

Preparation of Tertiary Alkyl Isocyanates by the Zinc Iodide Catalyzed Reaction of Tertiary Alkanoyl Chlorides with Trimethylsilyl Azide¹

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Tertiary cyclo(polycyclo)alkyl isocyanates were prepared in near quantitative yield by the zinc iodide catalyzed reaction of tertiary alkanoyl chlorides and trimethylsilyl azide. In comparison the reaction of tertiary alkyl halides with trimethylsilyl isocyanate in the presence of Lewis acids such as SnCl₄ gives only poor yields of the corresponding isocyanates.

Introduction

Preparation of 1-adamantyl isocyanate was reported by Stetter and Wulff^{2a} from 1-aminoadamantane hydrochloride^{2b} and an alkali-metal cyanate in low yield. Alkyl isocyanates are generally prepared in a one-pot reaction by treating the corresponding acyl chloride with ammonium or alkali-metal azide without isolating the intermediate acyl azides.^{3,4} The latter undergo Curtius rearrangement, leading to isocyanates.³ Various isocyanate reagents have also been reported for the preparation of alkyl isocyanates.⁴ Thus, (phenylthio)methyl or (methylthio)methyl isocyanates were prepared in modest yields (ca. 52%)^{4a,5} from the corresponding chlorides using silver isocyanate. 1-Adamantyl isocyanate was prepared⁶ in only 20% yield from 1-adamantyl chloride and trimethylsilyl isocyanate under Lewis acid (TiCl₄) catalysis.

Zinc iodide catalyzed reaction of trimethylsilyl azide^{7a} with aroyl chlorides gives thermally stable aroyl azides, which have been isolated.^{7b} Trimethylsilyl azide is also known to undergo similar Lewis acid catalyzed reaction with aldehydes and ketones to give the analogous α -siloxy compounds.⁸ The more reactive ortho esters give mainly alkoxy/azido group exchange⁹ and acetals and ketone acetals give monoazide and diazide derivatives.¹⁰ In contrast, reaction of trimethylsilyl azide with alkanoyl and substituted-alkanoyl chlorides yields thermally unstable (sometimes explosive) alkanoyl azides that rearrange under moderate thermal conditions to the corresponding isocyanates in high yield.¹¹ [This procedure affords mainly the preparation of primary alkyl isocyanates and has been further extended to the preparation of similar isocyanates from anhydrides.¹²]

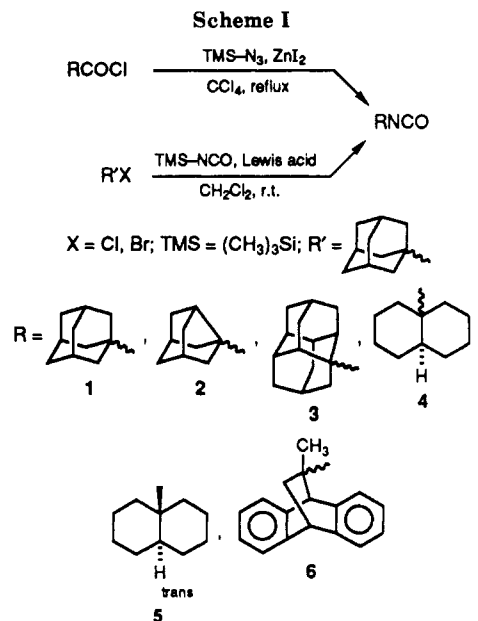


Table I. Zinc Iodide Catalyzed Preparation of Tertiary Isocyanates with TMS-N₃

alkanoyl chloride	reaction time (h)	% yield isocyanate
1	06	99
2	12	98
3	14	95
4	16	98
5	13	96
6	12	96

In continuation of our studies on the use of organosilicon reagents in synthesis, we have found a useful application of trimethylsilyl azide as an effective synthon in the preparation of tertiary alkyl (polycycloalkyl) isocyanates and herein report our results.

