

Conversion of Alkyl Carbamates into Amines *via* Treatment with Trimethylsilyl Iodide

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Summary Reaction of the alkyl carbamates (1) with trimethylsilyl iodide (2) followed by methanolysis of the resulting trimethylsilyl carbamates (4), affords high yields of the corresponding amines (5), even in the case of very sensitive compounds such as 2,3-diazabicyclo[2.2.1]-heptane (5h).

THE carbamate functionality is a useful and common protecting group for primary and secondary amines. While many specific carbamates have been developed for their ease of conversion back into the amines under mild conditions,¹ the simple, more easily obtainable alkyl carbamates have not been often employed because of the harsh conditions usually necessary.^{2,3} Two exceptions to this are benzyl carbamates,⁴ which can be converted into the amines

carbamic acid (8) which spontaneously decarboxylates to produce the amine (5). The intermediate formation of the trimethylsilyl carbamate (4) is demonstrated by the isolation of (4b) [m.p. 136–136.5 °C (from CCl₄); δ 6.9–7.6 (5H, m), 6.5–6.8br (1H, s), and 0.35 (9H, s)] from (1b) in 60% yield.

The alkyl carbamates are slightly more reactive toward trimethylsilyl iodide than the corresponding alkyl esters (reaction time at 50 °C: methyl carbamate, 2.5 h; methyl ester, 4–20 h). Presumably the initial complexation is enhanced by the presence of the lone pair on nitrogen, thus causing the equilibrium to lie more on the side of the complex for the carbamates than for the esters.

The conditions necessary for this dealkylative hydrolysis are generally much milder than those of other hydrolytic

TABLE. Reaction of alkyl carbamates with trimethylsilyl iodide

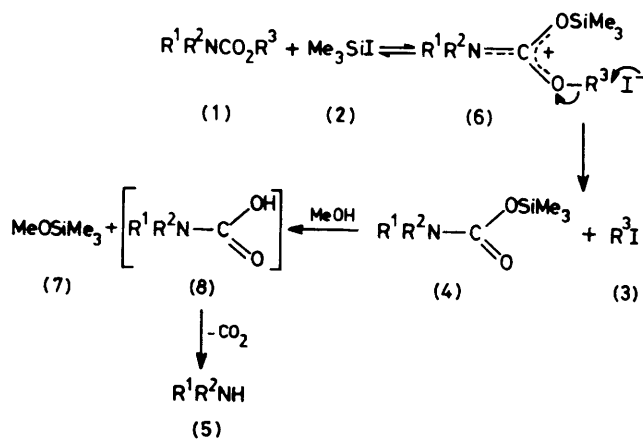
	R ¹	R ²	R ³	Solvent	Temp./°C	Time/h	% Yield ^a of (4)	% Yield ^b of (5)
a	Ph	H	Me	CDCl ₃	50	2.5	100	70
b	Ph	H	Et	CDCl ₃	55	6	95(60) ^c	—
c	Ph	Ph	Et	CDCl ₃	50	8	—	93
d	H	H	CH ₂ Ph	[CH ₂] ₄ SO ₂	25	<0.1	100	—
e	—CH ₂ CH ₂ OCH ₂ CH ₂ —	—	Et	CDCl ₃	60	3	100 ^d	—
f	C ₆ H ₁₃	C ₆ H ₁₃	Et	CDCl ₃	60	2.5	100	92
g	C ₁₀ H ₂₁	C ₁₀ H ₂₁	Et	CDCl ₃	60	2.5	100	89
h ^e				CDCl ₃	60	2.5	100	—
				CHCl ₃	70	3	—	71
				CHCl ₃	60	5	—	77 ^f

^a Determined by integration of the pertinent peaks in the ¹H n.m.r. spectrum. ^b Yield of isolated, purified material. ^c Yield of recrystallized material, m.p. 136–136.5 °C. ^d Prolonged reaction times with excess of trimethylsilyl iodide did not effect the ether linkage to an extent detectable by n.m.r. spectroscopy. ^e See displayed formula. ^f Isolated as the hydroiodide salt.

under mild conditions (hydrogenolysis,^{5a} irradiation,^{5b} or treatment with acid^{5c}), and *t*-butyl carbamates⁴ which are easily cleaved in acid.⁶ We report an efficient and general procedure for the conversion of simple alkyl carbamates into the corresponding amines under mild, non-aqueous conditions.

