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THE PREPARATION OF N-ALKYL AND N-ARYLGLYCINES FROM GLYOXYLIC ACID USING CARBONYLHYDRIDOFERRATE AS A REDUCING AGENT

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N-Substituted glycines were prepared from glyoxylic acid and a variety of primary amines using carbonylhydridoferrate(0).

Potassium tetracarbonylhydridoferrate(0) derived from iron pentacarbonyl and potassium hydroxide has been shown to be a useful reducing agent for a variety of organic functional groups.1) The ferrate, however, has little activity for the reduction of carbonyl groups. Although a reducing power of the ferrate is not strong, the ferrate appears to have a wide applicability as a selective reductant. Recent papers have demonstrated that the ferrate is active for the reductive alkylation of amines under mild conditions.2) In this communication, we wish to report a convenient method for synthesis of N-alkyl and N-arylglycines from glyoxylic acid and primary amines using carbonylferrates. Glycine is industrially prepared from chloroacetic acid and ammonia3) but few successful attempt to prepare glycine derivatives by the reductive amination of glyoxylic acid has been done.4)

In the general procedure, to a mixture of iron pentacarbonyl(11 mmol) and alcoholic 1N-potassium hydroxide(33-44 mmol) were added an amine(11-22 mmol), glyoxylic acid(11 mmol), and ethanol(20-30 ml) and the mixture was stirred for 24 hr at room temperature under carbon monoxide. The reaction proceeded smoothly with an absorption of carbon monoxide. White precipitates produced in the reaction were separated by filtration, washed with ethanol and ether, acidified with hydrochloric acid, and extracted with ethanol. An extract gave a residue including salts of N-substituted glycines, $RNHCH_2COOH\cdot HCl$, after evaporating the solvent. After recrysatallization from alcohol/acetone, products were analyzed by means of ir and nmr spectra, m.p., and chemical analyses.

TABLE. PREPARATION OF N-ALKYL AND N-ARYLGLYCINES FROM GLYOXYLIC ACID[a)]

Exp. No.	Amine	Product ($RNHCH_2COOH \cdot HCl$)	Yield %
1	Ammonium Hydroxide	R: H	40
2	Methylamine	Methyl	49
3	n-Butylamine	n-Butyl	34
4	n-Hexylamine	n-Hexyl	38
5	Cyclohexylamine	Cyclohexyl	46
6	Benzylamine	Benzyl	82
7	Aniline	Phenyl	75
8	p-Toluidine	p-Tolyl	55
9	p-Anisidine	p-Methoxyphenyl	65
10	p-Chloroaniline	p-Chlorophenyl	35
11	β-Naphthylamine	β-Naphthyl	50

a) At room temperature for 24 hr. Carbon monoxide absorbed, 0.4-0.8 mol/mol-ferrate.

Some representative results are listed in Table. Both aliphatic and aromatic primary amines gave the corresponding N-alkyl and N-arylglycines in fairly good to excellent yields. Ammonium hydroxide also gave glycine. The reaction seems to include the reduction of a carbon-nitrogen double bond, $RN{=}CHCOO^-$, with the ferrate: the more reactive C=N bond is selectively reduced and the carboxyl group remains unchanged. The result may indicate that the ferrate acts as a selective reducing agent in this reaction. This procedure may afford a simple and convenient method for synthesis of N-substituted glycines using a variety of primary amines, especially in laboratory scale. Further study on synthesis of amino acids by the reductive amination of α-keto acids using carbonylhydridoferrates is in progress.

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