

CYCLIZATION REACTION OF N-(HALOACYL)- OR N-(PHTHALOYLGLYCYL)HYDROXYAMINO ACID ESTERS WITH AMMONIA

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A new type of cyclization of  $\beta$ -methoxy derivatives of N-haloacyl- or N-phthaloylglycyl- $\alpha$ -hydroxyamino acid esters with ammonia to 2-carbamoyl-4-imidazolidone is described.

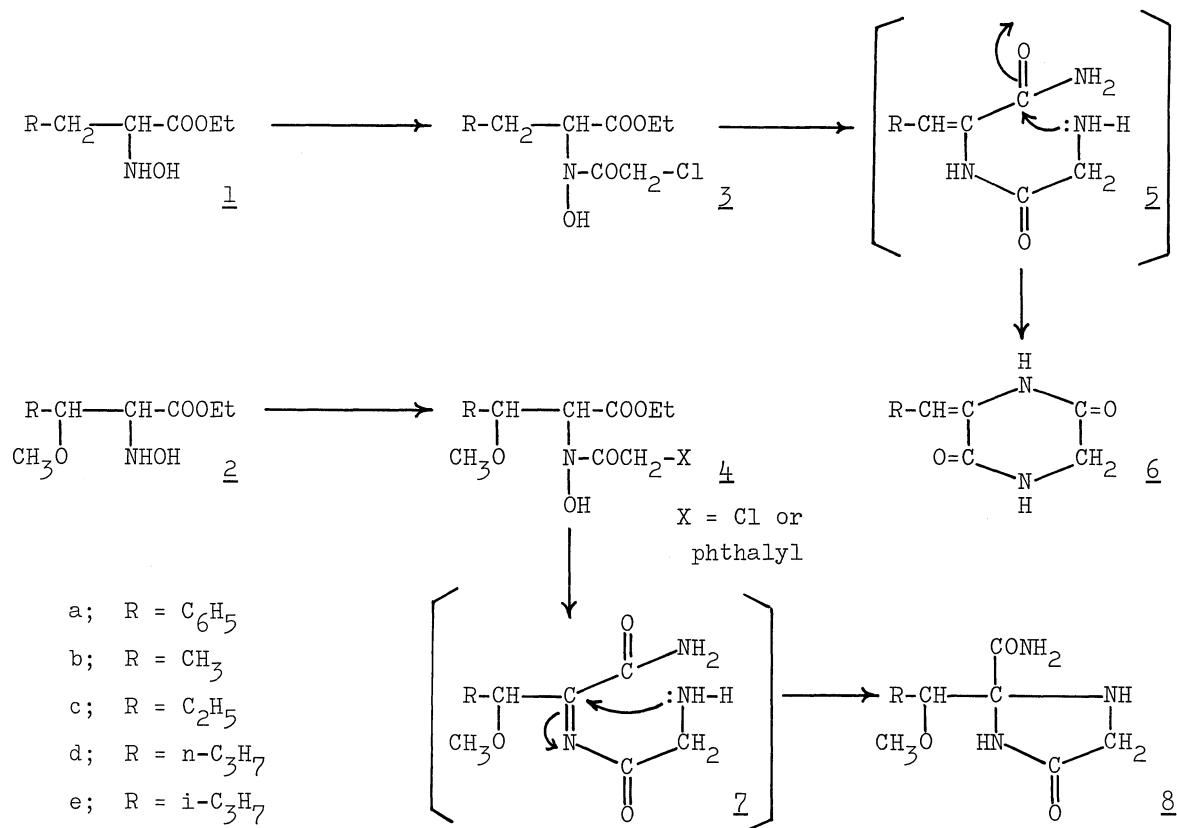
It has been well known that the treatment of N-haloacyl- $\alpha$ -hydroxyamino acid esters (3) with ammonia or hydroxylamine affords 1-hydroxy- or 1,4-dihydroxy-2,5-piperazinediones, respectively.<sup>1)</sup>

In this paper, we wish to communicate a new type of cyclization of  $\beta$ -methoxy derivatives of 3 into 2-carbamoyl-4-imidazolidone (8).

The reaction of  $\alpha$ -hydroxyamino acid ethyl ester (1) or their  $\beta$ -methoxy derivatives (2)<sup>2)</sup> with chloroacetyl chloride gave N-chloroacetyl- $\alpha$ -hydroxyamino acid ethyl ester (3) or its  $\beta$ -methoxy derivative (4), for example, 3a; yield 22.4%. mp 64-65°C. Nmr(in CDCl<sub>3</sub>,  $\delta$ ) 7.54s (-OH), 5.42t ( $\alpha$ -H), 3.22d ( $\beta$ -2H),  $J_{\alpha\beta}$  = 8.2Hz, 4a; yield 58.0%. mp 108-109°C. Nmr(in CDCl<sub>3</sub>,  $\delta$ ) 7.40s (-OH), 5.35t ( $\beta$ -H), 4.88d ( $\alpha$ -H),  $J_{\alpha\beta}$  = 6.2Hz, respectively, together with their O-acyl isomers, which were easily converted into 3 or 4 in the presence of base.

When an ethanol solution of 3a was saturated with ammonia and allowed to stand overnight at room temperature,  $\beta$ -benzylidene-2,5-piperazinedione [6a: yield 30.0%. mp 278-280°C(decomp.)]<sup>3,4)</sup> was obtained. Similar cyclization of 4 gave 2-carbamoyl-2-( $\alpha$ -methoxybenzyl)-4-imidazolidone [8: a; 194-195°C, b; 188-189°C, c; 185-187°C, d; 192-194°C, e; 181-182°C] in 23-51% yield, which was converted into the corresponding 1,3-diacyl derivatives by treatment with acetic anhydride at 130°C for 1 hr. This mode of cyclization was generally confirmed by use of  $\beta$ -methoxy- $\alpha$ -N-chloroacetyl- or phthaloylglycylhydroxyamino acid esters.<sup>2)</sup> All products were characterized by elementary and spectroscopic (Nmr and ir) analyses.

The cyclization reaction of 3 may proceed through an imino intermediate (7) formed by the dehydration of 4, while in the case of 2 the corresponding imino intermediate readily isomerizes to the tautomeric enamine (5)<sup>5,6)</sup> and then cyclizes to 6.



#### References

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