Isocyanates Derived from Fatty Acids by the Trimethylsilyl Azide Modification of the Curtius Rearrangement[1]

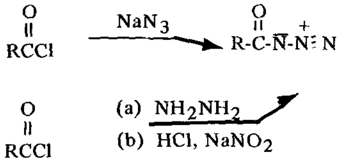
S.S. WASHBURNE and **W.R. PETERSON, JR.**, Department of Chemistry,
Temple University, Philadelphia, Pennsylvania 19122

ABSTRACT

Five fatty acid chlorides–myristoyl (14:0), palmitoyl (16:0), linoleoyl (18:2), oleyl (18:1) and stearoyl (18:0)–were smoothly converted in a one-pot, one-step reaction to the isocynates with one less carbon atom in the alkyl chain by treatment with trimethylsilyl azide in aromatic solvents at 100 C. The yields were consistently greater than 70%, and NMR and IR spectra of the products were consistent with the assigned isocyanate structures.

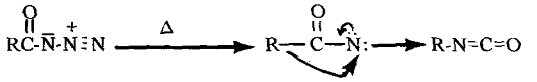
INTRODUCTION

We have recently reported (1) a simple modification of the Curtius Degradation (2) that affords high yields of isocyanates when acid chlorides are heated with trimethylsilyl azide in a nonpolar solvent. The Curtius Degradation is but one of four rearrangements, the others being the Schmidt, Hoffman and Lossen, commonly used for the conversion of an acid to the next lower amine. All these rearrangements proceed through a common intermediate, an isocyanate, but usually only the Curtius Degradation allows isolation of the isocyanate; due to these compounds rapid reaction with the protic solvents is typically employed in the other three rearrangements. Classical recipes for the Curtius Degradation (2) call for a two-step sequence: (a) isolation of an acyl azide, prepared either by treatment of an acyl chloride with sodium azide or by diazotization of an acyl hydrazide; and (b) thermolysis of the acyl azide in an aprotic solvent giving a nitrene after elimination of nitrogen, followed by rearrangement to the isocyanate.



$$\overset{O}{\overset{\|}{RCCl}} \xrightarrow{NaN_3} R\text{-}\overset{O}{\overset{\|}{C}}\text{-}\bar{N}\text{-}\overset{+}{N}\equiv N \qquad [1]$$

$$\overset{O}{\overset{\|}{RCCl}} \xrightarrow[(b)\ HCl,\ NaNO_2]{(a)\ NH_2NH_2}$$



$$R\overset{O}{\overset{\|}{C}}\text{-}\bar{N}\text{-}\overset{+}{N}\equiv N \xrightarrow{\Delta} R\text{—}\overset{O}{\overset{\|}{C}}\text{—}\ddot{N}\text{:} \longrightarrow R\text{-}N{=}C{=}O \qquad [2]$$

Although the Curtius Degradation has been utilized with fatty acid chlorides (2-6) with acceptable yields, the ever-present danger of explosion of an acyl azide has made the reaction less than completely practical. Fatty acid-derived isocyanates are potentially useful as additives in urethane resin formulations, and through their ready hydrolysis to amines as precursors for cationic surfactants.

Silyl azides are readily available via metathesis of chlorosilanes and sodium azide in dipolar aprotic solvents (7), and have an advantage over other sources of the N_3 group in that they are exceptionally thermally stable, perhaps the most stable azide compounds known (8). A further advantage of silyl azides over inorganic azides for organic reactions lies in their ready solubility in organic media, allowing a homogenous reaction medium for the Curtius Rearrangement, and making prior activation (9) of the inorganic azide unnecessary.

EXPERIMENTAL PROCEDURES

General Comments

Trimethylsilyl azide was prepared as described previously by us (7). Fatty acid chlorides were either commercial samples (Eastman or Fisher Scientific) or were prepared by treatment of the corresponding acid with thionyl chloride in dry benzene. They were distilled at reduced pressure immediately before use. IR spectra were determined as liquid smears between NaCl plates on Perkin Elmer Spectrophotometers, Models 21 and 700. Absorptions are reported as very strong (*vs*), strong (*s*), medium (*m*), weak (*w*) and shoulder (*sh*). NMR spectra were determined as ca. 15% solutions in $CDCl_3$ or CCl_4 containing 2% tetramethylsilane on Varian model T60 and XL100-15 spectrometers. Chemical shifts are given in δ units, ppm downfield from internal tetramethyl-silane. Liquid chromatography was performed on a Waters Associates Model ALC 202/401 Liquid Chromatograph using a 2 ft x 1/8 in. column of 10% Carbowax 400 on Porasil with chloroform as eluent. Microanalyses were performed by Schwartzkopf Microanalytical Laboratories, Woodside, N.Y. All reactions with silyl azides were carried out in an efficient fume hood.

