Aromatic Acetonylation by Using Aryltins with Acetonylium Equivalents under the Palladium Catalysis

Masanori KOSUGI,* Yoshio MIYAJIMA, Hideyuki NAKANISHI, Hiroshi SANO, and Toshihiko MIGITA*
Department of Chemistry, Faculty of Engineering, Gunma University, Kiryu, Gunma 376
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Synopsis. Palladium-catalyzed reactions of heteroaromatic tins with 2-ethoxyallyl diethyl phosphate and of nitrophenyltins with 2-methoxymethoxyallyl chloride were found to give the coupling products, which can be hydrolyzed to the corresponding acetonylated aromatics in good yields.

Although a number of methods for aromatic acetonylation were reported so far,[1] there is still in need of an efficient method for aromatics having electron-withdrawing groups or heteroaromatics. Previously, we reported that acetonyltributyltin prepared in situ from methoxytributyltin and isopropenyl acetate reacted with aryl bromide under the palladium catalysis to give the arylacetone in good yield.[2] The reaction, however, was hardly applied to the aryl bromides having electron-withdrawing groups, although recent survey brought some improvements.

On the other hand, we report here an alternative method of preparing acetonyl aromatics, that is, the reaction of aryltins with acetonylium equivalent under the palladium catalysis.

$$Bu_3SnAr + CH_3COCH_2^+ \xrightarrow{[Pd]} ArCH_2COCH_3 + Bu_3Sn^+ \quad (1)$$

Acetonyl halide is the most simple reagent for acetonylium synthon, but is not suitable for the present reaction, because it has a carbonyl group which is reactive toward aryltins. Among the other acetonylium equivalents, 2-methoxyallyl bromide[3] which is labile and 2-trimethylsiloxyallyl halide[4] which is also labile in the presence of palladium complexes are not proper for the present reaction. On the basis of the stability of the compounds and the easiness of their preparation, we chose the following compounds; 2-ethoxyallyl diethyl phosphate,[5] 2-ethoxyallyl acetate,[6] and 2-ethoxyallyl carbonate,[7] 2-methoxymethoxyallyl chloride,[8] and 1-chloromethylvinyl diethyl phosphate.[9] These allylic compounds are converted into π-allyl palladium complexes by the palladium catalyst, and then react with aryltin compounds to give the coupled products.[10] Treatment of the products with aqueous acid would give the expected acetonylated products.

$$Bu_3SnAr + CH_2{=}C(OR)CH_2X \xrightarrow{[Pd]} ArCH_2C(OR){=}CH_2 \xrightarrow{H^+} ArCH_2COCH_3 \quad (2)$$

Palladium-catalyzed reactions of the phenyltributyltin with the various acetonylium equivalents gave the results as shown in the following equations.

$$PhSnBu_3 + CH_2{=}C(OEt)CH_2OPO(OEt)_2 \xrightarrow{[Pd]} PhCH_2C(OEt){=}CH_2 \quad 74\% \quad (3)$$

$$PhSnBu_3 + CH_2{=}C(OEt)CH_2OAc \xrightarrow{[Pd]} PhCH_2C(OEt){=}CH_2 \quad 49\% \quad (4)$$

$$PhSnBu_3 + CH_2{=}C(OEt)CH_2OCO_2Me \xrightarrow{[Pd]} PhCH_2C(OEt){=}CH_2 \quad 17\% \quad (5)$$

$$PhSnBu_3 + CH_2{=}C(OMOM)CH_2Cl \xrightarrow{[Pd]} PhCH_2C(OMOM){=}CH_2 \quad 79\% \quad (6)$$

(OMOM = OCH_2OCH_3)

$$PhSnBu_3 + CH_2{=}C(CH_2Cl)OPO(OEt)_2 \xrightarrow{[Pd]} PhCH_2C[OPO(OEt)_2]{=}CH_2 \quad 58\% \quad (7)$$

2-Methoxymethoxyallyl chloride and 2-ethoxyallyl diethyl phosphate gave the products in good yields.

Palladium-catalyzed reactions of 2-ethoxyallyl diethyl phosphate with nitrophenyltributyltins, pyridyltributyltins, and thienyltributyltins which are chosen as representatives of aromatics having electron-withdrawing group and heteroaromatics, are described in Table 1.

As Table 1 shows, although the yields of *p* and *m*-nitrophenylacetone were rather low, good yields for the reaction of heteroaryltins were obtained. As acetonylpyridines were labile, the coupled products were isolated without hydrolysis.

Results of palladium-catalyzed reactions of 2-methoxymethoxyallyl chloride with aryltributyltins were shown in Table 2.

