Tetrahedron Letters No. 28, pp 2601 - 2602.
©Pergamon Press Ltd. 1979. Printed in Great Britain.

0040-4039/79/0708-2601$02.00/0

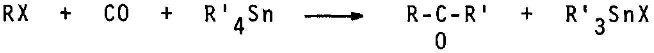
UNSYMMETRICAL KETONE SYNTHESIS FROM ORGANIC HALIDES, CARBON MONOXIDE, AND ORGANOTIN COMPOUNDS CATALYZED BY A PALLADIUM COMPLEX

Masato Tanaka
National Chemical Laboratory for Industry,
Honmachi, Shibuya-ku, Tokyo 151, Japan

Summary: Palladium complex catalyzed carbonylation of organic halides in the presence of organotin compounds to give unsymmetrical ketones in moderate to excellent yields is disclosed.

Although several stoichiometric unsymmetrical ketone synthesis from organic halides utilizing carbon monoxide with transition metal complexes are known,[1,2] there seems to be no successful catalytic method reported so far.[3] Recently, Yamamoto and co-workers have shown that ketonization of aromatic halides with carbon monoxide and Grignard reagents can be catalyzed by some nickel complexes, but the method is of a limited synthetic value due to the reaction of the Grignard reagents to ketones formed.[4] On the other hand, alkylation of metal-halogen bonds with organotin compounds has been one of standard methods to synthesize alkyl-metal complexes. Furthermore, most functional groups are tolerant to organotin compounds, which allowed the allylation of fuctionalized aromatic halides[5] as well as the alkylation of acid halides[6] catalyzed by palladium complexes.

In this paper, we wish to report a successful unsymmetrical ketone synthesis from organic halides, carbon monoxide, and organotin compounds in the presence of a palladium complex catalyst.



$$RX + CO + R'_4Sn \longrightarrow R\text{-}\underset{O}{C}\text{-}R' + R'_3SnX$$

Typical procedure is as follows; a stainless steel autoclave was charged with 10.5 mg (1.25×10^{-2} mmol) of $C_6H_5PdI[P(C_6H_5)_3]_2$, 3 ml of HMPA, 0.84 ml (7.5 mmol) of iodobenzene, and 1.23 ml (3.75 mmol) of tetrabutyltin. Carbon monoxide (30 atm at room temperature) was indroduced, and the mixture was stirred at 120°C overnight (judging from the pressure decrease, the reaction seemed to have finished within a few hours). The reaction mixture was poured into a 20 ml water-50 ml ether mixture. The ether layer was washed with water, treated with excess potassium fluoride,[7] filtered, washed again with water, dried over magnesium sulfate, and was concentrated. The residue was distilled (kugelrohr) to give 441 mg of valerophenone, which was identified by glc, ir, and pmr. Glc analysis of the reaction mixture showed no butylbenzene formed as a by-product, which was readily formed when the reaction was conducted in the

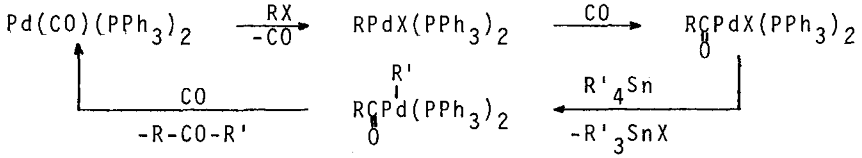
Table. Ketone synthesis from RX, CO, and R'_4Sn with $PhPdI(PPh_3)_2$ as catalyst

RX	R' in R'_4Sn	Product	Yield (%)[a]
C_6H_5I	CH_3	C_6H_5-CO-CH_3	123 (85)
C_6H_5I	CH_3	C_6H_5-CO-CH_3	105[b]
C_6H_5I	n-C_4H_9	C_6H_5-CO-n-C_4H_9	79 (73)
C_6H_5I	C_6H_5	C_6H_5-CO-C_6H_5	68
$C_6H_5CH_2Cl$	CH_3	$C_6H_5CH_2$-CO-CH_3	— (86)
trans-$C_6H_5CH{=}CHBr$	CH_3	*trans*-$C_6H_5CH{=}CH$-CO-CH_3	— (62)[c]
$C_2H_5OOCCH_2Br$	C_6H_5	$C_2H_5OOCCH_2$-CO-C_6H_5	— (67)

a) The figures in parentheses indicate isolated yields. b) The catalyst amount used was one tenth of the standard run. c) A polymeric material was also formed in 14% yield: its amount increased when the reaction was not discontinued as soon as the carbon monoxide absorption ceased.

absence of carbon monoxide.

Some typical results are collected in the table (the yield is not optimized). Since a second alkyl group of organotin compounds (i.e., $(CH_3)_3SnI$) also has some reactivity for this reaction, the yield for iodobenzene reactions with tetramethyltin exceeded 100%. Although no attempt to find the best conditions for the reaction, including the use of other transition metal complex catalysts, has been made, turnover number of more than 3000 was attained, at least, for the iodobenzene-tetramethyltin combination. The following reaction scheme which consists of oxidative addition of a halide, insertion of carbon monoxide, and reductive elimination of a ketone may be postulated for this reaction.[8] In view of the tolerance of most functional groups, this reaction might have considerable utility for ketonization of organic halides.



References and notes

1) J. P. Collman, S. R. Winter, and D. R. Clark, *J. Amer. Chem. Soc.*, 94, 1788 (1972).
2) I. Rhee, M. Ryang, T. Watanabe, H. Omura, S. Murai, and N. Sonoda, *Synthesis*, 1977, 776.
3) For symmetrical ketone synthesis from carbon monoxide and organomercurials, organolead or tin compounds in the presence of palladium or rhodium complex catalysts, see R. F. Heck, *J. Amer. Chem. Soc.*, 90, 5546 (1968).
4) T. Yamamoto, T. Kohara, and A. Yamamoto, *Chem. Lett.*, 1976, 1217.
5) M. Kosugi, K. Sasazawa, Y. Shimizu, and T. Migita, *ibid.*, 1977, 301.
6) D. Milstein and J. K. Stille, *J. Amer. Chem. Soc.*, 100, 3636 (1978), and the references cited therein.
7) J. E. Leibner and J. Jacobus, *J. Org. Chem.*, 44, 449 (1979).
8) For mechanisms of palladium catalyzed carbonylation reactions, see P. E. Garrou and R. F. Heck, *J. Amer. Chem. Soc.*, 98, 4115 (1976).

(**Received** in Japan 30 March 1979)