cis-8-Heptadecenyl Isocyanate

A solution of 17.6 g (0.059 moles) of oleyl chloride in 30 ml toluene was stirred at 75-90 C, while 8.1 g (0.07 moles) of trimethylsilyl azide was added dropwise. A gas buret was used to measure nitrogen evolution. The mixture was heated at reflux for 24 hr, after which more than 90% of the theoretical amount of nitrogen had been evolved. The addition funnel was replaced with a variable reflux-ratio stillhead. After ca. 7 ml trimethylchlorosilane (bp 57-59 C) and the toluene had been removed by distillation at atmospheric pressure, the residual pale yellow oil was fractionated affording 14.4 g (89%) of *cis*-8-heptadecenyl

TABLE I

Isocyanates Derived from Fatty Acid Chlorides Using Trimethylsilyl Azide

Chloride	Isocyanate	Solvent	Conditions	Yield, %
14:0	$CH_3(CH_2)_{12}NCO$	CCl_4	16 hr, reflux	81
16:0	$CH_3(CH_2)_{14}NCO$	None	16 hr, 125 C	82
18:0	$CH_3(CH_2)_{16}NCO$	Toluene	3 hr, reflux	84
18:1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7NCO$	Toluene	24 hr, reflux	89
18:2	$CH_3(CH_2)_3(CH_2CH{=}CH)_2(CH_2)_7NCO$	Xylene	1 hr, 105 C	70

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[1] "Interaction of Carbonyl Compounds with Organometallic Azides," Part 3; for Part 2, see Reference 1; for Part 1, see Washburne, S.S., and W.R. Peterson, Jr., J. Org. Chem. 37:1738 (1972).

isocyanate, bp 133-135 C (0.15 mm) lit (6) bp 148 (0.5 mm). IR: 3040 (*sh*), 2950 (*s*), 2880 (*s*), 2280 (*vs*), 1655 (*w*), 1465 (*m*), 1445 (*sh*), 1405 (*w*), 1370 (*sh*), 1360 (*m*), 975 (*w*), 870 (*w*), and 720 (*m*) cm^{-1}. NMR: δ 0.90 (3H, *t*), 1.25-1.8 (22H, *m*), 2.04 (4H, broad quartet), 3.28 (2H, *t* J = 6.5 Hz), and 5.36 (2H, *t* with further splitting) ppm. The butyl urea derivative, prepared by heating the isocyanate with an excess of *n*-butylamine in benzene, had after recrystallization from $EtOH/H_2O$, mp 70-73 C, lit (6) mp 65 C. IR: 3350, 1640, 1585 cm^{-1}. It gave one peak upon liquid chromatographic analysis.

Tridecyl Isocyanate

10.0 g (0.04 moles) myristoyl chloride and 4.7 g (0.042 moles) trimethylsilyl azide, heated at reflux in CCl_4, afforded by a similar procedure 7.55 g (81%) of tridecyl isocyanate, bp 119 C (0.67 mm). IR: 2980 (*s*), 2850 (*s*), 2250 (*vs*), 1785 (*w*), 1460 (*m*), 1347 (*w*), 1055 (*w*). NMR: δ 0.90 (3H, *t*), 1.1-1.8 (22H, *m*), 3.26 (2H, *t*) ppm.

Pentadecyl Isocyanate

7.7 g (0.028 moles) palmitoyl chloride and 3.4 g (0.03 moles) trimethylsilyl azide heated 16 hr at 125 C without solvent gave 5.8 g (82%) pentadecyl isocyanate, bp 108-109 C (0.1 mm). IR: 2920 (*s*), 2850 (*s*), 2258 (*vs*), 1465 (*m*) 1355 (*w*), 720 (*w*) cm^{-1}. NMR: δ 0.90 (3H, *t*), 1.1-1.8 (26H, *m*), 3.25 (2H, *t*) ppm.

