The Conversion of Methyl 12-Ketostearate to 1, 12-Diisocyanatooctadecane

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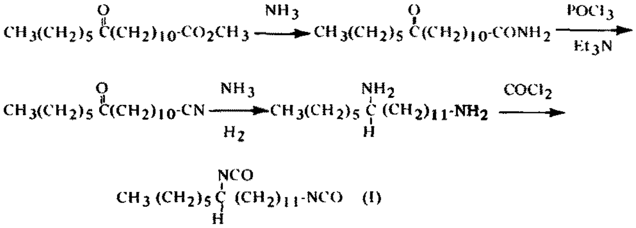
ABSTRACT

A method has been developed for the preparation of 1, 12-diisocyanatooctadecane in good purity and overall yield of 42%. Methyl 12-ketostearate is converted via the amide into 12-ketostearonitrile and then by reductive amination into 1, 12-diaminoctadecane. The corresponding diisocyanate was prepared by phosgenation of the diamine, its dihydrochloride or its carbamate salt. Variables in reaction conditions were examined to maximize yield and purity of these products.

INTRODUCTION

We have examined the preparation of 1, 12-diisocyanatooctadecane (I) by the following route:



$$CH_3(CH_2)_5\overset{O}{\overset{\|}{C}}(CH_2)_{10}\text{-}CO_2CH_3 \xrightarrow{NH_3} CH_3(CH_2)_5\overset{O}{\overset{\|}{C}}(CH_2)_{10}\text{-}CONH_2 \xrightarrow[Et_3N]{POCl_3}$$

$$CH_3(CH_2)_5\overset{O}{\overset{\|}{C}}(CH_2)_{10}\text{-}CN \xrightarrow[H_2]{NH_3} CH_3(CH_2)_5\underset{H}{\overset{NH_2}{C}}(CH_2)_{11}\text{-}NH_2 \xrightarrow{COCl_2}$$

$$CH_3(CH_2)_5\underset{H}{\overset{NCO}{C}}(CH_2)_{11}\text{-}NCO \quad (I)$$

The diisocyanate is of interest because it can be used as a chemical intermediate and as a monomer for preparing a variety of interesting polymeric products. It should give nonyellowing urethane polymers valuable in many industrial applications in contrast to urethane polymers from aromatic diisocyanates which suffer from yellowing. The diisocyanate has not been reported previously, although the intermediate diamine and its precursors have been described in several patents (1,2). In the first of these 12-ketostearin from castor oil was hydrolyzed to 12-ketostearic acid and subsequently combined with ammonia in the vapor phase at 360 C over a borophosphoric acid catalyst to give 12-ketostearonitrile in 43% yield. Reductive amination of this ketonitrile using a cobalt catalyst produced a 63% yield of the diamine (1).

The present research was directed toward making a significant improvement in the yield of these intermediate products as well as developing a method for preparing the diisocyanate. In addition an alternate method suitable for the laboratory was desired to replace the high temperature, vapor phase dehydration of ketoamide to ketonitrile. To monitor these conversions it was necessary to develop thin layer chromatography (TLC) systems not previously reported.

EXPERIMENTAL PROCEDURES

Chemicals

Methyl 12-ketostearate was obtained by dehydrogenation of methyl 12-hydroxystearate (3). Phosphorus oxychloride (Matheson, Coleman and Bell), 1,1,2,2-tetrachloroethane and triethylamine (Eastman) and tetrahydrofuran (THF) (Aldrich Chemical Company) were all reagent grade. The latter two chemicals were dried over Linde Type 4A molecular sieves (Matheson, Coleman and Bell) before use. Raney nickel catalyst was purchased from W.R. Grace and Co. Lithium aluminum hydride was obtained from Alfa Inorganics, Inc.

Preparative Procedures

12-Ketostearamide: a 1 liter Magnedrive stirred autoclave was charged with 100 g (0.32 mole) of methyl 12-ketostearate. After the autoclave had been flushed with nitrogen, it was cooled to -5 C in an ice-acetone bath, and 109 g (6.4 moles) of anhydrous ammonia was added. The autoclave was then heated for 21 hr at 150 C, cooled to room temperature, and excess ammonia was vented. The crude product was slurried in acetone at room temperature and filtered to remove any residual starting material. The solid obtained in this way was recrystallized from methanol to give 81 g (0.27 mole, 85%) of 12-ketostearamide, mp 119.4-120.0 C (lit. 120-122 C [2]).

