## A CONVENIENT METHOD FOR THE SYNTHESES OF 2(1H)-IMIDAZOLONE DERIVATIVES

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It was established that N-protected 2(lH)-imidazolone derivatives are conveniently prepared by the reaction of benzyl N-potassium-N-cyanocarbamate [Ia] or ethyl N-potassium-N-cyanocarbamate [Ib] with %-halo carbonyl compounds. N-Protecting group, benzyloxycarbonyl or ethoxycarbonyl group, was easily removed either by hydrogenation on Pd-C or alkaline hydrolysis to afford 2(lH)-imidazolone in good yields.

In the previous paper, a convenient method for the preparation of benzyl N-alkyl-N-cyanocarbamates by the reactions of benzyl N-potassium-N-cyanocarbamate with various alkyl halides has been reported. 1)

In the present study, it was found that 2(lH)-imidazolone derivatives are obtained in good yields by the treatment of benzyl N-potassium-N-cyanocarbamate [Ia] or ethyl N-potassimm-N-cyanocarbamate [Ib] with \(\alpha\)-halo carbonyl compounds. \(^{2a-c}\) For example, 4-acetyl-3-benzyloxycarbonyl-5-methyl-2(lH)-imidazolone and 4-acetyl-5-methyl-2(lH)-imidazolone were obtained in 64% and 18% yields, respectively, by treating benzyl N-potassium-N-cyanocarbamate with \(\alpha\)-chloroacetylacetone in boiling acetonitrile for 5 hr. Similarly, the reaction of benzyl N-potassium-N-cyanocarbamate with methyl \(\alpha\)-chloroacetoacetate afforded the corresponding 2(lH)-imidazolone derivative (see Table I). These reactions may involve the following three steps; namely, a nucleophilic displacement of benzyl N-potassium-N-cyanocarbamate with alkyl halide and the subsequent formation of 2-imino-4-oxazoline derivative through the intramolecular nucleophilic attack of the enol oxygen to the cyano group. The 2-imino-4-oxazoline is then transformed into the corresponding 2(lH)-imidazolone derivative via "Chapmann-type" rearrangement. \(^3\)

The following experimental results support this mechanism; namely 3-benzyl-oxycarbonyl-2-imino-5-phenyl-4-oxazoline [II] was isolated in 71% yield by the reaction of benzyl N-potassium-N-cyanocarbamate with phenacyl bromide in dimethyl-formamide at room temperature for 20 hr and [II] was transformed into 3-benzyloxy-carbonyl-5-phenyl-2(1H)-imidazolone by heating at 135~140°C or by treating with weak acid such as silica gel. On the other hand, benzyl N-phenacylcyanocarbamate [III] was obtained in quantitative yield when the same reaction was carried out in acetonitrile at room temperature for 4 hr.

$$C_{6}H_{5}CCH_{2}Br + KN(Z)CN$$

$$C_{6}H_{5}CCH_{2}N(Z)CN$$

$$C_{6}H_{5}CCH_{2}N(Z)CN$$

$$C_{6}H_{5}CCH_{2}N(Z)CN$$

$$C_{6}H_{5}CCH_{2}N(Z)CN$$

$$C_{6}H_{5}$$

It was also established that when benzyl N-acetonylcyanocarbamate was treated with hydrogen chloride in methanol at room temperature, 3-benzyloxycarbonyl-5-methyl-2(lH)-imidazolone was obtained in 76% yield. On the other hand, the above mentioned carbamate was not transformed into the corresponding 2(lH)-imidazolone derivative by heating or by the treatment with weak acid.

$$KN(\overset{\circ}{COR})CN + R^1\overset{\circ}{CCH}_2C1 \longrightarrow R^1\overset{\circ}{CCH}_2N(\overset{\circ}{COR})CN$$
[IV]

HC1 HN NCOR
[V]

Similarly, 5-acetylthiomethyl-3-benzyloxycarbonyl-2(lH)-imidazolone, 3-ethoxycarbonyl-5-methyl-2(lH)-imidazolone and 5-acetylthiomethyl-3-ethoxycarbonyl-2(lH)-imidazolone were obtained in good yields from the corresponding  $\alpha$ -chloro carbonyl compounds. These results are summarized in Table I.

