HETEROCYCLES, Vol 12, No 7, 1979

THE SYNTHESIS OF BENZOLACTONES BY PALLADIUM CATALYZED CARBONYLATION[**]

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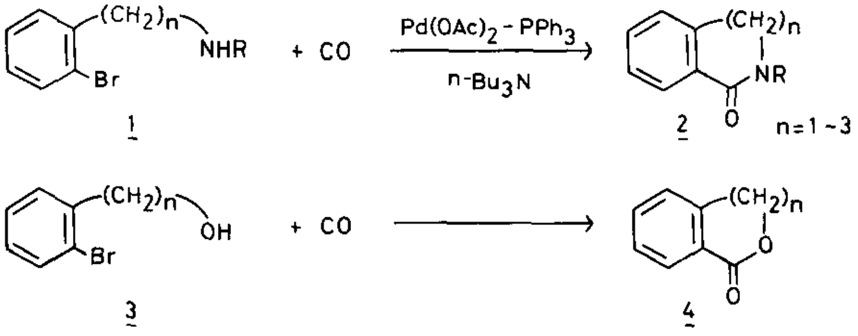
Phthalide was easily prepared from o-bromobenzyl alcohol in the presence of a catalytic amount of $Pd(OAc)_2$ and PPh_3 under an atmospheric pressure of carbon monoxide in a good yield. When a large amount of PPh_3 was used as a ligand, a better result was obtained. The six- and seven-membered benzolactones were synthesized by the same procedure.

We have recently reported the new synthesis of benzolactams(2) by palladium catalyzed carbonylation by a very simple procedure,[1] which has been extended to the total synthesis of the alkaloid, sendaverine.[2] It might be readily assumed that a similar treatment of o-bromo-ω-hydroxyalkylbenzene(3) would afford benzolactones(4).



In the present paper, we describe a simple procedure of the synthetic method of benzolactones(4) by use of this palladium catalyzed carbonylation.

[**] This paper is dedicated to Professor Emeritus Tetsuo Nozoe on the occasion of his 77th birthday.

The typical procedure is demonstrated in the following: A whole mixture of o-bromobenzyl alcohol(3a, 1 eq.), a catalytic amount of $Pd(OAc)_2$(2 mol%), PPh_3 (4 mol%) and $n-Bu_3N$(3a, 1 eq.) was added to the reaction vessel connected to a balloon filled with a carbon monoxide and heated at 100° for 26 h to give the expected phthalide(4a, 19.6%, mp 73.5-75°) and o-carboxybenzyl alcohol(5, 4.9%). However, the yield was lower than that of the synthesis of five-membered benzolactam (2, n=1, $R=CH_2Ph$). Therefore, this reaction was surveyed under the various conditions(Table 1). It was turned out that the addition of a large amount of PPh_3 to the reaction mixture provided a good result and a higher temperature also increased the yield of the desired product(4a, 81.9%).

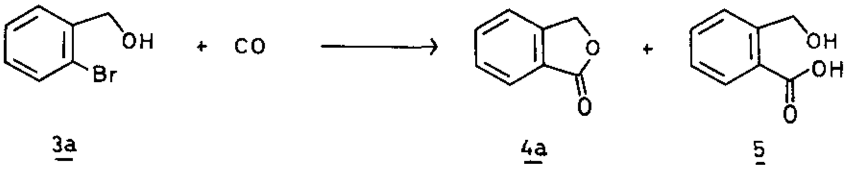
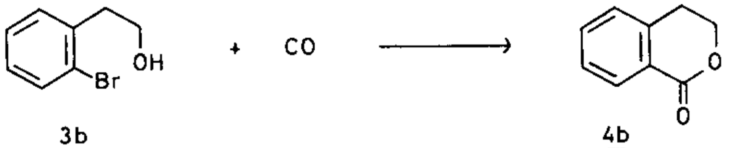