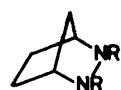
Treatment of an alkyl carbamate (1) in chloroform or sulpholan solution with trimethylsilyl iodide (2) at 50–60 °C gives the trimethylsilyl carbamate (4) and the alkyl iodide (3). The trimethylsilyl carbamate (4) can then be isolated by work-up under anhydrous conditions, or converted directly into the amine (5) by addition of methanol, removal of the volatile components, and purification by distillation or chromatography. Results for a series of carbamates are in the Table.

The mechanism proposed for this transformation (Scheme) is analogous to the one suggested for the reaction of alkyl esters with trimethylsilyl iodide.⁷ The first step is a fast reversible complexation of the trimethylsilyl group with the carbamate forming the intermediate (6) which can then proceed to the trimethylsilyl carbamate (4) and alkyl iodide (3) *via* an S_N1 or S_N2 process. Methanol then cleaves the oxygen–silicon bond of the trimethylsilyl carbamate to afford methyl trimethylsilyl ether (7) and the



SCHEME

methods. For example, the deprotection of the biscarbamate (1h) has been effected by several groups^{3,8} using potassium hydroxide in refluxing alcoholic solvents. Although the bicyclic hydrazine (5h) could be isolated with care from the reaction mixture, owing to its lability to



(1h) R = CO₂Et
(5h) R = H

air-oxidation⁹ it was usually contaminated with the oxidation product, the corresponding azo-compound. Other preparations of the compound are known, but these utilize somewhat specialized azodiester derivatives.¹⁰ Our conditions for the hydrolysis of the diethyl biscarbamate (1h) (70 °C; 3 h) are not only much milder than those reported previously^{3,9,10b} but also permit the simple isolation of the sensitive hydrazine (5h) itself in 71% yield as a low-melting white solid. The hydroiodide salt of (5h) was easily obtained by the use of 3 equiv. of (2) (60 °C; 5 h) in 77% yield.† Either of these compounds could be converted into

† The m.p., and n.m.r. and mass spectrum of (5h) were in agreement with those reported in refs. 9 and 10. Work-up involved initial evaporation of the volatile component [solvent and slight excess of (2)], addition of degassed methanol (for hydrolysis of the silyl carbamates), evaporation of volatile materials (removal of methanol and decarboxylation), and final distillation under reduced pressure. A somewhat impure sample of the hydroiodide of (5h) melted with decomposition at 165–170 °C. The n.m.r., i.r., and mass spectrum of this sample were consistent with its proposed structure and were analogous to those reported for similar compounds (ref. 9b and J. P. Snyder, M. L. Heyman, and V. T. Bandurco, *Tetrahedron Letters*, 1971, 4693).

‡ In the case of the nucleophilic amines (5f) and (5g), methanol pretreated with gaseous HCl was used to quench the reaction so that the amine was protonated as formed. This eliminated a side reaction between the amine and the silyl carbamate to form the symmetrical urea which otherwise accounted for 5–10% of the isolated material. In these cases 1 equiv. more of sodium methoxide was added in the next operation.

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the azo-compound by several known oxidation methods.³

The following is a general experimental procedure. To a 2M solution of 1 equiv. of the carbamate (1) in chloroform (or CDCl₃), sealed in a reaction vessel under nitrogen, was added 1.2 equiv. of trimethylsilyl iodide (2) via a dry syringe. The mixture was then heated (usually to 50–60 °C) and the progress of the reaction was followed by n.m.r. spectroscopy. When reaction was complete, 3–4 equiv. of methanol were added† and the volatile components were removed under reduced pressure. The residue was taken up in methanol and 0.5 equiv. of sodium methoxide was added.‡ The volatile components were removed under reduced pressure again and the amine (5) was distilled from the residue.

The present results, in conjunction with previous publications¹¹ indicate the wide versatility of trimethylsilyl iodide in synthetic applications.

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