Results and Discussion

Trimethylsilyl azide was added dropwise to a well-stirred solution of 1-adamantanecarbonyl chloride and a catalytic amount of ZnI₂ in CCl₄, and the reaction mixture was slowly refluxed for 6 h (Scheme I). After workup 1-adamantyl isocyanate was obtained in nearly quantitative yield. In the absence of ZnI₂ the reaction is incomplete and difficult to control. Similar ZnI₂-catalyzed reaction of a series of polycycloalkanoyl chlorides with trimethylsilyl azide gives quantitative yield of the corresponding iso-

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Table II. GC-MS and ¹³C NMR Data of Tertiary Isocyanates

tertiary isocyanates	GC-MS	¹³ C NMR
1	177 (M ⁺ , 48), 149 (2), 135 (M - NCO, 26), 120 (100)	C ₃ = C ₅ = C ₇ = 29.73 (d), C ₄ = C ₆ = C ₁₀ = 35.79 (t), C ₂ = C ₈ = C ₉ = 45.29 (t), C ₁ = 55.72 (s), C _α = 122.70 (s)
2	163 (M ⁺ , 17.5), 121 (M - NCO, 11), 120 (100), 80 (43)	C ₁ = C ₆ = 37.26 (d), C ₂ = C ₈ = 51.40 (t), C ₃ = 65.88 (s), C ₄ = 45.74 (d), C ₅ = C ₉ = 43.12 (t), C ₇ = 33.59 (t), C _α = 121.58 (s)
3	229 (M ⁺ , 2), 213 (100), 187 (M - NCO, 11), 130 (39), 117 (18)	C ₄ = 24.45 (d), C ₉ = 25.0 (d), C ₈ = C ₁₀ = 34.45 (t), C ₆ = 35.73 (d), C ₇ = C ₁₁ = 35.95 (d), C ₃ = C ₁₄ = 36.47 (t), C ₅ = 37.07 (t), C ₁ = 37.48 (s), C ₂ = C ₁₂ = 38.45 (d), C ₁₃ = 40.83 (t), C _α = 123.73 (s)
4	179 (M ⁺ , 46), 137 (M - NCO, 21), 136 (100), 122 (31), 117 (28), 108 (24), 93 (22), 79 (72)	21.95 (t), 27.62 (t), 28.94 (t), 42.58 (t), 45.08 (d), 61.53 (s), C _α = 121.40 (s)
5	179 (M ⁺ , 49), 137 (M - NCO, 21), 136 (100), 122 (38), 117 (29), 108 (24), 93 (19), 79 (16)	22.02 (t), 25.8 (t), 29.01 (t), 40.02 (t), 45.15 (d), 62.07 (s), C _α = 121.79 (s)
6	178 (M - C ₂ H ₃ NCO, 100), 152 (5), 89 (2), 69 (2)	142.81 (s), 142.65 (s), 140.00 (s), 135.34 (s), 126.81 (d), 126.60 (d), 126.28 (d), 126.12 (d), 125.96 (d), 124.51 (d), 123.37 (d), 123.32 (d), 52.20 (d), 51.41 (d), 43.44 (d), 38.19 (t), C _α = 122.72 (s)

cyanates as isolated products (Table I). All of the prepared isocyanates were characterized by elemental analysis and by IR, ¹³C NMR, and GC-MS analysis (Table II).

For comparison, attempted SnCl₄-catalyzed direct preparation of 1-adamantyl isocyanate from 1-chloro- or 1-bromoadamantane and trimethylsilyl isocyanate gave only low yields (10–20%) similar to the TiCl₄-catalyzed reaction of 1-chloroadamantane with trimethylsilyl isocyanate.⁶

Whereas primary as well as some secondary alkyl isocyanates^{11,12} can be readily prepared from their corresponding alkanoyl chlorides and trimethylsilyl azide without any catalysis, preparation of tertiary alkyl isocyanates from similar precursors is successful only with selective Lewis acid catalysis. The ZnI₂-catalyzed reaction of tertiary alkanoyl chlorides with trimethylsilyl azide affords a convenient method for the preparation of tertiary alkyl isocyanates.

Experimental Section

1-Chloro- and 1-bromoadamantanes and 1-adamantanoyl chloride were available from Aldrich in high purity (>95%) and used as received. 3-Noradamantanecarbonyl chloride was prepared from the corresponding carboxylic acid (Aldrich) by a conventional method using SOCl₂. 1-Diamantanoyl chloride was similarly prepared from the corresponding carboxylic acid obtained from the corresponding carbonitrile.¹³ Trimethylsilyl azide and isocyanate were purchased from Petrarch Systems. ZnI₂ (Aldrich) and AlCl₃ (Fluka) were of high purity and used as received. Carbon tetrachloride and methylene chloride, respectively, were dried over P₂O₅ under reflux.

