-2H-azepin-2-one (IVb-Ac) and 1-acetyl-3,6,7-trihydro-2H-azepin-2-one (IVa-Ac). In Table I are listed the peak positions, chemical shifts and calculated coupling constants for the acetylated derivatives.

TABLE I

PROTON NMR DATA OF THE N-ACETYLATED MIXTURE OF IVa AND IVb (δ, TMS)

IVa-Ac	IVb-Ac	Multiplet centers	J, Hz
		~5.7	
		A = 6.01[a] B = 6.51[a]	11.5
$CH_2C{=}CCC{=}O$		2.3	
	$CH_2C{=}CC{=}O$ ($\underbrace{\quad}_{J}$)	2.3	5.8
$C{=}CCH_2C{=}O$		3.45	
	$NCCH_2C$	1.95	
$-NCH_2-$		4.12	
	NCH_2	3.84	
		2.41[a]	
		2.38	

[a] Denotes actual chemical shifts.

When sodium alkoxides such as sodium ethoxide and sodium propoxide has been used for the dehydrobromination of α-bromocaprolactam, respective alkoxycaprolactams were also obtained, the yield of which depended upon the reaction conditions. The nmr spectra (Table II) revealed that these compounds were β-alkoxycaprolactams.

This result indicates that the formation of these compounds involved dehydrobromination and subsequent 1,4 addition to the formed α,β unsaturated system.

In Figure I are summarized the band locations of the infrared spectra for the various caprolactam derivatives that were synthesized in the course of this work. The lines indicate the positions of the particular bands; the numbers in parentheses are relative intensities with respect to the carbonyl absorption of the lactam moiety.

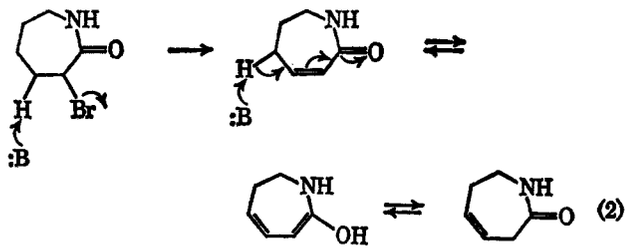
Discussion

The formation of the β,γ unsaturated caprolactam IVa could be explained by a shift of the double bond from the α,β position because of possible steric strain occasioned by the coplanarity of the C=C and C=O groups. If this were true, however, formation of IVa should occur independently of the synthetic procedure applied for the introduction of a double bond in the α,β position. An examination of the data reported by Donat and Nelson,[4] who synthesized the α,β unsaturated lactam (IVb) by Beckmann rearrangement of *syn*-2-cyclohexenone oxime, showed that they had the pure IVb. According to the procedures these authors employed in isolating their reaction product, it would have been impossible to fail to notice any amount of IVa that could have been formed. In addition, if its structure were sterically favored over that of IVb, it would be difficult to rationalize the observed ease with which IVa participates in the described reactions which are typical 1,4 additions. Therefore, the formation of IVa must be the result of the specific dehydrobromination procedures employed in this work. A mechanistic scheme such as eq 2, appears to be consistent with the experimental conditions and observations, and explains the formation of the two isomers. This

TABLE II

PROTON NMR BAND CENTER LOCATIONS (δ, TMS) FOR $HNCH_2CH_2CH_2\underset{\displaystyle OR}{\underset{|}{C}}HCH_2C{=}O$

	$-CH_3$	$-CH_2-$	$-(CH_2)_3$ (ring)	$-CH_2CO-$	CH_2N	$\overset{\displaystyle OCH_2}{\underset{|}{HC}}$	NH
$-CH_2CH_3$ (XI)	1.13		1.8	2.6	3.2	3.5	8.1
$-CH_2CH_2CH_3$ (XII)	0.91	1.54	1.8	2.6	3.2	3.5	8.1



(2)

mechanism is quite analogous to one recently suggested by Overberger and Kaye[9] to explain the formation of double bond rearranged mixtures of 6 hydroxyhexenoic acid lactones.

Experimental Section

Spectra.—The nmr spectra were obtained at 60 MHz on a Varian A-56/60 nmr spectrometer and at 100 MHz on a Varian 100-MHz spectrometer using carbon tetrachloride solutions that contained a small amount of tetramethylsilane. The infrared spectra were obtained on a Beckman IR-12 infrared spectrometer.