12-Ketostearonitrile: A 2 liter round bottom flask was charged with 73.3 g (0.246 mole) 12-ketostearamide, 600 ml tetrahydrofuran and 69 ml triethylamine. The mixture was stirred and heated to reflux. Then with the heat source removed a solution of 28.2 g (0.184 mole) of $POCl_3$ in 50 ml THF was added at a rate sufficient to maintain gentle reflux. The mixture was refluxed for an additional 0.5 hr after addition was complete.

After filtration and removal of volatiles, the residue was taken up in 300 ml ether and filtered again, then washed twice with a saturated sodium chloride solution. An emulsion formed during the washing which was broken by filtering off the small amount of solid material in the emulsified layer. The combined ether layers were dried over magnesium sulfate, the solvent was removed, and the residue was distilled through a Berl saddle-packed column. The fractions boiling at 157-169 C/6 μ weighed 57.6 g (0.206 mole, 84%). On cooling, the liquid 12-ketostearonitrile solidified to a product melting at 42.1-42.2 C (lit. 34.5 C [1]). Analysis calculated for $C_{18}H_{33}NO$: C, 77.36%; H, 11.90%; N, 5.01%. Found: C, 77.4%; H, 11.8%; N, 4.99%.

1, 12-Diaminooctadecane from 12-Ketostearonitrile: A 1 liter stirred autoclave was charged with 62.3 g (0.224 mole) 12-ketostearonitrile, 1.06 g ammonium chloride, 21.2 g Raney nickel and 500 ml methanol. The autoclave was flushed with nitrogen, cooled to 2 C, and 76 g (4.5 moles) of ammonia was added. The mixture was heated 2 hr at 125 C; then hydrogen was admitted to give a total pressure of 2000 psig. Hydrogenation was conducted 2.5 hr at 125 C.

The autoclave was cooled and vented, then the reaction mixture was filtered through Celite and washed with chloroform to effect complete solution of the product. Solvent was removed from the filtrate and the crude diamine was distilled. The fraction boiling at 149-160 C/5 μ weighed 54.5 g (0.192 mole, 86%). The diamine when protected from air melted at 33.8-34.0 C (lit. 32 C [1]). Analysis calculated for $C_{18}H_{40}N_2$: C, 75.98; H, 14.17; N, 9.85. Found: C, 75.8; H, 14.0; N, 9.69.

12-Aminostearamide: A 300 ml stirred autoclave was charged with 10 g (0.034 mole) 12-ketostearamide, 0.17 g ammonium chloride, 3.4 g Raney nickel and 110 ml

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[1] W. Market. Nutr. Res. Div., ARS, USDA.

TABLE I

Preparation of 1,12-Diisocyanatooctadecane

Method	Run no.	Diamine or diamine salt, g	Addition time, hr	Reaction temperature during addition, C	Reaction time after addition, hr	Reaction temperature after addition, C	Estimated purity of crude product by thin layer chromatography[d]	Yield after distillation, %
A[a] Diamine added dropwise	1	1	0.5	110-124	0.5	119-122	Medium	---
					0.5	127-135	High	---
	2	1	0.5	137-144	0.25	144	High	---
	3	5	0.75	137-143	0.5	142-145	High	69
	4	10	1.0	138-145	1.5	142-144	Low	---
					1.25	143-145	High	---
					1.0	140-145	High	61
B[b] Dihydrochloride	5	1	---	---	0.5	111-115	Medium	---
					1.0	110	Medium	---
					1.0	138	High	---
	6	1	---	---	0.25	140-143	High	---
	7	5	---	---	0.25	140-143	Medium	---
					0.75	140-144	Medium-High	62
C[c] Carbamate salt added dropwise	8	1	1.0	109	0.5	114	High	---
	9	1	0.75	102-124	0.33	120-124	High	---

[a] Method A: 1 g Diamine in 20 ml 1,1,2,2-tetrachloroethane (TCE) at 25 C was added dropwise to a heated solution of $COCl_2$ in 20 ml TCE.

[b] Method B: HCl was passed through a solution of 1 g diamine in 40 ml TCE which was then heated until the dihydrochloride dissolved (ca. 110-126 C). $COCl_2$ was then passed through the heated solution.