All of the other carboxylic acid chlorides were prepared via reaction of carboxylic acid and freshly distilled thionyl chloride, generally at 65–70 °C for 30 min, and freshly distilled in vacuo before use.

General Procedure for Preparation of Tertiary Alkyl Isocyanates. (a) **From Trimethylsilyl Azide.** To a well-stirred solution of 24.0 mmol of polycycloalkanoyl chloride and a catalytic amount of ZnI₂ (usually 5–10 mg) in CCl₄ (~50 mL) was added 3.0 mL (28.8 mmol) of trimethylsilyl azide dropwise over a period of 5 min under dry argon and the reaction mixture was then refluxed for the stipulated reaction times (Table I). The reaction mixture was cooled to room temperature. Removal of solvent in vacuo gave crude isocyanate, which was subsequently purified

via column chromatography on silica gel (10% Et₂O/hexane eluent) to afford the pure isocyanate. Analytical samples were prepared by recrystallization/distillation.

(b) **From Trimethylsilyl Isocyanate.** To a well-stirred solution of 2 g (12 mmol) of 1-chloro(1-bromo)adamantane and 1.6 g (14.0 mmol) of trimethylsilyl isocyanate in CH₂Cl₂ was added 3.6 g (14 mmol) of SnCl₄ slowly at 0 °C during a period of 5 min. After the addition of SnCl₄ was complete, the reaction mixture was maintained with stirring at ambient temperature for 18 h and then quenched with ice-sodium bicarbonate. Extraction with CH₂Cl₂ followed by removal of solvent gave crude 1-adamantyl isocyanate together with adamantane and unreacted halo-adamantane. The isocyanate was separated by column chromatography as described in the above procedure.

1-Adamantyl Isocyanate (1). From the reaction of 1-adamantanecarboxylic acid chloride and trimethylsilyl azide the corresponding 1-adamantyl isocyanate (1) was obtained; IR (KBr) 2260 cm⁻¹; mp 143 °C (lit.⁶ mp 144–145 °C).

3-Noradamantyl Isocyanate (2). From the reaction of 3-noradamantanecarboxylic acid chloride and trimethylsilyl azide was obtained the corresponding 3-noradamantyl isocyanate as a colorless microcrystalline solid: mp 57 °C (from hexane); IR (KBr) 2264 cm⁻¹. Anal. Calcd for C₁₀H₁₃NO: C, 73.62; H, 7.98. Found: C, 73.89; H, 8.06.

3-Diamantyl Isocyanate (3). From the reaction of 3-diamantanecarboxylic acid chloride and trimethylsilyl azide was obtained the corresponding 3 as a colorless microcrystalline solid: mp 126 °C (hexane); IR (KBr) 2263 cm⁻¹. Anal. Calcd for C₁₅H₁₉NO: C, 78.60; H, 8.30. Found: C, 78.52; H, 8.21.

α-Decalin Isocyanate (4). From the reaction of α-decalin-carboxylic acid chloride and trimethylsilyl azide was obtained the corresponding 4 as a colorless liquid: bp 84 °C/2.7 mm; IR (CCl₄) 2258 cm⁻¹. Anal. Calcd for C₁₁H₁₇NO: C, 73.74; H, 9.50. Found: C, 73.43; H, 9.49.

trans-α-Decalin Isocyanate (5). From the reaction of trans-α-decalin-carboxylic acid chloride and trimethylsilyl azide was obtained the corresponding 5 as a liquid: bp 81 °C/2.7 mm; IR (CCl₄) 2263 cm⁻¹. Anal. Calcd for C₁₁H₁₇NO: C, 73.74; H, 9.50. Found: C, 73.66; H, 9.33.

7-Methyl-2,3,5,6-dibenzobicyclo[2.2.2]oct-7-yl Isocyanate (6). From the reaction of 7-methyl-2,3,5,6-dibenzobicyclo[2.2.2]octane-7-carboxylic acid chloride and trimethylsilyl azide was obtained the corresponding 6 as a colorless liquid: bp 136 °C/0.1 mm; IR (CCl₄) 2258 cm⁻¹. Anal. Calcd for C₁₈H₁₅NO: C, 82.73; H, 5.79. Found: C, 82.56; H, 5.77.

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