

A NEW METHOD FOR THE PREPARATION OF 3,4-DIHYDRO- $\beta$ -CARBOLINES  
VIA ALKYLTHIOIMINIUM SALT

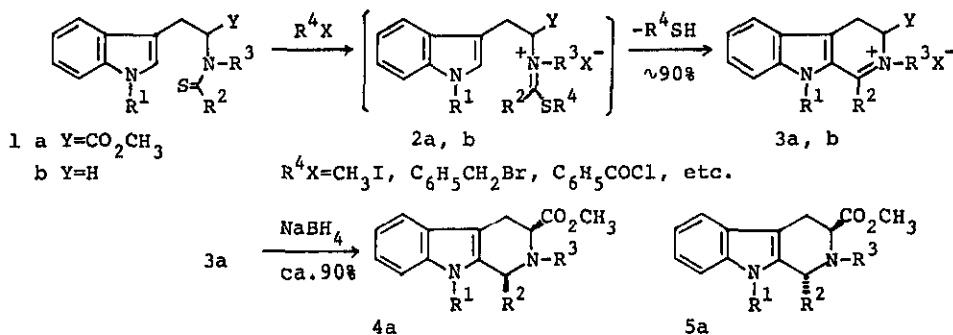
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The Bischler-Napieralski reaction under acidic conditions has been widely used for the preparation of 3,4-dihydro- $\beta$ -carbolines. We report here that N-alkylthio-carbonyl tryptophan (1a) and tryptamine analogs (1b) can be converted into the corresponding 3,4-dihydro- $\beta$ -carbolines (3a,b) under milder and non-acidic conditions. Reduction of 3a to 1,2,3,4-tetrahydro- $\beta$ -carbolines is also discussed.

Treatment of 1 with methyl iodide or benzyl bromides in an appropriate solvent (acetone, dichloromethane, acetonitrile, etc.) gave alkylthioiminium salt (2) as an intermediate, which, at room temperature or in the refluxing solvent, spontaneously cyclized and released alkanethiol to give 3 in good yields. Some of acyl halides such as benzoyl chloride in place of alkyl halides are equally effective for this cyclodesulfurization.

Reduction of 3a ( $R^3=H$ ) with sodium borohydride proceeded almost stereoselectively to give cis-1,3-disubstituted tetrahydro- $\beta$ -carboline (4a). On the other hand, reduction of 3a ( $R^3=CH_2C_6H_5$ ) afforded 1,3-trans isomer (5a) predominantly, together with a small amount of 4a ( $R^3=CH_2C_6H_5$ ).

Cyclization of optically active (L)-1 and (D)-1 ( $R^1=R^3=H$ ,  $R^2=CH_3$ ) gave (L)-3 and (D)-3, in good yields, respectively. Optical purity of both compounds was confirmed by converting them into the known tetrahydro derivatives, (L)-4a and (D)-4a ( $R^1=R^3=H$ ,  $R^2=CH_3$ ).



$R^1=H, CH_3$ ;  $R^2=CH_3, C_2H_5, C_6H_5, C_6H_{11}, C(CH_3)_3$ ;  $R^2=R^3=-(CH_2)_3-$ ;  $R^3=H, CH_2C_6H_5$