SODIUM BOROHYDRIDE DESULPHURIZATION OF THIOLACTAMS TO AMINES

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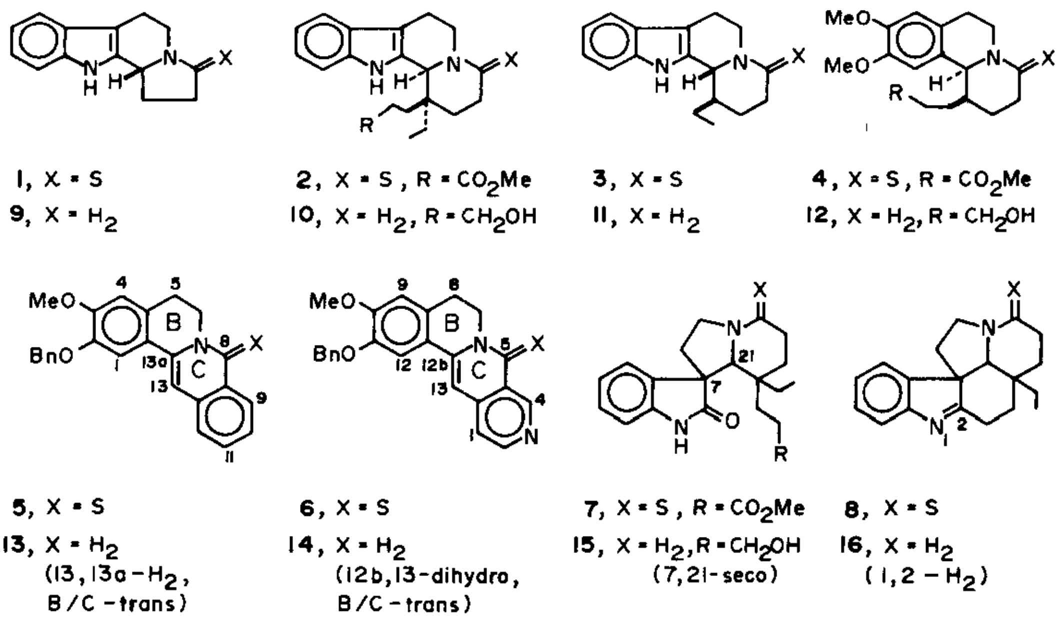
Abstract - Sodium borohydride desulphurizes a variety of thiolactams(1-8) in t-butanol/ methanol mixture under reflux to the respective amines (9-16) in good yield.

Thiolactams are usually reduced to amines by Raney nickel[1] which can also desulphurize many sulphur containing groups[2]. Aluminium amalgam in neutral alcoholic solution[3] has also been used in some cases. However, to the best of our knowledge, the use of $NaBH_4$ in this conversion is not yet known. Herein we wish to report an efficient method of desulphurization of thiolactams (**1-8**) to the corresponding amines (**9-16**) (Scheme 1) in ca. 70-94% yield (Table 1) using $NaBH_4$ in t-butanol/methanol mixture, a reagent recently shown to reduce esters[4] and tertiary δ-lactams[5].

In a typical experiment, MeOH (4 ml) was added dropwise over a period of 2-5 h to a refluxing mixture of a thiolactam (0.5 mmol) and $NaBH_4$ (6-8 mmol) in t-BuOH (6 ml). Usual work-up followed by column chromatography and crystallization afforded the desired amine (70-94%). In case of compounds **5** and **6**, since during purification the products were getting easily transformed to the lactams, further reduction of the enamine double bond was ensured to fully characterise

Scheme I



1, X = S
9, X = H_2

2, X = S, R = CO_2Me
10, X = H_2, R = CH_2OH

3, X = S
11, X = H_2

4, X = S, R = CO_2Me
12, X = H_2, R = CH_2OH

5, X = S
13, X = H_2
(13,13a-H_2,
B/C -trans)

6, X = S
14, X = H_2
(12b,13-dihydro,
B/C -trans)

7, X = S, R = CO_2Me
15, X = H_2, R = CH_2OH
(7,21-seco)

8, X = S
16, X = H_2
(1,2 - H_2)

the product. This was done by cooling the reaction mixture to 0°C followed by successive addition of HOAc (5 ml) and $NaBH_4$ (~ 2 mmol) with stirring for 20 min at room temperature. It was basified and after usual work-up the product was purified by chromatography.

Table 1. Desulphurization of Thiolactams (**1-8**) to Amines (**9-16**)

Thiolactams	$NaBH_4$ (mol ratio)	Time (h)	Product (Yield%)	Observed mp (°C)	Reported mp (°C)	Ref.
1	12	5	**9**(83)	168-169	172.5-173.5	6
2	16	2	**10**(90)	126-128	128-129	5
3	12	2	**11**(85)	88-90	90-93	7
4	16	2	**12**(90)	107-109	109-110	5
5	12	3	**13**(70)	98-101	100-102	8
6	12	4	**14**(78)	Foam	-	9
7	16	3	**15**(94)	Wax	-	9
8	16	2	**16**(71)	104-107	108-110	10

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