CYCLIZATION OF α -HALOAMIDE WITH INTERNAL DOUBLE BOND BY USE OF THE LOW-VALENT METAL COMPLEX

Miwako Mori, Izumi Oda and Yoshio Ban* (Faculty of pharmaceutical Sciences, Hokkaido University, Sapporo 060 Japan)

Summary ——— The α -haloamide having internal double bond was allowed to react with a catalytic amount of Pd(PPh₂)₄ in the presence of proton sponge to produce a cyclized product in a fairly good yield possibly through the intermediation of σ -alkylmetal complex although it was not isolated.

Aryl or vinylmetal complexes which are formed by oxidative addition of aryl or vinyl halide to the low valent metal complexes are the useful intermediates for organic syntheses. However, in general, the alkyl halides were assumed not to afford the alkylmetal complexes of the transition metals because of the instability of the compounds due to their easy decomposition to olefins when they possessed β -hydrogen with respect to the metals.

$$\operatorname{RCH}_{2}\operatorname{CH}_{2} X \xrightarrow{\operatorname{M}^{\circ}\operatorname{Ln}} \left(\begin{array}{c} H_{2}^{H_{2}} \\ \operatorname{RCH}^{-}\operatorname{CH}_{2}^{-}\operatorname{M} X \operatorname{Lm} \end{array} \right) \xrightarrow{} \operatorname{RCH}=\operatorname{CH}_{2} + \operatorname{HM} X \operatorname{Lm}$$

It was anticipated that the reaction of α -halo-carbonylated compound with the low-valent metal complex¹ would afford a fairly stable σ -alkylmetal complex 2. We report here the successful results of the cyclization reaction of α -haloamide having internal double bond² with the low-valent metal complex. The general reaction scheme was shown as follows.



N-Benzyl-N-allyl- α - iodoacetamide(la) was warmed with an equimolar amount of Pd(PPh₃)₄ in dimethylformamide(DMF) at 65° for 5.5 h to afford N-benzyl-3methylene-2-pyrrolidone(4a) and N-benzyl-3-iodomethyl-2-pyrrolidone(5a) in the yield of 14% and 23 %, respectively. The former compound was an expected product possibly through the intermediation of σ -alkylmetal complex 2 and the latter one 5a was considered to be the reductive elimination product from 3.



Compound lb was also treated in the same manner to afford the desired cyclized product, 4b, 8 and 5b. To confirm these structures, compound 4b or 8 was hydrogenated with PtO, under an atmosphere of hydrogen to afford N-benzy1-3ethyl-2-pyrrolidone(9). Compound 5b was reduced with $NaBH_A$ in the presence of $n-Bu_4NBr$ in toluene^{3°} to afford the same product 9. This reaction was carried out under the various conditions in order to survey the reaction course(Table 1). In some cases, migration of the double bond or reduction of α -haloacetamide group of the starting material occurred to produce the compound 6 or N-acetyl derivative 7. As for the solvent, acetonitrile or toluene gave the same result, but the yield was rather low. There occurred no reaction in the absence of Pd(PPh3)4, but in the presence of an equimolar amount of Ni(PPh3)4, 4a was obtained in the yield of 10 %. The reaction proceeded catalytically with $Pd(PPh_3)_4$, namely, when 5 mol % of $Pd(PPh_3)_4$ was used in this reaction, the expected cyclized product 5a was obtained in the yield of 18 %, and 10 mol % of the same catalyst gave 25 % yield of 5a. A catalytic amount of Pd(OAc) 2-PPh3 gave a small amount of the desired product but the divalent palladium complex [Pd(acac)] without ligand did not afford the desired product. To avoid the formation of the phosphonium salt of the starting material, tri-o-tolylphosphine was used instead of PPh3, but the cyclized product was not obtained. These results suggest that this reaction proceeded via alkylpalladium complex 2 formed from 1 with the low-valent metal complex. On the other hand, N-ally1-N-benzy1-2-bromoacetamide was treated in the same manner to afford only a