Good yields of the arylacetones were obtained from the reaction with the *m* and *p*-nitrophenyltin, but moderate yields from the thienyltins. And the reaction with the pyridyltins did not give the product. Thus, suitable reagents for acetonylium synthon are differ-

Table 1. Pd-Catalyzed Reaction of $CH_2{=}C(OEt)$-$CH_2OPO(OEt)_2$ with Aryltins

Ar in Ar-$SnBu_3$	GLC Yield/%, Product	
Ph-	74	$PhCH_2C(OEt){=}CH_2$
p-NO_2-C_6H_4-	56, 48[a]	*p*-$NO_2C_6H_4CH_2COCH_3$
m-NO_2-C_6H_4-	40, 34[a]	*m*-$NO_2C_6H_4CH_2COCH_3$
2-Pyridyl-	60[a]	2-Pyridyl-$CH_2C(OEt){=}CH_2$
3-Pyridyl-	84[a]	3-Pyridyl-$CH_2C(OEt){=}CH_2$
2-Thienyl-	83[a]	2-Thienyl-CH_2COCH_3
3-Thienyl-	72[a]	3-Thienyl-CH_2COCH_3

a) Isolated yield.

Table 2. Pd-Catalyzed Reaction of $CH_2=C(OMOM)-CH_2Cl$[a] with Aryltins

Ar in Ar-$SnBu_3$	Isolated Yield/%, $ArCH_2COCH_3$	
H-C_6H_4-	79[b]	$PhCH_2COCH_3$
m-NO_2-C_6H_4-	71	*m*-$NO_2C_6H_4CH_2COCH_3$
p-NO_2-C_6H_4-	70	*p*-$NO_2C_6H_4CH_2COCH_3$
2-Thienyl-	42	2-Thienyl-CH_2COCH_3
3-Thienyl-	55	3-Thienyl-CH_2COCH_3

a) OMOM=OCH_2OCH_3. b) GLC yield.

ent with the kind of aromatic tin compounds.

There are a number of methods for the conversion of allyl acetate or phosphate into the corresponding allylstannane.[11] If such a conversion could be attained, the same coupling products could be obtained from the 2-alkoxyallylstannane and aryl halide. Unfortunately, many trials for the preparation of the 2-alkoxyallylstannane failed.

However, palladium-catalyzed reaction of a ternary system composed of bromobenzene, hexabutyldistannane, and 2-methoxymethoxyallyl chloride or 2-ethoxyallyl diethyl phosphate gave the expected product in moderate yields, although the reaction with substituted aryl bromides gave the product in lower yields.

$$PhBr+Bu_3SnSnBu_3+CH_2=C(OMOM)CH_2Cl \xrightarrow{[Pd]} PhCH_2C(OMOM)=CH_2 \quad 69\% \quad (8)$$

$$PhBr+Bu_3SnSnBu_3+CH_2=C(OEt)CH_2OPO(OEt)_2 \xrightarrow{[Pd]} PhCH_2C(OEt)=CH_2 \quad 53\% \quad (9)$$

The reaction seems to proceed through the formation of aryltributyltin prepared in situ by the reaction of aryl bromide with hexabutyldistannane under the palladium catalysis,[12] followed by its reaction with acetonylium equivalent under the reaction conditions.

Experimental

Instruments. JASCO Model A-100 for infrared spectra, Varian Associates Model EM-360 for ^1H NMR spectra, JEOL Model JMS-DX302 for mass spectra, JAI Model LC-08 for liquid chromatography, and Ohkura Model for gas chromatography using 10% Silicone SF96 or SE30 on Celite 545 were used.

Materials. 2-Bromothiophene (bp 65—75 °C/15 mmHg; 1 mmHg=133.322 Pa) was prepared by the bromination of thiophene.[13] 3-Bromothiophene (bp 75—77 °C/46 mmHg) was prepared by the bromination of thiophene giving 2,3,5-tribromothiophene (bp 135 °C/16 mmHg), followed by the treatment with zinc in acetic acid.[14] 2-Ethoxyallyl diethyl phosphate,[5] 2-ethoxyallyl acetate,[6] 2-ethoxyallyl carbonate,[7] 2-methoxymethoxyallyl chloride,[8] and 1-chloromethylvinyl diethyl phosphate[9] were prepared according to the method described in the literatures. Phenyltributyltin was prepared by the reaction of phenylmagnesium bromide with tributyltin chloride [prepared from bis(tributyltin) oxide and hydrochloric acid].[15] *m*-, *p*-Nitrophenyltributyltin were prepared by the reaction of the corresponding aryl bromide with hexabutyldistannane in the presence of palladium complexes.[12] 2-, 3-Pyridyl- and 2-,3-thienyltributyltin were prepared by the reaction of the corresponding pyridyl or thienyl bromide with butyllithium, followed by the reaction with tributyltin chloride.[16] Hexabutyldistannane was prepared by the reaction of the tributyltin hydride [prepared from bis(tributyltin) oxide and poly(methylhydrosiloxane)] in the presence of palladium complexes.[17] Tetrakis(triphenylphosphine)palladium,[18] dichlorobis(triphenylphosphine)palladium,[19] and tris(benzylideneacetone)dipalladium,[20] were prepared by the methods described.

