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REACTION OF α-HALOESTER HAVING INTERNAL DOUBLE BOND WITH THE LOW-VALENT METAL COMPLEX

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Abstract———The α-haloester having an internal double bond was allowed to react with a catalytic amount of $Pd(PPh_3)_4$ to afford a cyclized product in a fairly good yield and the same product was obtained by treatment with $Pd(OAc)_2$ to ketene silyl acetal.

In general, the aryl or vinyl halide can oxidatively add to the low-valent metal complex to afford the aryl or vinylmetal complex, while an alkyl halide can not afford such an alkylmetal complex.[1] On the other hand, the cyclization of α-haloamide with internal double bond in the presence of $Pd(PPh_3)_4$ has been already reported from this laboratory.[2] These results stimulated our interest in this type of reaction and attention has been focussed to a reaction of α-haloester[3] with the low-valent metal complex, since it may be assumed that the alkyl halide possessing sp_2-carbon at the α-position of halogenated carbon could afford an σ-alkylmetal complex 3 (Chart 1).

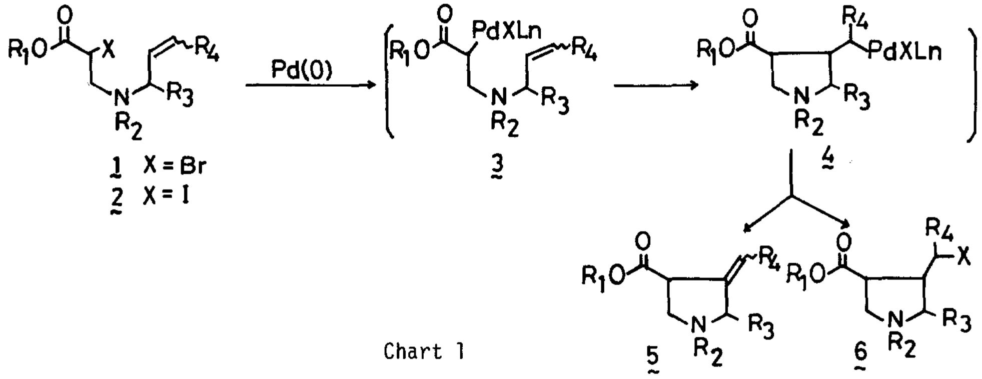
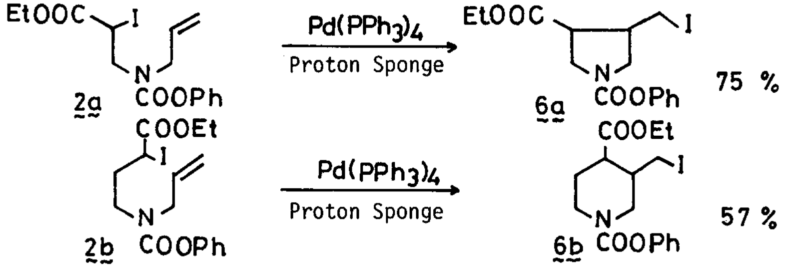
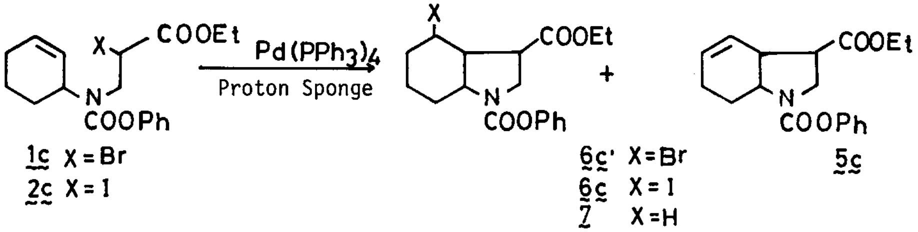


Chart 1

The idea was substantially realized, which reactions of 1 and 2 smoothly proceeded to afford the haloalkyl derivatives 6 as main products, along with the olefinic compounds 5, as a result to have effected the intramolecular addition reaction of the carbon-halogen bond of α-haloester to an olefinic linkage in the presence of $Pd(PPh_3)_4$.

