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NOVEL HYDROXYMETHYLATION OF ARYL BROMIDES BY MEANS OF ORGANOTIN REAGENTS

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Direct transformation of aryl bromides to benzylic alcohols by means of hydroxymethyltributyltin in the presence of palladium complex was attained in moderate yields, although the catalytic efficiencies were rather low, and the reaction could not be applied to aryl bromides having strong electron-withdrawing group. These problems were solved by using the trimethylsilyl-protected tin compound.

Development of agents for hydroxymethylation of organic halides is a current interest.[1)] Our earlier findings about a novel aromatic methoxymethylation by using methoxymethyltributyltin[2)] prompted us to investigate the possibility of hydroxymethylation of bromobenzene. We wish to report that this novel aromatic hydroxymethylation with hydroxymethyltributyltin in the presence of palladium complex proceeds with tolerable smoothness. It is notable that such direct hydroxymethylation can be done without any protection of the hydroxy group in the reagent.

$$Bu_3SnCH_2OH \quad + \quad PhBr \xrightarrow{[Pd]} PhCH_2OH \quad + \quad Bu_3SnBr$$

In a typical procedure, a mixture of hydroxymethyltributyltin[3)] (3.0 mmol), bromobenzene (2.0 mmol), $Pd(PPh_3)_4$ (0.1 mmol), and 1,4-dioxane (2 ml) was heated under argon at 80 °C for 20 h. After evaporation of the solvent, column chromatography of the residue (silica gel; cyclohexane followed by benzene, and finally ether as an eluent) provided the benzyl alcohol in the ethereal elute, from which the product was isolated by using Kugelrohr under reduced pressure.

As shown in Table 1, however, the reaction required a rather large amount of the catalyst (5 mol%), and the reaction could not be applied to the aryl bromides having strong electron-withdrawing substituents, such as p-acyl, p-cyano, p-nitro, etc. These disadvantages were overcome by using trimethylsilyl-protected tin compound ($Bu_3SnCH_2OSiMe_3$), where the reaction required higher temperature (120 °C) and longer reaction time (48 h), but by using only 1 mol% of the catalyst, p-acetylbenzyl alcohol (48%), p-cyanobenzyl alcohol (66%), and p-nitrobenzyl alcohol (52%) were obtained after hydrolytic treatment of the reaction mixtures.

Table 1. The reaction of aryl bromides with hydroxymethyltributyltin

X-C_6H_4Br	Catalyst (mol%)[a]	Temp / °C	Solvent	Yield of $ArCH_2OH$ / %[b]
H	none	80	PhH	0
H	A (1)	80	PhH	23
H	B (1)	80	PhH	14
H	C (1)	80	PhH	trace
H	D (1)	80	PhH	0
H	E (1)	80	PhH	0
H	A (1)	60	PhH	12
H	A (1)	100	PhH	11
H	A (1)	80	DMF	11
H	A (1)	80	HMPA	0
H	A (1)	80	1,4-Dioxane	28
H	A (1)	80	EtOH	23
H	A (3)	80	1,4-Dioxane	42
H	A (5)	80	1,4-Dioxane	60
H	A(10)	80	1,4-Dioxane	63
p-CH_3	A (5)	80	1,4-Dioxane	52
m-CH_3	A (5)	80	1,4-Dioxane	62
o-CH_3	A (5)	80	1,4-Dioxane	80
p-Cl	A (5)	80	1,4-Dioxane	73
o-Cl	A (5)	80	1,4-Dioxane	71
p-CH_3O	A (5)	80	1,4-Dioxane	53
o-CH_3O	A (5)	80	1,4-Dioxane	83
p-CH_3CO	A (5)	80	1,4-Dioxane	0
p-CN	A (5)	80	1,4-Dioxane	0
p-NO_2	A (5)	80	1,4-Dioxane	0

a) A; $Pd(PPh_3)_4$, B; $PdCl_2(PPh_3)_2$, C; $PdCl_2[P(o\text{-}tolyl)_3]_2$, D; $RhCl(PPh_3)_3$, E; $RuCl_2(PPh_3)_3$.

b) Isolated yields based on the bromides.

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References

1) K. Tamao, N. Ishida, and M. Kumada, J. Org. Chem., 48, 2120 (1983) and references cited therein.

2) M. Kosugi, T. Sumiya, T. Ogata, H. Sano, and T. Migita, Chem. Lett., 1984, 1225.

3) Hydroxymethyltributyltin was prepared by the reaction of tributylstannyl lithium with formaldehyde: D. E. Seitz, J. J. Carroll, C. P. Cartaya M., S-H. Lee, and A. Zapata, Synthetic Commun., 13, 129 (1983).

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