Table I. Yields of 2(1H)-Imidazolone Derivatives

		Conditions	Products(%)
[Ia]	сн <sub>3</sub> соснс1сосн <sub>3</sub>	CH <sub>3</sub> CN reflux 5 hr	HN NZ HN NH C-CH <sub>3</sub> C-CH <sub>3</sub> C-CH <sub>3</sub> (64) (18)
[Ib]	сн <sub>3</sub> соснс1сосн <sub>3</sub>	CH <sub>3</sub> CN reflux 4 hr	HN NCOET  CH <sub>3</sub> C-CH <sub>3</sub> (67)
[Ia]	сн <sub>3</sub> соснс1со <sub>2</sub> сн <sub>3</sub>	CH <sub>3</sub> CN reflux 6 hr	HN NZ HN NH  CH <sub>3</sub> CO <sub>2</sub> CH <sub>3</sub> CH <sub>3</sub> CO <sub>2</sub> CH <sub>3</sub> (56) (10)
[Ia]	сн <sub>3</sub> сосн <sub>2</sub> с1	CH <sub>3</sub> CN reflux 6 hr then MeOH-HCl r.t. 4 hr	HN NZ CH <sub>3</sub> (61)
[Ib]	сн <sub>3</sub> сосн <sub>2</sub> с1	${ m CH_3CN}$ reflux 4.5 hr then ${ m C_6H_6}{ m -AcOH}{ m -AC_2O}{ m -HCl}$ r	HN NCOET  CH <sub>3</sub> (52)
[Ia]	о о сн <sub>3</sub> cscн <sub>2</sub> ccн <sub>2</sub> c1	CH <sub>3</sub> CN reflux 3 hr then C <sub>6</sub> H <sub>6</sub> -AcOH-AC <sub>2</sub> O-HCl	HN NZ CH <sub>2</sub> SAC (50)
[dl]	о о сн <sub>3</sub> ësсн <sub>2</sub> ëсн <sub>2</sub> с1	${ m CH_3CN}$ reflux 3 hr then ${ m C_6H_6-AcOH-AC_2O-HCl}$ r	HN NCO <sub>2</sub> Et

Further, it is noted that the benzyloxycarbonyl group of the 2(1H)-imidazolone was removed by catalytic hydrogenation on Pd-C or by the treatment with 30% HBr in acetic acid. The ethoxycarbonyl group of the 2(1H)-imidazolone was easily removed by alkaline hydrolysis; for example, 4-methyl-2(1H)-imidazolone was obtained in quantitative yield by the treatment of 3-ethoxycarbonyl-5-methyl-2(1H)-imidazolone with potassium hydroxide in methanol at room temperature for 1 hr. These results are summarized in Table II.

Table II.	Removal of	Benzyloxycarbony	1 or	Ethoxycarbonyl	Group
	1101110 1 42 02				OF C GP

	Conditions	Products	Yield(%)	mp.(°C)
	CONGILIONS		11610(0)	mp. ( C)
HN NZ	н <sub>2</sub> /Pd-С 95% EtOH	HN NH	quantitative	202-204
HN C-OCH <sub>3</sub>	H <sub>2</sub> /Pd-C 95% EtOH	HN C-OCH <sub>3</sub>	quantitative	200-201
HN NZ C-CH <sub>3</sub>	н <sub>2</sub> /Рd-С 95% ЕtОН	HN C-CH <sub>3</sub>	60	175-180 (dec.)
HN NZ CH <sub>2</sub> SAC	30% HBr-AcOH	HN NH CH <sub>2</sub> SAC	39	201-204 (dec.)
HN NCO <sub>2</sub> Et	KOH-MeOH r.t. l hr	HN NH	quantitative	202-204
HN NCO <sub>2</sub> Et  CH <sub>2</sub> SAC	NaOMe-MeOH r.t. 30 min	HN NH CH <sub>2</sub> SH		

<sup>\*</sup> By the reaction of this hydrolyzed product with benzyl bromide, 4-benzylthiomethyl-2(lH)-imidazolone was obtained in 87% yield.

## REFERENCES

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