The initial α-haloesters 1 and 2 having internal double bond as the substrates were prepared from amino acids.[4,5] Compound 2a was treated with a catalytic amount of $Pd(PPh_3)_4$(10 mol %) in the presence of 1,8-dimethylaminonaphthalene(proton sponge) in HMPA under an atmosphere of argon at 65°. The reaction was completed in 15 min to give the iodo-compound as the sole product [6a, 75 % yield, MASS m/e 403(M^+)]. Similarly, compound 2b gave a piperidine derivative 6b[MASS m/e 417(M^+)] in a yield of 57 %. The cyclohexenyl derivative 1c was treated in the same manner to give the indoline derivative 6c' in the yield of 65 % along with 5c and 7(6 % yield), but the α-iodoester 2c gave 6c and 5c in the yield of 30 % and 34 %, respectively. Though the starting material disappeared after 4 hr on the reaction of 1c, only 15 min was enough for the completion of the cyclization of 2c. An octahydroquinoline derivative 5d was obtained from 2d in a similar manner in good yield. In this reaction, α-bromoester 1d gave the desired compound 6d' in the yield of only 18 %. These results suggest that the reactivity of





Substrate	X	6c or 6c'	5c	7
1c	Br	65 %		6 %
2c	I	30	34 %	

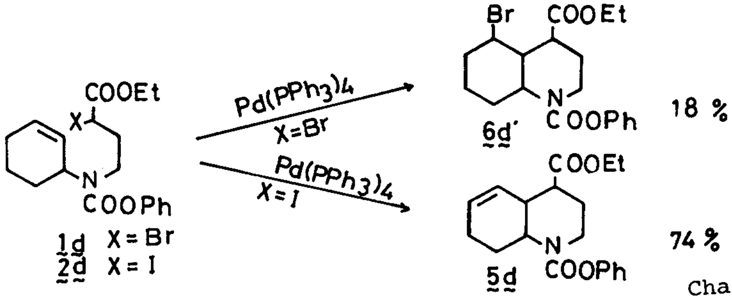


Chart 2

α-iodoesters **2** is much superior to that of the α-bromoesters **1**. Steric repulsion between an ethoxycarbonyl group and a large palladium iodide group may contribute to the formation of the dehydrohalogenation products **5c** and **5d**. Though the iodo-compound **6** should be obtained by reductive elimination of alkyl halide from **4**, the reason why the unusual and interesting result was obtained has not been clear yet. The intermediate of this reaction was considered to be an σ-alkylmetal complex **3** derived from α-haloester **1** or **2**, which was reacted with internal double bond to produce the cyclized products **5** and 6(Chart 1).

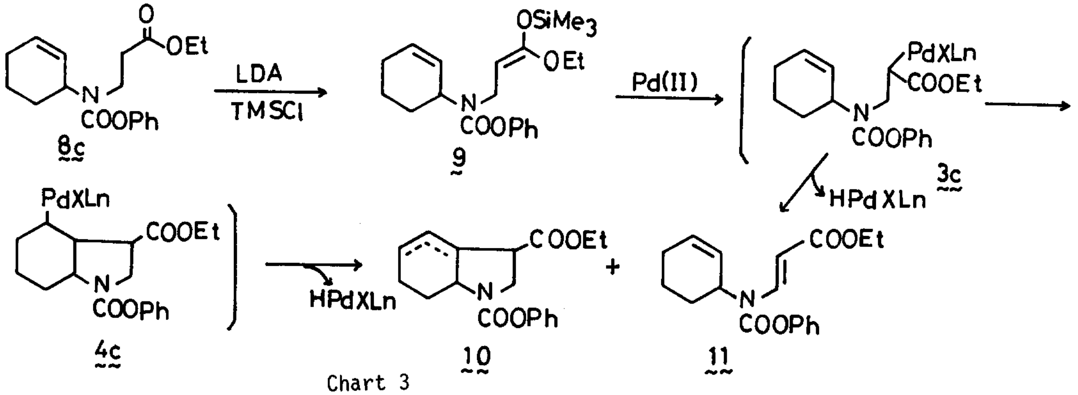


Chart 3

Furthermore, it was assumed that the same intermediate **3** should be formed from ketene silyl acetal and Pd(II).^{6} Thus, compound **8c**(0.63 mmol) was allowed to react with lithium diisopropylamide(LDA)(0.63 mmol) followed by treatment with trimethyl silyl chloride(TMSCl)(1.26 mmol) in THF^7 to give the ketene silyl acetal **9**. After evaporation of the solvent and diisopropylamine, $Pd(OAc)_2$(0.63 mmol) was added to the residue dissolved in acetonitrile(3.5 ml) and then a solution was stirred at room temperature overnight. The desired cyclized product **10** was obtained though a yield was rather low(17 % yield). The dehydrohalogenation product **11**(40 % yield) should be obtained by elimination of HPdXLm from **3c**. The other divalent palladium complexes such as $PdCl_2(CH_3CN)_2$ and $PdCl_2(PhCN)_2$ do not give the good results and no reaction occurs in the absence of TMSCl. It was very interesting that the low-valent metal complex[$Pd(PPh_3)_4$] could be reacted with α-haloester to produce σ-alkylmetal complex, while the same σ-alkylmetal complex could be formed from ketene silyl acetal and the divalent metal complex[$Pd(OAc)_2$].

