REDUCTION OF N-ALKOXYCARBONYLLACTAMS WITH $NaBH_4/EtOH\text{-}H^+$: A FACILE SYNTHESIS OF α-ETHOXYURETHANES

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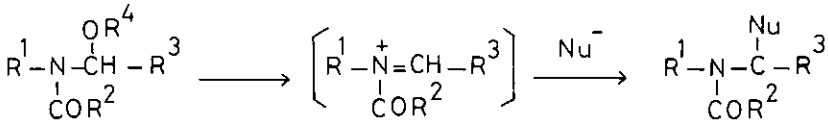
Abstract — Reduction of N-alkoxycarbonyllactams with $NaBH_4/H^+$ in ethanol (Speckamp's condition) afforded α-ethoxyurethanes (Shono's compounds) in good yields.

New methods for the carbon-carbon bond formation at the α-position of amines via acyliminium ion (2) have been developed in recent years.[1] Among these, α-alkoxyamides[2] (1; R^2 = alkyl) and α-alkoxyurethanes[3] (1; R^2 = alkoxy), precursors for 2, are conveniently available from the reduction of imides with $NaBH_4/EtOH\text{-}H^+$ or from the anodic oxidation of urethanes, respectively. In this paper, a convenient alternative method for the synthesis of cyclic N-alkoxycarbonyl-2-ethoxyamines (7 - 9) is described.

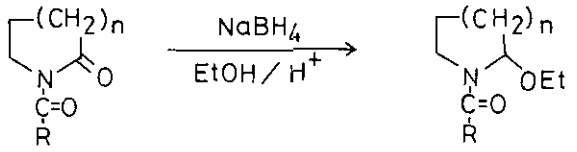


1 2 3

Although the reduction of N-acyllactams (e. g. 4a, 4b, 5a) with $NaBH_4$ did not afford α-ethoxyamides (e. g. 7a, 7b, 8a), the reductinon of N-alkoxycarbonyl-lactams (4c-g - 6c-g) in a similar condition gave the desired α-ethoxyurethanes (7 - 9) in good yields. The results are shown in Table 1. The reaction was carried out by the modification of Speckamp's procedure[2]: A small amount of bromocresol green (pH 3.8 yellow - 5.4 blue) was used as an internal indicator and the optimum reaction temperature was between -6° and 0°.

The investigation of the carbon-sulfur, carbon-nitrogen and carbon-carbon bonds formation at the α-position of amines using these α-ethoxyurethane are now in progress.

Table 1. Reduction of N-Alkoxycarbonyllactams[a] to α-Ethoxyurethanes[b]



4 n = 1 7 n = 1
5 n = 2 8 n = 2
6 n = 3 9 n = 3

Yield (%)[c] and bp (°C/mmHg) of Products (7, 8, 9)

R	7		8		9	
a : Me	0[d]		0[d]		-	
b : Ph	0[d]		-		-	
c : OMe	80	(120°/3)	79	(85°/4)	-	
d : OEt	83	(83°/2)	-		64	(83°/2)
e : OCH_2Ph	83	(110°/2)	80	(-[e])	88	(-[e])
f : O^tBu	88	(75°/2)	70	(70°/2)	65	(78°/2)
g : $OCH_2CH=CH_2$	88	(105°/2)	-		-	

a) N-Alkoxycarbonyllactams (4 - 6) were prepared by the alkoxycarbonylation of lactams with chloroformates (or di-tert-butyl dicarbonate for tert-butoxycarbonylation) and sodium hydride in 60-80% yields. b) All the products gave satisfactory ir, ^{1}H-nmr and ms spectra. c) Isolated yield. d) In the case of N-acyllactams, the cleavage of N-acyl groups and the reduction of the ring-opened compounds were observed. e) Purified by chromatography.

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