[c] Method C: CO_2 was bubbled into a solution of 1 g of diamine in 20 ml TCE at 109 C (8th run) or 50-55 C (9th run). This solution was added dropwise to a solution of 20 ml TCE at 109 (8th run) or 30 ml TCE at 102-124 C (9th run) through which $COCl_2$ was bubbled.

[d] High, 90-95%; medium, 60-90%; low $<$60% by estimation of thin layer chromatography spots.

methanol. It was flushed with nitrogen, cooled to 1 C, and 17 g (1.0 mole) ammonia was added. After heating 4 hr at 100 C, the autoclave was pressurized with hydrogen to 2000 psig, and heating was continued 2 hr at 100 C. After cooling and venting the autoclave, the contents were filtered through Celite with 500 ml hot methanol. Removal of the solvent produced a solid residue which was dissolved in 75 ml hot methanol, and precipitated by adding the solution to 750 ml water. The resulting solid was purified by dissolving it in aqueous acetic acid followed by reprecipitation with aqueous ammonium hydroxide (4). Recrystallization from 50% aqueous methanol gave 7.49 g (0.025 mole, 75%) of 12-aminostearamide melting at 83.4-84.7 C (lit. 86-88 C [4]).

1, 12-Diaminooctadecane from 12-Aminostearamide: A 200 ml round bottom flask was charged with a slurry of 2.0 g (0.053 mole) lithium aluminum hydride and 20 ml THF. To this stirred mixture was added over 16 min a slurry of 7.46 g (0.025 mole) of 12-aminostearamide in 50 ml THF. The temperature rose from 24-39 C and the mixture gelled. An additional 45 ml THF was added, and the mixture was heated to 66 C for 1 hr, then cooled to room temperature and allowed to stand overnight.

After hydrolysis of the mixture with sodium hydroxide (5) and filtration from inorganic salts, the THF was evaporated. Distillation of the crude product afforded the diamine identical to that obtained above.

1, 12-Diisocyanatooctadecane: A flask containing 100 ml of 1,1,2,2-tetrachloroethane (TCE) was heated to 144 C while phosgene was bubbled into the solvent. To this mixture was added dropwise a solution of 5.0 g (0.018 mole) of 1, 12-diaminooctadecane in 100 ml TCE over 45 min while maintaining the reaction temperature at 137-143 C. After the mixture had been heated for an additional 30 min (142-145 C) with phosgene, heating was stopped. TCE was removed by distillation under reduced pressure (48 C/22 mm). The crude diisocyanate was then distilled through a short, jacketed head to give 4.05 g (0.012 mole, 69%) of 1, 12-diisocyanatooctadecane bp 168-184 C/4 μ. Analysis calculated for $C_{20}H_{36}N_2O_2$: C, 71.38; H, 10.78; N, 8.32. Found: C, 71.6; H, 10.7; N, 8.27. Its IR spectrum contained a strong NCO band at 2270 cm^{-1}. Mass spectral analysis gave a fragmentation pattern consistent with the diisocyanate structure. Molecular ion: calculated, 336.2776; found, 336.2749.

Thin Layer Chromatography

Prescored Uniplates (Analtech, Inc.) coated with 250 μ of Silica Gel G were spotted with 5-10 μliters of chloroform solutions containing 10 mg/ml of the compound to be examined using disposable micropipettes. Methyl 12-ketostearate and 12-ketostearamide were well separated using the developing solvent benzene-methanol-acetic acid 90:10:2. This solvent system was also used to separate 12-ketostearamide and 12-ketostearonitrile. The separation of the ketostearonitrile and the diamine was achieved using methylene chloride-methanol-ammonium hydroxide 90:12:2, which also separated the aminostearamide and the diamine. Either of these solvent systems satisfactorily separated a mixture of amino, hydroxy (6) and ketostearamides. Hydroxystearamide was included because it was a likely byproduct in the reductive amination of 12-ketostearamide.

The diisocyanate could not be analyzed directly by TLC because of its reaction with the developing solvent or TLC plate, or both. Instead it was converted to a urea derivative and analyzed by the following procedure: To a flask containing 10 mg diisocyanate was added 0.13 ml of a solution of 6.45 g di-*n*-butylamine in 100 ml THF (or 100 ml ether). The flask was shaken for 5-10 sec and heated at 75 C/17 mm to remove volatiles. After diluting the residue with chloroform it was spotted on the plate and developed with benzene-methanol-ammonium hydroxide 80:20:1 along a 10 cm path.