1,5,6,7- (1,3,6,7-) Tetrahydro-2H-azepin-2-one (IV).—A mixture of 384.0 g of α-bromocaprolactam and 384 ml of 2,6-lutidine was heated to reflux with stirring for 3 hr. After cooling, the formed precipitate was filtered and washed with benzene. Combining the filtrates resulted in more precipitate which was filtered from the benzene solution. The precipitate (374 g) was identified as 2,6-lutidine hydrobromide, mp 213° (yield 100%). Benzene and 2,6-lutidine were distilled from the product The oil obtained was vacuum distilled, giving a colorless liquid, bp 65° (0.50 mm). Upon standing, this oil partially crystallized to a solid–oil mixture. The mixture was put into cold petroleum ether (bp 30–60°), where most of the oil was dissolved. The remaining solid was recrystallized from hot petroleum ether and had a melting point of 79° (IVa).

Anal. Calcd for C_6H_9NO: C, 64.80; H, 8.10; N, 12.60. Found: C, 64.75; H, 8.12; N, 12.57.

The oil, which was dissolved in cold petroleum ether, was recovered by evaporating the petroleum ether. It was dissolved in hot hexane and came out of solution upon cooling. This treatment was repeated until a purified oil was obtained: $n^{25}D$ 1.5267 (IVb).

Anal. Calcd for C_6H_9NO: C, 64.80; H, 8.10; N, 12.60. Found: C, 64.72; H, 8.22; N, 12.60.

β-(Dicarbethoxymethyl)caprolactam (V).—Clean sodium (50.6 g) was allowed to react with 3 l. of absolute ethanol. The resulting solution was refluxed and 640 g of diethyl malonate was added dropwise. The clear solution was refluxed for 3 hr. A benzene solution of IV prepared from 384.0 g of α-bromocaprolactam was added dropwise. Refluxing was continued for 5 hr. After cooling, the ethanol and benzene were removed. The resulting liquid was dissolved in ether. It was extracted with small portions of 4% HCl solution, then with saturated $NaHCO_3$ solution until neutral, and finally with water. The ether solution was dried. The ether and diethyl malonate were removed by distillation. The remaining oil was extracted with petroleum ether until it solidified. Recrystallization from hexane yielded 351 g (70% yield) of V which melted at 49–50°.

Anal. Calcd for $C_{13}H_{21}NO_5$: C, 57.50; H, 7.80; N, 5.20. Found: C, 57.38; H, 7.69; N, 5.32.

Dipotassium Salt of β-(Dicarboxymethyl)caprolactam (VI).—KOH (175 g) was dissolved in 1 l. of absolute ethanol. A solution of 351 g of V in 0.5 l. of absolute ethanol was added dropwise to the KOH solution. The reaction mixture was refluxed for 6 hr. The precipitate was filtered and washed with dry ethanol, followed by ethyl ether; 378 g of VI was obtained, a quantitative yield.

β-(Dicarboxymethyl)caprolactam (VII).—VI (378 g) was dissolved in 250 ml of water and 241 ml of concentrated HCl was added dropwise to the solution at −5°. The precipitate was filtered and washed with cool methonol, followed by ether. VII (252 g, 90% yield) was obtained. The product could be recrystallized from methanol and melted at 162° with decomposition.

β-(Carboxymethyl)caprolactam (I).—IV (20 g) was added in small quantities to *o*-dichlorobenzene at 160°, when the evolution of CO_2 had ceased, the mixture was heated to 170°. The clear solution was allowed to cool to room temperature. I (18.4 g) was obtained from the dichlorobenzene upon cooling, (92% yield). The product was recrystallized from water, mp 193–194°.

Anal. Calcd for $C_8H_{13}NO_3$: C, 56.12; H, 7.61; N, 8.20. Found: C, 55.98; H, 7.50; N, 8.12.

β-(Carbethoxymethyl)caprolactam (IX).—I (21 g) was mixed with a solution of 120 ml. of absolute ethanol, 20 ml. of benzene and 2 ml of concentrated H_2SO_4. The mixture was heated to reflux and 250 ml of solvents were removed by distillation. Fresh benzene and ethanol were added to replace the distilled solvents. After 3 hr, the mixture was cooled to room temperature. The solvents were removed by distillation. The remaining oil was dissolved in chloroform and neutralized with $NaHCO_3$ solution. The chloroform solution was dried and the solvent distilled from the product. The yield was 23.1 g (95%) of IX which was recrystallized from hexane, mp 78.5–80°.

