

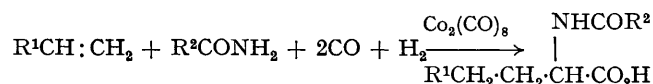
## Synthesis of *N*-Acyl Amino-acids by a Carbonylation Reaction

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**Summary** A novel cobalt carbonyl-catalysed reaction gives an *N*-acyl amino-acid from an aldehyde, an amide, and carbon monoxide.

In the course of our studies on the hydroformylation of  $\alpha\beta$ -unsaturated nitriles, a novel cobalt carbonyl catalyzed reaction has been found to give *N*-acyl- $\alpha$ -amino-acids by carbonylation.



The scope of the reaction is wide, giving various *N*-acyl- $\alpha$ -amino-acids.

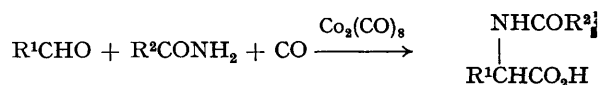
In the case of the synthesis of *N*-acetylalanine, the ratio of  $\alpha$ - to  $\beta$ -alanine, after hydrolysis, is 550:1.

TABLE  
Reaction Conditions

Aldehyde (50 mmol)	Amide (50 mmol)	Solv.	Temp.	Time (min.)	Products	(mmol)
Formaldehyde	Acetamide	Dioxan	110°	15	<i>N</i> -Acetyl glycine	13
Acetaldehyde	Acetamide	EtOAc	115°	10	<i>N</i> -Acetylalanine	34
Propionaldehyde	Acetamide	AcOH	150°	60	<i>N</i> -Acetyl- $\alpha$ -amino-n-butyric acid	23
Isobutyraldehyde	Acetamide	Dioxan	120°	60	<i>N</i> -Acetylvaline	35
Phenylacetaldehyde	Acetamide	Dioxan	140°	70	<i>N</i> -Acetylphenylalanine	27
$\beta$ -Formylpropionitrile	Acetamide	Dioxan	120°	80	<i>N</i> -Acetyl- $\gamma$ -cyano- $\alpha$ -amino-n-butyric acid	29
Methyl $\beta$ -formylpropionate	Acetamide	EtOAc	120°	25	<i>N</i> -Acetyl- $\gamma$ -methylglutamate	35
$\beta$ -Methylmercaptopropionaldehyde	Acetamide	EtOAc	120°	20	<i>N</i> -Acetylmethionine	32
Acetaldehyde	Benzamide	Dioxan	120°	95	<i>N</i> -Benzoylalanine	15
Acetaldehyde	Lauramide	EtOAc	120°	15	<i>N</i> -Lauroylalanine	40
$\beta$ -Formylpropionitrile	Lauramide	Dioxan	120°	20	<i>N</i> -Lauroyl- $\gamma$ -cyano- $\alpha$ -amino-n-butyric acid	34
Acetaldehyde	<i>N</i> -Ethylacetamide	Dioxan	130°	70	<i>N</i> -Acetyl- <i>N</i> -ethylalanine	29

A 100 ml capacity autoclave and 50 ml of the specified solvent were used.

Catalyst:  $Co_2(CO)_8$ , 300 mg. Initial gas pressure: CO 150 kg/cm<sup>2</sup>, H<sub>2</sub> 50 kg/cm<sup>2</sup>



The reaction proceeds under exactly the same conditions as used for the hydroformylation reaction. Thus it can be advantageously coupled with an oxo process.

Benzaldehyde and acetamide give *N*-acetylbenzylamine under these reaction conditions. Furfural and acetaldehyde also give anomalous results.

With a stoichiometric amount of dicobalt octacarbonyl, the reaction proceeds under atmospheric pressure and at room temperature.

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