Visualization was most satisfactory for all the compounds tested with a modified spray reagent made by dissolving 3 g copper acetate in 60 ml water and adding to this solution 40 ml of 85% phosphoric acid (7). The sprayed plate was charred on a hot plate.

RESULTS AND DISCUSSION

Preparation of Intermediates

Improved yields over patented procedures were obtained in the series of reaction steps leading to diisocyanate. Ammonolysis to 12-ketostearamide was best carried out without a solvent. At 150 C reaction was incomplete after 7 hr and 12 hr, but was essentially complete in 21 hr yielding 85% product. Several procedures were attempted to dehydrate the amide to the corresponding nitrile. The use of thionyl chloride in benzene or $POCl_3$ without solvent was unsuccessful. The use of $POCl_3$ in THF with triethylamine was successful. This reaction was vigorous and exothermic, so that it is best controlled by dropwise addition of $POCl_3$. In THF but in the absence of triethylamine the reaction required 3.5 hr to come to completion on a 5 g scale in contrast to 14 min in the presence of triethylamine. The desirability of conducting the dehydration of amides with the combination of $POCl_3$ in the presence of triethylamine appears to be largely ignored in the literature. Runs were made in which $POCl_3$ was employed in excesses of 100, 50, 25 and 12% over theory, while triethylamine was used in excesses of 240, 200 and 133%. The highest yield of product (84%) was obtained when 50% excess $POCl_3$ and 133% excess triethylamine were used.

1, 12-Diaminooctadecane was best obtained by reductive amination of 12-ketostearonitrile. By conducting the reaction between the ketonitrile and ammonia for 2 hr at 125 C and the hydrogenation for 4.5 hr at 100 C or 2.5 hr at 125 C, yields of 84-88% were obtained and purity (estimated by TLC) was 95% or greater. The diamine reacts with CO_2 in the air to form a carbamate salt as is well known for primary and secondary amines (8). Material of broad melting range (94-101 C) was eventually obtained which contained about one molecule of CO_2 for every two molecules of diamine as was shown by elemental analysis. Regeneration of diamine from its carbamate salt occurs under vacuum distillation. The diamine was also prepared by lithium aluminum hydride reduction of 12-aminostearamide, a procedure useful for laboratory preparations on a small scale. The carbamate salt, diamine and dihydrochloride were used in the phosgenation studies.

Preparation of 1, 12-Diisocyanatooctadecane

Three methods for preparing the diisocyanate were investigated as shown in Table I. Of these, Method A gave the highest yield and was the simplest to carry out. This result was not anticipated because it was expected that the reaction of the diamine with diisocyanate to form polyureas would predominate over the reactions of the diamine with phosgene to form diisocyanate. On a 1 g scale reactions were run to determine completeness of reaction and product purity. On a 5 or 10 g scale crude products were distilled and yields were determined.

Of those runs in which yield was determined the highest yield of product was obtained using the conditions of Run 3. Because of the high purity of the crude diisocyanate formed in this run, it could probably be used directly for further reactions without additional purification. This would be advantageous because during distillation of the diisocyanate some of it polymerized so that only 69% of theory was isolated. Molecular distillation, used in Run 4, appears to be preferable to conventional distillation as the heat sensitive diisocyanate is heated for a much shorter time.

Results obtained by phosgenation of the diamine dihydrochloride are summarized under Method B. Solvents commonly used for this reaction such as toluene, xylene, amylbenzene, chlorobenzene, etc., were not suitable for the preparation of our diisocyanate because of the limited solubility of the dihydrochloride in the boiling solvents. In 1,1,2,2-tetrachloroethane (TCE), the dihydrochloride was soluble and reaction was rapid. It was used for all reactions described in Table I. Recovered product in Run 7 was almost as high as that obtained by Method A.

Phosgenation of the carbamate salt (Method C) rather than the diamine has also been reported (9). Runs 8 and 9 show conditions which gave good conversions to the diisocyanate using this method. Method C was not as convenient as Methods A and B and on a larger scale gave a lower yield of product. The use of Methods A or B provides an attractive route for obtaining the diisocyanate in good yield and high purity.

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