Run	Starting Material	Catalyst(mol eq.)	Solvent	Yield of the Cycilzed Product	1 4 ~	Rat	5 2) (:	of 6(or	1 8) 7 ~	Reco	over	У
1	la	Pd(PPh3)4	(1.00)	DMF	37 %	1	:	1.	6		-		-	
2	ĩp	Pd(PPh3)4	(1.00)	DMF	37	1.3	3:]	.4	:	1	-		-	
3	la ~~	Pd (PPh3)4	(1.00)	сн _з си	28	2	:	11	.:	1	17	8	-	
4	lb	Pd(PPh3)4	(1.00)	toluene	30			9	:	1	7		-	
5	la	PPh ₃	(0.25)	DMF	0						7		58	¥
6	la	Ni(PPh3)4	(1.00)	DMF	10	1	:	0	:	0	-		-	
7	la	$Pd(PPh_3)_4$	(0.05)	DMF	18	0	:	1	:	0	15		26	
8	la	Pd(PPh3)4	(0.10)	DMF	25	0	:	1	:	0	27		-	
9	1b	$Pd(PPh_3)_4$	(0.10)	DMF	35	1	:	4			16		-	
10	la	Pd(acac) ₂	(0.05)	DMF	0						-		71	
11	la ~~	Pd(OAc) ₂ -PPh ₃	(0.05) (0.20)	DMF	4	0	:	1	:	0	21		53	
12	la ~~	Pd(OAc) -(o-tolyl)3	(0.05) (0.20)	DMF	0						29		61	
13	la ~~	Pd(PPh3)4 Proton Spon	(0.10) ge(1.20)	DMF	48			2	:	1	-		-	
14	lb ~~	Pd (PPh 3) 4 Proton Spon	(0.10) ge(1.20)	DMF	45	0	:	1	:	0	-		-	

Table 1 Reaction of the compound 1 with palladium complex under various conditions

The reaction mixture was stirred under an atmosphere of argon at room temperature for 30 min. and then warmed at $60-65^\circ$ for 6 h.

small amount of the desired compound 4a(6%) and 6(2%). To regenerate the zerovalent metal complex from hydride metal complex, the base such as NEt₃ or n-Bu₃N was required. Since such bases should afford the ammonium salts of the starting material, the reaction was carried out in the presence of bis(1,8-dimethylamino)-naphthalene(proton sponge) as the base to afford the desired cyclized product in a fairly good yield. Compound lb was also treated in the same manner in the presence of proton sponge to afford 5b in 44.8 % yiled.

Moreover, compound 1c which was prepared by condensation of 1-bromo-2-cyclohexene with benzylamine followed by treatment with chloroacetyl chloride and then potassium iodide, was treated with $Pd(PPh_3)_4$ in DMF at 65° in the presence of

proton sponge to afford 4c and 5c in the yield of 26.2 % and 19.9 %, respectively, along with 7c. To confirm these structures, compound 5c was converted to 4c with treatment of 1,8-diazabicyclo-[5,4,0]-7-undecene(DBU)⁴ in DMSO in the yield of 74 %. Compound 4c was treated with 5 % Pd-C in cymene⁵ under an atmosphere of argon to produce N-benzyl oxindole(10) and N-benzylhexahydro-oxindole(11) in the yield of 32.6 % and 40.6 %, respectively.



These results suggest that β -oxo-alkylpalladium complexes¹ can be obtained from α -halo-carbonylated compounds with low-valent metal complexes and these complexes are useful intermediate for organic syntheses.

Further studies are in progress.

References and Notes

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- 7. Recently, Ito, et al. reported the Pd(II)-promoted cyclization and its intermediate was assumed to be σ-alkylpalladium complex 14 via oxo-π-allyl palladium complex 13 formed from silyl enol ether 12 with Pd(II)Cl₂(PhCN)₂.