Anal. Calcd for $C_{10}H_{17}NO_3$: C, 60.28; H, 8.60; N, 7.05. Found: C, 60.12; H, 8.58; N, 7.21

β-(Carbamidomethyl)caprolactam (X).—A solution of 14.7 g of IX and 125 ml of concentrated ammonium hydroxide was held at room temperature for 16 hr. The solvent was removed and the remaining solid was recrystallized from ethanol. X (7.5 g) was obtained (60% yield): mp 206–208°.

Anal. Calcd for $C_8H_{14}N_2O_2$: C, 56.45; H, 8.29; N, 16.46. Found: C, 56.43; H; 8.11; N, 16.26.

Dibromohexahydro-2H-azepin-2-one (VIII).—IVa (500 g) was dissolved in 100 ml of ethyl ether. The solution was cooled to −5.0°, and 7.20 g of bromine was added dropwise to the solution. Dibromide VIII (9.4 g) precipitated from the reaction mixture (77% yield). The product was recrystallized from ethanol: mp 134–136°.

The same procedure was used employing the oil. It gave an 80% yield of dibromide VIII that melted at 135.5–137° upon recrystallization from ethanol. The mixture melting point of the products derived from IVa and the oil was 134–137°.

Anal. Calcd for $C_6H_9NOBr_2$: C, 26.55; H, 3.32; N, 5.17; Br, 59.1. Found for Ia: C, 26.80; H, 3.54; N, 5.10; Br, 59.3. Found for Ib: C, 26.78; H, 3.39; N, 5.12; Br, 59.4.

Hydrogenation of IV.—IVa (1.0 g) was dissolved in 20 ml of absolute ethanol and added to a dry flask containing a small scribed previously.[10] The solution was stirred, while hydrogen was fed into the flask until no further reaction occurred. The Pd–C was collected on a filter and the ethanol was allowed to evaporate. Caprolactam (1.0 g) was obtained, 98% yield, mp 69°. A mixture melting point with caprolactam was unchanged; 208 ml of hydrogen had reacted. Using the same method 1.0 g of the oil was also converted into caprolactam quantitatively.

1-Acetyl-5,6,7-trihydro-2H-azepin-2-one (IV-Ac).—Unfractionated IV (28 g) was mixed with 31 g of acetic anhydride and refluxed for 4 hr. The acetic acid and the unreacted acetic anhydride were distilled from the reaction mixture. Distillation of the remaining oil [bp 40° (0.03 mm)] yielded 31 g of product (80.5%), $n^{25}D$ 1.5086.

Anal. Calcd for $C_8H_{11}NO_2$: C, 62.8; 7.20; N, 9.16. Found: C, 63.1; H, 7.31; N, 9.28.

The vapor phase chromatogram showed that the product consisted of two closely boiling isomers at a ratio of 58.7:41.3.

β-(Ethoxy)caprolactam (XI).—Sodium (27.9 g) was treated with 1.5 l. of anhydrous ethanol. When all of the sodium had reacted, the solution was brought to reflux. Then 111.0 g of IV in 400 ml of anhydrous ethanol was added. The mixture was refluxed for 1 hr. Upon cooling the ethanol was removed. The solution was dissolved in benzene, the solid which precipitated was filtered. The benzene solution was extracted with a small portion of 10% HCl solution, followed by a saturated $NaHCO_3$ solution. The benzene extract was dried and the solvent was distilled, bp 93° (0.05 mm). It solidified upon standing to give white crystals, mp 59–60°. The yield was 109.0 g (70%) of XI.

(9) C. G. Overberger and Howard Kaye, *J. Amer. Chem. Soc.*, **89**, 5640 1967).

(10) Gatterman and Wieland, "Laboratory Methods of Organic Chemistry," Macmillan & Co. Ltd., London, 1941, p 376.

Anal. Calcd for $C_8H_{15}NO_2$: C, 61.15; H, 9.55; N, 8.92. Found: C, 61.02; H, 9.46; N, 9.35.