Table 1. Carbonylation of 3a under the various conditions

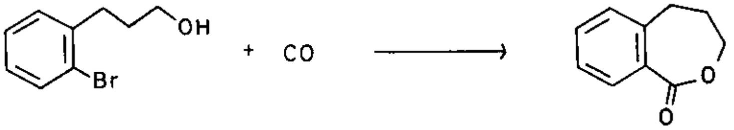
Reaction Temp.	mol% of $Pd(OAc)_2$	mol% of PPh_3	Reaction Time(h)	Yield of 4a(%)
100°	2.0	4.0	26	24.5*
100°	2.2	4.0	63.5	29.6
130°	2.2	5.3	26	56.4
130°	2.2	60.0	26	81.9

* The total yield of 4a and 5

Moreover, under similar conditions, six-membered benzolactone[4b, ν_{max} 1740 cm^{-1}, m/e 148(M^+), 69.8%] and seven-membered benzolactone[4c, ν_{max} 1705 cm^{-1}, m/e 162 (M^+), 41.6%] were also obtained from o-bromophenethyl alcohol(3b) and o-bromophenylpropyl alcohol(3c), respectively.

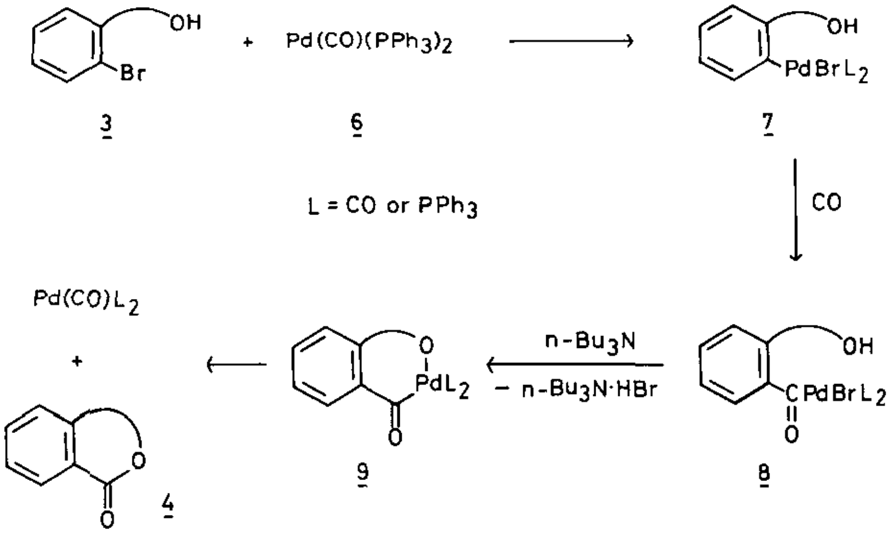


3b 4b



3c 4c

The reaction scheme might be considered as follows. It has been known that palladium (II) acetate could be reduced by carbon monoxide in the presence of the alcohol and a tertiary amine.[3] Zerovallent palladium complex(6) should be inserted to aryl halide(3) afford the arylpalladium complex(7),[4] which should be transformed to 9 via 8 by the insertion of carbon monoxide. The reductive elimination of palladium might give benzolactone(4) and zerovallent palladium(6).



These reactions are very useful because the starting material is readily available and carbon monoxide could be easily handled.

Further studies are in progress.

ACKNOWLEDGEMENT: This work was supported by a Grant-in-Aid for Scientific Research(No. 303023 and 367375) from the Ministry of Education, Sciences and Culture, Japan, which are gratefully acknowledged.

REFERENCES:

1. M.Mori, K.Chiba and Y.Ban, J. Org. Chem., 43, 1684 (1978).
2. M.Mori, K.Chiba and Y.Ban, Heterocycles, 6, 1841 (1977).
3. a) A.Schoenberg, I.Bartoletti and R.F.Heck, J. Org. Chem., 39, 3318 (1974).
   b) M.Hidai, M.Kokura and Y.Uchida, J. Organometall. Chem., 52, 431 (1973).
4. K.Kudo, M.Sato, M.Hidai and Y.Uchida, Bull. Chem. Soc. Japan, 46, 2820 (1973).

Received, 7th May, 1979