

STUDIES ON LACTAMS IX.<sup>1)</sup> A CONVENIENT SYNTHESIS OF LACTAM RINGS

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The auto-cyclization reaction has been employed for the synthesis of lactam rings by means of reduction from  $\omega$ -carboxybenzoylamino acid active esters in high dilution method.

In the previous paper, we reported availability of the  $N,N'$ -disuccinimidyl carbonate (DSC)<sup>2)</sup> and  $N$ -succinimidyl diphenylphosphate (SDPP)<sup>3)</sup> for the preparation of active ester reagents. In this paper, we report the lactam synthesis from active esters by removal of the protected group, followed by auto-cyclization.

$\omega$ -Amino carboxylic acid,  $\beta$ -alanine,  $\gamma$ -aminobutylic acid,  $\delta$ -aminovaleric acid, and  $\epsilon$ -aminocaproic acid were reacted with carbobenzoxy chloride (Z-Cl) to yield  $\omega$ -Z-amino acids (1), respectively.

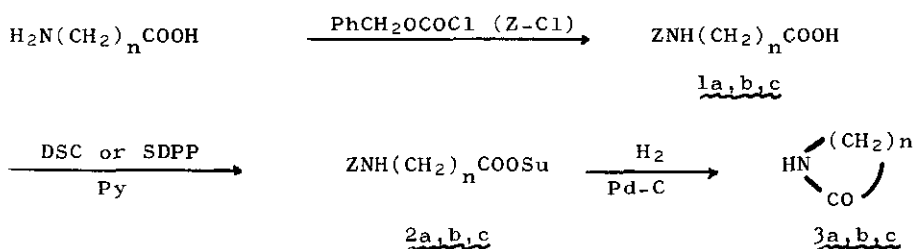


Chart 1

Table I. Yields of the Products

	n	Yield (%)	
		<u>2</u>	<u>3</u>
a	3	100	86
b	4	95	91
c	5	98	88

$\omega$ -Z-Amino acids (1a,b,c) were treated with DSC or SDPP to give active esters of  $\omega$ -Z-amino acid (2a,b,c) in good yields. The active esters of  $\omega$ -Z-amino acid (2a,b,c) were reduced catalytically in the presence of 10% palladium carbon in high dilution method in ethyl acetate, and auto-cyclization product, lactams (3a,b,c) were obtained (Chart 1).

Similarly, 2-amino(L)-6-hexanelactam (7) was obtained as follows: Boc-Lys(Z)-OH (4) was reacted with DSC to give Boc-Lys(Z)-OSu (5) in a quantitative yield. This compound (5) was reduced under the same conditions as above to yield 2-Boc-amino(L)-6-hexanelactam (6) in good yield. This compound (6) was treated with HBr in dry ether to afford 2-amino(L)-6-hexanelactam hydrobromide (7) in a quantitative yield as shown in Chart 2.

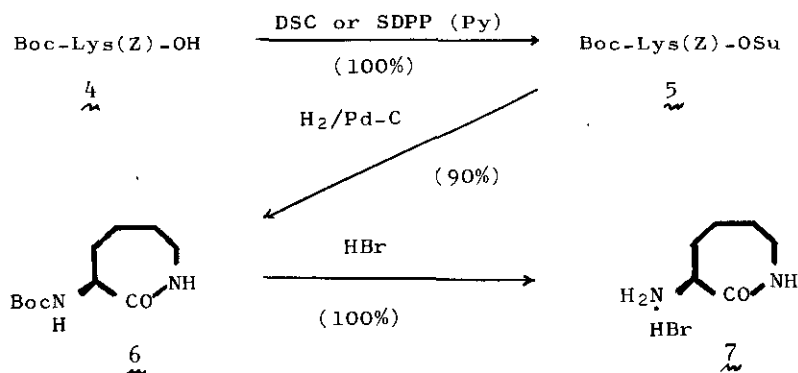


Chart 2

This auto-cyclization reaction is not applicable to  $\beta$ -alanine derivatives, and the  $\beta$ -lactam rings could not be obtained.

#### REFERENCES

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