Heptadecyl Isocyanate

13.6 g (0.045 moles) stearoyl chloride and 5.5 g (0.048 moles) trimethylsilyl azide heated in toluene for 3 hr gave 10.7 g (84%) heptadecyl isocyanate, bp 130-131 C (0.15 mm), lit (6) bp 151 C (0.4 mm). IR: 2910 (*s*), 2850 (*s*), 2255 (*vs*), 1480 (*m*), 1355 (*w*), and 720 (*w*)cm^{-1}. NMR: δ 0.88 (3H, *t*), 1.05-1.65 (30H, *m*), 3.25 (2H, *t*) ppm.

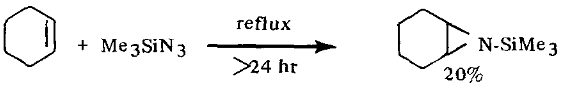
cis, cis-8,11-Heptadecadienyl Isocyanate

44.5 g (0.15 moles) linoleoyl chloride and 17.5 g (0.152 moles) trimethylsilyl azide heated 1 hr at 105 C in 80 ml xylene gave 29.0 g (70%) of the isocyanate, bp 156-158 C (0.15 mm), lit (6) bp 172 (3mm). IR: 2945(*m*), 2910 (*s*), 2260 (*vs*), 1695 (*w*), 1462 (*m*), 1370 (*sh*), 1358 (*m*), 1260 (*w*), 1055 (*w*), 965 (*w*), 905 (*w*), 860 (*w*), 720 (*m*) cm^{-1}. NMR: δ 0.90 (3H, *t*), 1.2-1.6 (18H, *m*), 2.05 (4H, broad quartet), 2.75 (2H, *t*), 3.21 (2H, *t*), 5.30 (4H, triplet with further splitting) ppm.

RESULTS AND DISCUSSION

The interaction of fatty acid chlorides and trimethylsilyl azide (Table I) smoothly gives the isocyanates with one less carbon atom in the alkyl chain. There is little effect of solvent upon yield or ease of work-up. As the product is distilled directly from the reaction flask, the experimental procedure is especially simple. The completeness of the reaction is easily monitored by following nitrogen evolution. This is reflected in the uniformly high distilled yields of pure product, which are in excess of 80%, except in the case of the diene isocyanate, where a viscous pot residue was obtained in large quantity. Even though this reaction was conducted under a blanket of dry nitrogen to minimize polymerization, it is evident that some occurred, causing a reduction of yield.

Although the olefinic bond is known to be reactive to trimethylsilyl azide (cyclohexene gives 7-trimethylsilyl-7-azabicyclo(4.1.0)heptane (10) (equation 3), we observed no reaction at the unsaturated centers of oleyl and linoleoyl chlorides. This is probably a manifestation of the lesser reactivity toward silyl azide of the olefinic center relative to the acid chloride function. Even at low silyl azide concentration, the chloride competes favorably with the olefinic center for azide, for the isocyanate-forming reactions go essentially to completion. Although we did not isolate the acyl azides, their intermediacy in the Curtius Degradation is well documented (9).



[3]

The spectral data of the products are in good accord with the assigned structure. The isocyanate peak is a very strong absorption in the 2260 cm^{-1} region, while the presence of unreacted acid chloride can be shown by absorption around 1790 cm^{-1}. Only in the case of tridecyl isocyanate was a weak peak observed in this region. The presence of medium absorption at 720 cm^{-1} and only weak absorption at 970 cm^{-1} in the olefinic isocyanates is good evidence that little, if any, isomerization about the double bonds occurred during the reaction.

NMR spectroscopy has been shown to be a powerful tool in fatty acid chemistry (11). All of the isocyanates prepared in this study exhibited a triplet resonance around δ 3.25 for the $-CH_2-$ hydrogens immediately adjacent to the N=C=O group. As this occurs in a region of the spectrum removed from other resonances, its presence can be considered diagnostic for the CH_2-N=C=O moiety.

Silyl azides other than trimethyl were investigated as reactant in some preliminary studies, but appeared to offer no advantage over the more readily available trimethylsilyl azide, even in reactions with perfluoroalkanoyl chlorides, where the isocyanate products had boiling points similar to that of Me_3SiCl, the expected silicon product. Details of those investigations will be published elsewhere.

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