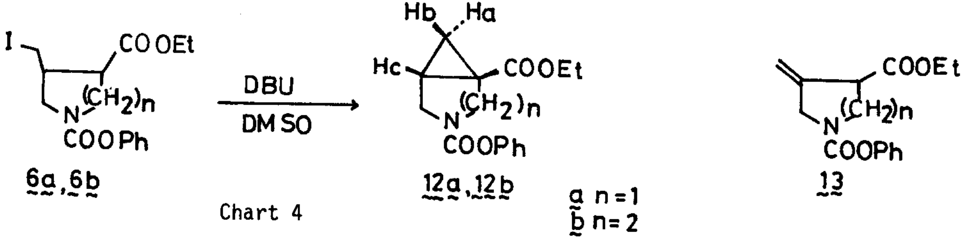


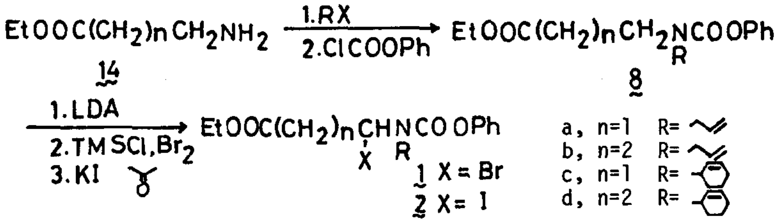
Chart 4

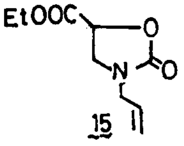
To confirm the structure of the five membered ring, dehydrohalogenation of 6 was carried out by use of 1,8-diazabicyclo[5.4.0]undecene-7(DBU). When compound 6a was warmed in DMSO at 90° for 2 days in the presence of DBU, 1-ethoxycarbonyl-3-phenoxycarbonyl-3-azabicyclo[3.1.0]hexane(12a)[NMR δ ($CDCl_3$) 0.95(dd, 1 H, J= 4.9 Hz, 5.4 Hz, Ha), 1.67(dd, 1 H, J=4.9 Hz, 8.3 Hz, Hb), 2.14(ddd, 1 H, J=8.3, 5.4, 4.2 Hz, Hc); MASS, m/e 275(M^+)] was obtained in 66 % yield instead of the elimination product 13. Similarly, compound 6b was treated in the same manner, the three membered compound 12b was obtained in a yield of 67 %. These results were very interesting because of the easy formation of the three membered ring under mild conditions.

The intramolecular addition reaction of α-haloester to olefin was very useful synthetic method for the heterocyclic compounds and an application of these reactions are now being studied.

REFERENCES AND NOTES

1. For the alkyl halides, methyl, benzyl and allyl halides can oxidatively add to the low-valent metal complex to produce σ-alkylmetal complexes. P. Fitton, M. P. Johnson and J. E. Mckepn, J. C. S. Chem. Comm., 1968, 6. G. Pearson and P. E. Figdore, J. Am. Chem. Soc., 102, 1541 (1980).
2. M. Mori, I. Oda and Y. Ban., Tetrahedron Lett., 23, 5315 (1982).
3. It was already known that the condensation of the carbonyl compound with organozinc derivative of α-haloester yielded β-hydroxyester. Reformatskii, Ber., 20, 1210 (1887). R. L. Shriner, Organic Reactions, 1, (1942). M. W. Rathke, Organic Reactions, 22, 423 (1975).
4. Though it was not so easy to get the α-haloesters having amino group, they could be obtained by the following method. Haloganation of the ester 8 was effected smoothly via ketene silyl acetal followed by reaction with bromine. α-Iodoester 2 was prepared from α-bromoester 1 by treatment with potassium iodide in acetone.





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5. For the protection of the amino group, phenoxycarbonyl group was chosen because of the easy formation of oxazolidone derivative 15 by treatment with KI to compound 1 protected with carbomethoxy group instead of carbophenoxy group.
6. Recently, Saegusa and Ito have reported the interesting results of the reaction of silyl enol ether with $PdCl_2(PhCN)_2$. They claimed that the intermediate of that reaction was assumed to be σ-alkylmetal complex via oxo-π-allyl palladium complex formed from silyl enol ether with Pd(II). Y. Ito, H. Aoyama and T. Saegusa, J. Am. Chem. Soc., 102, 4521 (1980).
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