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A NOVEL METHOXYMETHYLATION OF ARYL BROMIDE BY METHOXYMETHYLTRIBUTYLTIN IN THE PRESENCE OF PALLADIUM COMPLEX

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The reaction of aryl bromides with methoxymethyltributyltin in the presence of a catalytic amount of dichlorobis(triphenylphosphine)palladium was found to give arylmethyl methyl ether. The reaction is a novel aromatic methoxymethylation.

The cross-coupling of an organometallic with an organic halide catalyzed by a transition metal is an important, versatile method of stereo- and regiospecific carbon-carbon bond formation.[1,2] Various organometallic reagents have now been developed for the transformation.[3] Among these, organotin compounds appeared to be especially attractive,[4] because they can be conveniently prepared.

Cross-coupling of organic halides with α-heterosubstituted organometallic reagents, such as Metal-CH_2OCH_3, Metal-CH_2SCH_3, etc., has received recent interests. Many trials were reported by Negishi and his co-workers, but the results appeared not to be always satisfactory.[5] In this letter, we wish to show a novel aromatic methoxymethylation of aryl bromides by methoxymethyltributyltin in the presence of a catalytic amount of dichlorobis(triphenylphosphine)palladium.

$$Bu_3SnCH_2OCH_3 + ArBr \xrightarrow{[Pd]} ArCH_2OCH_3 + Bu_3SnBr$$

The following reaction procedure was typical; the mixture of methoxymethyltributyltin (6.5 mmol), bromobenzene (5.0 mmol), $PdCl_2(PPh_3)_2$ (0.05 mmol), and hexamethylphosphoric triamide (HMPA) (2.5 ml) was heated with stirring at 80 °C for 20 h under argon. After the reaction mixtures were poured into water to remove HMPA, and treated with aquous potassium fluoride to remove the tributyltin bromide, organic layer was extracted with ether and dried over magnesium sulfate. Distillation gave benzyl methyl ether in 73% yield based on bromobenzene. The results are shown in Table 1.

The reaction gave moderate yields of the products and could be applied to a wide variety of aryl bromides bearing functional substituents, such as carbonyl, cyano, and nitro groups. With o-bromotoluene, rather long reaction time was needed for completion of the reaction.

Table 1. The Reaction of Aryl Bromide with Methoxymethyltributyltin

Aryl Bromide R-C_6H_4Br	Catalyst	Solvent	Yield of $ArCH_2OCH_3$ % a)	Bp (°C/mmHg)
H-	-	HMPA	(0)	
	$PdCl_2(PPh_3)_2$		(76), 73	73/30
	$PdCl_2[P(o\text{-}toly)_3]_2$		(17)	
	$Pd(PPh_3)_4$		(31)	
	$PdCl_2(PPh_3)_2$	PhH	(8)	
o-Me-		HMPA	80 b)	74/22
m-Me-			72	70/15
p-Me-			67	79/23
o-Cl-			61	72/22
p-Cl-			70	87/26
o-MeO-			trace b)	
p-MeO-			68	78/15
p-Ac-			64	108/15
p-CN-			57	105/16
p-NO_2-			65	110/15

a) Isolated yield based on the bromide (GLC yield in parentheses).
b) Reaction time for 70 h.

The substitution of aryl bromide was tried to extend, using diethoxymethyltributyltin and thiomethoxymethyltributyltin as organotin reagents, but the reaction did not take place under similar conditions, and the starting materials were recovered. Quite interestingly, however, hydroxymethylation of bromobenzene by using the corresponding organotin compound occurred rather smoothly. Further works on the scope of the reaction are in progress.

$$Bu_3SnCH_2OH + PhBr \xrightarrow[\text{in THF}]{[Pd]} \underset{60\%}{PhCH_2OH} + Bu_3SnBr$$

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References

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