Tetrahedron Letters,Vol.23,No.24,pp 2491-2494,1982 0040-4039/82/242491-04$03.00/0
Printed in Great Britain

DIRECT CONVERSION OF ALLYLIC ALCOHOLS INTO N-ACYL-α-AMINO ACIDS BY CATALYTIC AMIDOCARBONYLATION BY MEANS OF HOMOGENEOUS BINARY SYSTEMS

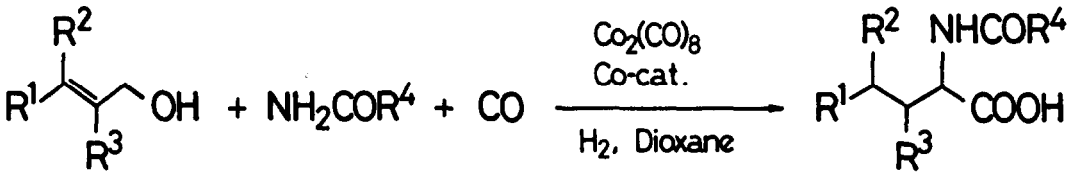
Kenji HIRAI, Yoshitaka TAKAHASHI, and Iwao OJIMA*
Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa 229 (Japan)

Summary: N-Acyl-α-amino acids are synthesized by the amidocarbonylation of allylic alcohols catalyzed by homogeneous binary systems which consist of cobalt carbonyl and rhodium (or iron or palladium) complexes.

Transition metal carbonyl catalyzed carbonylation of olefins, halides, and alcohols have been extensively studied for a long time because of their importance both as laboratory methods and as industrial processes[1]. One of the most interesting reaction using carbon monoxide is the cobalt-catalyzed amidocarbonylation of aldehydes which leads to the formation of N-acyl-α-amino acids. This reaction was first reported by Wakamatsu in 1971[2] and reinvestigated precisely by Pino in 1979[3] with regard to the synthetic potentiality and the reaction mechanism. On the other hand, the isomerization of allylic alcohols to the corresponding aldehydes or ketones has been shown to proceed by the catalysis of Group VIII metal complexes.[4] Thus, if the isomerization of allylic alcohols to the corresponding aldehydes is effectively combined with the amidocarbonylation, we could obtain N-acyl-α-amino acids directly from allylic alcohols. In fact, this combination has been done successfully. Now, we wish to describe here a new and convenient route to N-acyl-α-amino acids from allylic alcohols by combining transition metal catalyzed isomerization and cobalt catalyzed amidocarbonylation.

The amidocarbonylation of allylic alcohols (1) was carried out with amide (2), carbon monoxide catalyzed by dicobalt octacarbonyl and co-catalyst to give

N-acyl-α-amino acids (3) in good yields. It was found that under the present reaction conditions, hydroformylation and hydrogenation of the allylic alcohols (1) were depressed and isomerization followed by subsequent amidocarbonylation occurred predominantly leading to the formation of N-acyl-α-amino acids (3).



1 2 3

Typically, the reaction of crotyl alcohol (1b) with acetamide and carbon monoxide was carried out as follows. In a 100 ml stainless steel autoclave, a mixture of crotyl alcohol (50 mmol) and acetamide (100 mmol) in dioxane (50 ml) was placed, and dicobalt octacarbonyl, $Co_2(CO)_8$, (1.7 mmol) and carbonylhydridotris(triphenylphosphine)rhodium, $HRh(CO)(PPh_3)_3$, (0.17 mmol) were added. Then, a 1:1 mixture of carbon monoxide and hydrogen was introduced to the autoclave (initial pressure: 100 atm at ambient temperature). The autoclave was heated up to 110°C, at which temperature the pressure was 110 atm, the mixture was stirred for 17 hours at the same temperature (usually the pressure decreased to about 80 atm), and then the autoclave was cooled to ambient temperature and depressurized. After the solvent was removed under reduced pressure, the reaction mixture was treated with 10% aqueous sodium carbonate and extracted with ethyl acetate to remove unreacted acetamide and other side product(s). The aqueous solution was then acidified with phosphoric acid, extracted with ethyl acetate, and the solvent was removed in vacuo to afford 5.60 g of N-acetylnorvaline (3b) as colorless solid (70% yield based on 1b).

Similarly, the amidocarbonylation of allyl alcohol (1a), and prenyl alcohol (1c) were performed to give the corresponding N-acylhomoalanine (3a), and N-acylleucine (3c), respectively, in satisfactory yields. Results are summarized in Table 1. As Table 1 shows, the reaction proceeds to some extent without the cocatalyst for promoting the isomerization (Entry 13) since $HCo(CO)_4$ which should be generated under the reaction conditions, can act as an isomerization-catalyst

Table 1. Synthesis of N-Acyl-α-amino Acids by the Amidocarbonylation of Allylic Alcohols[a]