β-(n-Propoxy)caprolactam (XII).—Sodium (25.3 g) was treated with 1.2 l. of anhydrous *n*-propyl alcohol. At 60°, 192 g of α-bromocaprolactam in 600 ml and *n*-propyl alcohol was added in a dropwise fashion. The reaction mixture was refluxed for 3 hr. After cooling, the NaBr was filtered off and *n*-propyl alcohol was distilled. The oil was dissolved in chloroform, extracted with 10% aqueous HCl solution until neutral, then with a saturated $NaHCO_3$ solution and water. The chloroform solution was dried with anhydrous Na_2SO_4, the chloroform was removed, and the oil distilled: bp 68° (0.13 mm). The yield was 85.5 g (50.0%).

Anal. Calcd for $C_9H_{17}NO_2$: C, 63.20; H, 9.95; N, 8.20. Found: C, 63.09; H, 10.02; N, 8.35.

Registry No.—ε-Caprolactam, 105-60-2; I, 10139-43-2; IVa, 2228-79-7; IVa-Ac, 18753-61-2; IVb, 18761-61-0; IVb-Ac, 18753-62-3; V, 18753-63-4; VI (dipotassium salt), 18753-64-5; VII, 18753-65-6; VIII, 18753-66-7; IX, 10139-44-3; X, 18753-68-9; XI, 18753-69-0; XII, 18753-70-3.

Acknowledgment.—The authors are indebted to Mr. G. Babbitt for obtaining the nmr spectra.

Direct Liquid Phase Fluorination of Methyl Trichloroacetate and Acetic Anhydride

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Direct liquid phase fluorination of methyl trichloroacetate gave fluoromethyl trichloroacetate and difluoromethyl trichloroacetate. Under similar conditions, followed by hydrolysis of the fluorination mixture, acetic anhydride yielded fluoroacetic acid and difluoroacetic acid.

Selective, noncatalytic direct liquid phase fluorination of saturated aliphatic hydrocarbons has been the subject of only sporadic research efforts. In fact, less than a handful of publications dealing with this subject have appeared since Moissan's time.

Early attempts to fluorinate organic compounds with elementary fluorine resulted in explosions, firings, and complete destruction of substrate molecules to hydrogen fluoride and carbon tetrafluoride. The possibility of obtaining substitution products in this manner appeared very remote.[1]

In 1919, Hemiston[2] discovered that reactions between organic compounds and fluorine could be moderated considerably using fluorine diluted with inert gases such as carbon dioxide or nitrogen. However, even under these milder fluorination conditions, Hemiston was unable to obtain substitution products in the fluorination of acetone or chloroform. Hemiston's finding that carbon tetrachloride was relatively inert toward fluorine, and could be used as fluorination medium, contributed considerably to the subsequent development of the liquid phase fluorination technique.

Employing the fluorination conditions introduced by Hemiston, Bockemuller,[3] in 1933, investigated the fluorination of *n*-butyric acid, its anhydride, and chloride, obtaining mixtures of the corresponding β- and γ-fluoro derivatives. In the same work he reported fluorination of isobutyric acid to its β-fluoro derivative, and fluorination of cyclohexane and *n*-hexadecane to the corresponding monofluorocarbons. Bockemuller also attempted to fluorinate acetic, succinic, and glutaric anhydrides, and acetic acid in carbon tetrachloride solution, but found that these substrates were unreactive.

During the past several years, direct liquid phase fluorination technique has been successfully applied in the synthesis of N-fluoro derivatives. Fluorination of aqueous urea,[4] substituted urea,[3] alkyl carbamates,[5,6] simple amides,[5] and amines[7] yielded N-fluoro and N,N-difluoro derivatives. In all of the above cases the fluorination occurred selectively on nitrogen. "Burning" and explosions often reported in connection with direct fluorination reactions in earlier literature have not been encountered in these studies.

Recently, the direct liquid phase fluorination technique has been applied in the synthesis of fluorocarbons. Fluorodinitromethyl derivatives have been obtained in excellent yields in the fluorination of aqueous nitronate salts,[8,9] and aromatic electrophilic substitution leading to aromatic fluorocarbons has been reported.[10] This communication deals with direct liquid phase fluorination of methyl trichloroacetate and acetic anhydride.

Alkyl esters were considered in the search for inert solvents suitable as heat transfer media in direct liquid phase fluorination reactions. It was found, however, that simple alkyl acetates and formates reacted readily with fluorine and, therefore, could not be em-

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