A NOVEL SYNTHESIS OF CYCLIC IMIDES AND QUINOLONE BY USE OF PALLADIUM CATALYZED CARBONYLATION

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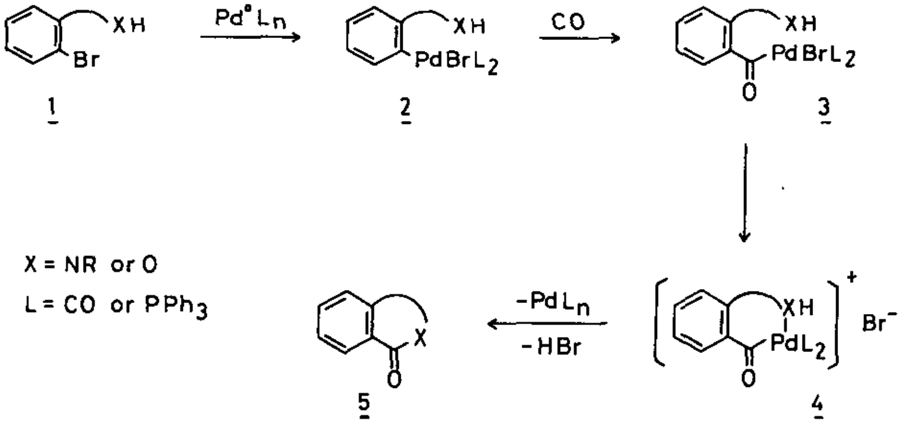
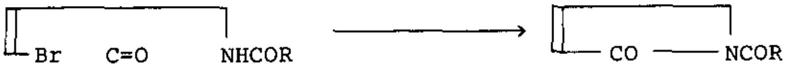
Abstract— The palladium catalyzed carbonylation of aryl and vinyl bromides bearing the internal amide group proceeded smoothly to give cyclic imides, such as phthalimide, N-acetylisoindolinone and N-acetylisoquinolone and quinolone.

We have developed a new synthesis of benzolactams[1] and benzolactones[2] by extention of Heck's method for palladium catalyzed carbonylation.[3] This reaction has been extended to the total synthesis of the natural compound, sendaverine.[4] It is assumed that the intermediate in the reaction is acylpalladium complex(3), in which the hetero atom, nitrogen or oxygen, coordinates to palladium to form the cyclic complex(4).



Thus, it was anticipated that the amide as a substrate could subject to carbonylation to form a similar complex(4), which would result in generation of the imide. The reaction can be indicated by Scheme 1.



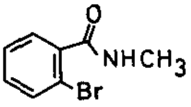
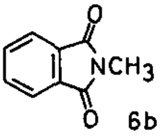
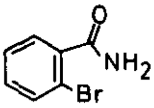
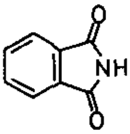
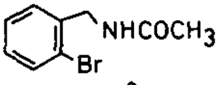
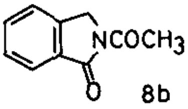
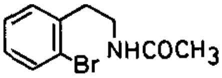
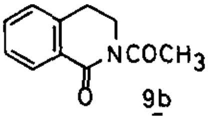
(Scheme 1)

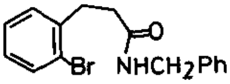
This idea has been substantially realized with aryl bromides bearing internal amide group. A typical procedure of the synthesis of cyclic imides was shown as follows.

A mixture of o-bromo-N-methylbenzamide(6a, *430.0 mg, 2.0 mmol*), a catalytic amount of Pd(OAc)$_2$(9.0 mg, 0.04 mmol), PPh$_3$(52.1 mg, 0.2 mmol) and n-Bu$_3$N(444.0 mg, 2.4 mmol) in HMPA(1.5 mmol) was heated at 100° under an atmospheric pressure of carbon monoxide for 36 h to produce N-methylphthalimide[6b, 269.9 mg, 83.6 %, mp 133-135°(lit. 133-134°,[5] from EtOH)] in a good yield.

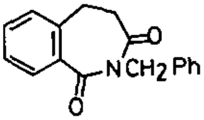
Other results of the carbonylation of halobenzene bearing internal amide group are shown in Table 1.

Table 1. The synthesis of cyclic imides by use of palladium catalyzed carbonylation

Entry	Substrate	Product	Yield(%)
1	 6a	 6b	83.6
2	 7a	 7b	71.6
3	 8a	 8b	23.1
4	 9a	 9b	17.0



10a

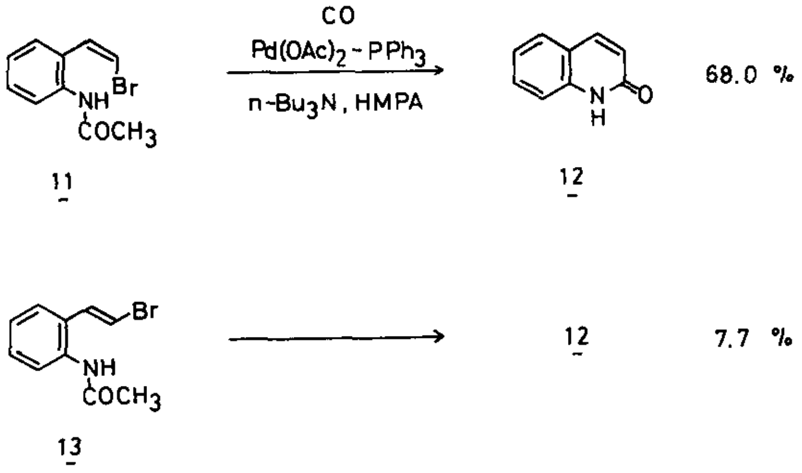


10b

Compounds bearing an electron withdrawing group ortho to bromine gave the good yields(Entries 1 and 2). This is consistent with the rate determining step being the oxidative addition of an aryl halide to a low valent metal complex.[6] Since the syntheses of the imides(8b and 9b) require aryl halides which lack an activating group at the ortho position, their yields were lower(Entry 3 and 4). Moreover, the compound(10a) did not give the cyclic imide(10b) at all even heating under carbon monoxide at 120° for 48 h.

On the other hand, the Z-isomer(11) of the vinyl halide involving an internal amide group smoothly proceeded with the same manner at 70° for 24 h to furnish 2-quinolone(12) in 68.0% yield with loss of N-acetyl group. But the corresponding E-isomer(13) gave only a 7.7% yield of the desired quinolone(12) at the same reaction conditions. The present results demonstrate that palladation occurs at the position of halogen atom of the vinyl halide.

Further studies are in progress.



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