Entry	N-Acyl-α-amino Acid	R^1	R^2	R^3	R^4	$Co_2(CO)_8$ (mol%)	co-catalyst	(mol%)	1/2	Solvent	CO/H_2[b] (atm/atm)	Time (h)	Isolated Yield(%)
1	3a	H	H	H	Me	2.0	$HRh(CO)(PPh_3)_3$	0.10	1/2	Dioxane	50/50	12	63
2						5.0	$Fe_2(CO)_9$	5.00	1/1	Dioxane	50/50	24	58
3						3.3	$RuCl_2(PPh_3)_3$	0.33	1/1	Dioxane	50/50	12	44
4	3a'	H	H	H	Ph	3.3	$RhCl(PPh_3)_3$	0.33	1/1	Dioxane	50/50	12	60
5	3b	Me	H	H	Me	3.3	$Fe_2(CO)_9$	6.60	1/1	Dioxane	50/50	18	75
6						1.7	$HRh(CO)(PPh_3)_3$	0.17	1/1	Dioxane	50/50	18	70
7						1.7	$HRh(CO)(PPh_3)_3$	0.17	1/1	AcOEt	50/50	18	49
8						1.7	$HRh(CO)(PPh_3)_3$	0.17	1/1	Benzene	50/50	18	34
9						1.7	$HRh(CO)(PPh_3)_3$	0.17	1/1	THF	50/50	18	48
10						1.7	$HRh(CO)(PPh_3)_3$	0.17	1/1	Acetone	50/50	18	34
11						3.3	$PdCl_2(PPh_3)_2$	0.33	1/1	Dioxane	50/50	18	77
12						3.3	$HRuCl(CO)(PPh_3)_3$	0.33	1/1	Dioxane	50/50	18	41
13						3.3	-----		1/1	Dioxane	50/50	18	46
14	3b'	Me	H	H	Ph	1.7	$HRh(CO)(PPh_3)_3$	0.17	1/2	Dioxane	50/50	18	36
15	3c	Me	Me	H	Me	1.7	$HRh(CO)(PPh_3)_3$	0.20	1/1	Dioxane	50/50	12	62
16	3c'	Me	Me	H	Ph	2.0	$HRh(CO)(PPh_3)_3$	0.20	1/2	Dioxane	50/50	12	66

a All the reactions were run with 30-50 mmol of allylic alcohol (1) and 30-100 mmol of amide (2) in 50-100 ml of solvent at 110°C. *b* Initial pressure at 25°C.

as well as the catalyst for amidocarbonylation. But it is apparent that the addition of $HRh(CO)(PPh_3)_3$, $Fe_2(CO)_9$ or $PdCl_2(PPh_3)_2$ significantly accelerates the reaction. Other co-catalysts such as $RuCl_2(PPh_3)_2$ and $HRuCl(PPh_3)_3$ did not bring about good results. As for the solvent, dioxane turned out to be the best as far as we examined (Entry 6-10). The amidocarbonylation seems to be sensitive to the steric bulkiness of the aldehyde generated in situ. Thus, the reaction of methallyl alcohol with acetamide in dioxane gave N-acetylvaline in rather low yield (25-35%) often together with an unidentified side product (0-39%). It is noteworthy that prenyl alcohol, which is known to be very difficult to isomerize to 3-methylbutanol,[6] reacts nicely to give N-acylleucine in good yield. The result clearly indicates that the aldehyde generated in situ by the isomerization of the allylic alcohol is immediately involved into the successive fast amidocarbonylation to yield N-acyl-α-amino acid.

Homoallyl alcohols, 3-buten-1-ol (4a) and 3-methyl-3-buten-1-ol (4b), were also employed as substrate under similar conditions to give the corresponding N-acylnorvaline (55%) and N-acylleucine (34%), respectively, in moderate yields.

In conclusion, the amidocarbonylation of allylic alcohols promoted by homogeneous binary catalyst systems provides a new and convenient route to N-acyl-α-amino acids. Further application of the catalyst systems is under active investigation.

REFERENCES AND NOTES

1. (a) I. Wender and P. Pino, in "Organic Syntheses via Metal Carbonyls," Vol. 2, Wiley-Interscience, New York, 1977. (b) J. Falbe, "New Syntheses with Carbon Monoxide," Springer-Verlag, Berlin, 1980.
2. H. Wakamatsu, J. Uda, and N. Yamakami, J.C.S. Chem. Commun., 1540 (1971). H. Wakamatsu, Sekiyu Gakkai Shi, 17, 105 (1974).
3. J.-J. Parnaud, G. Campari, and P. Pino, J. Mol. Catal., 6, 341 (1979).
4. e.g., W. T. Hendrix, F. G. Cowherd, and J. L. von Rosenberg, J.C.S. Chem. Commun., 97 (1968); F. G. Cowherd and J. L. von Rosenberg, J. Am. Chem. Soc., 91, 2157 (1969); A. Bright, J. F. Malone, J. K. Nicholson, J. Powell, and B. L. Show, J.C.S. Chem. Commun., 712 (1971); Y. Sasson and G. L. Rempel, Tetrahedron Lett., 4133 (1974); W. Strohmeier and L. Weigelt, J. Organomet. Chem., , 86, C17 (1975); C. F. Lochow and R. G. Miller, J. Org. Chem., 41, 3020 (1976).
5. Satisfactory microanalyses were obtained for all products, and physical properties and the spectral data confirmed the structures of the products.
6. D. Baudry, M. Ephritikhine, and H. Felkin, Nouv. J. Chim., 2, 355 (1978).

(Received in Japan 12 March 1982)