Reaction Procedures. In Eqs. 3 and 4, the mixture of aryltin (1.3 mmol), the acetonylating agent (1.0 mmol), and tetrakis(triphenylphosphine)palladium (1 mol%) in HMPA (1 mL) was heated in a sealed tube at 100 °C for 20 h. The product was analyzed by GLC. In Eq. 5, the reaction was carried out at 120 °C. In Eq. 6, at 120 °C and dichlorobis(triphenylphosphine)palladium in THF were used. In Eq. 7, the reaction was carried out at 120 °C by using tris(dibenzylideneacetone)dipalladium (0.5 mol%) plus triphenylphosphine (2 mol%) in HMPA. In Tables 1 and 2, three times of the scale and dichlorobis(triphenylphosphine)palladium in benzene or toluene were used. The reaction mixture was washed with aqueous potassium fluoride, followed by the extraction of organic layer with ether, then dried over anhydrous magnesium sulfate. The product was isolated by Kugelrohr distillation under reduced pressure. It was acetonylated by the use of column chromatogaraphy on silica gel.

Products. 2-Ethoxyallylbenzene, ^1H NMR (CCl_4) δ=1.30 (t, J=7 Hz, 3H), 3.30 (s, 2H), 3.65 (q, J=7 Hz, 2H), 3.70 (bs, 2H), 7.15 (s, 5H). 1-Benzylvinyl diethyl phosphate, ^1H NMR (CCl_4) δ=1.30 (t, J=7 Hz, 6H), 3.50 (s, 2H), 3.95 (q, J=7 Hz, 2H), 4.16 (q, J=7 Hz, 2H), 4.40 (s, 1H), 4.90 (s, 1H), 7.30 (s, 5H). (2-Methoxymethoxyallyl)benzene, ^1H NMR (CCl_4) δ=3.30 (s, 3H), 3.35 (s, 2H), 4.00 (s, 1H), 4.20 (s, 1H), 4.85 (s, 2H), 7.25 (s, 5H). These compounds were hydrolyzed to give phenylacetone. ^1H NMR (CCl_4) δ=2.05 (s, 3H), 3.65 (s, 2H), 7.35 (s, 5H). Its IR spectra were consistent with that of the authentic sample.[21] 3-(2-Ethoxyallyl)-pyridine, ^1H NMR ($CDCl_3$) δ=1.25 (t, J=7 Hz, 3H), 3.40 (s, 2H), 3.80 (q, J=7 Hz, 2H), 3.90 (bs, 2H), 7.1—8.7 (m, 4H). Exact MS, Found: m/z 163.0952, Calcd for $C_{10}H_{13}NO$: M, 163.0997. 2-(2-Ethoxy-2-propenyl)pyridine, ^1H NMR ($CDCl_3$) δ=1.30 (t, J=7 Hz, 3H), 3.60 (s), 3.80 (q, J=7 Hz) 4.00 (s) 6H, 6.9—8.6 (m, 4H). *p*-Nitroacetonylbenzene, ^1H NMR (CCl_4) δ=2.20 (s, 3H), 3.80 (s, 2H), 7.40, 8.25 (ABq, J=10 Hz, 4H). IR (CCl_4) 1715 (C=O), 1515 and 1345(NO_2) cm^{-1}. Exact MS, Found: m/z 179.0549, Calcd for $C_4H_9NO_3$: M, 179.0582. *m*-Nitroacetonylbenzene, ^1H NMR (CCl_4) δ=2.20 (s,3H), 3.80 (s, 2H), 7.5—8.3 (m, 4H). IR (KBr) 1715 (C=O), 1510 and 1340 (NO_2) cm^{-1}. Exact MS, Found: m/z 179.0526, Calcd for $C_4H_9NO_3$: M, 179.0582. *p*-Cyanoacetonylbenzene, ^1H NMR ($CDCl_3$) δ=2.20 (s, 3H), 3.80 (s, 2H), 7.45, 7.80 (ABq, J=10 Hz, 4H). IR (KBr) 2250(CN), 1718 (C=O) cm^{-1}. Exact MS, Found: m/z 159.0668, Calcd for $C_{10}H_9NO$: M, 159.0684. 2-Acetonylthiophene, ^1H NMR ($CDCl_3$) δ=2.20 (s, 3H), 3.90 (s, 2H), 6.8—7.4 (m, 3H). IR (neat) 1710 (C=O) cm^{-1}. Exact MS, Found: m/z 140.0289, Calcd for C_7H_8OS: M, 140.0296. 3-Acetonylthiophene, ^1H NMR ($CDCl_3$) δ=2.20 (s, 3H), 3.65 (s, 2H), 6.8—7.4 (m, 3H). IR (neat) 1720 (C=O) cm^{-1}, Exact MS, Found: m/z 140.0275, Calcd for C_7H_8OS: M, 140.0296.

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