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Communications

Palladium-catalyzed Acylation of β,β-Diphenyl-α-(trifluoromethyl)vinylstannane as a Novel Route to 1,3-Disubstituted 2-(Trifluoromethyl)indene Derivatives

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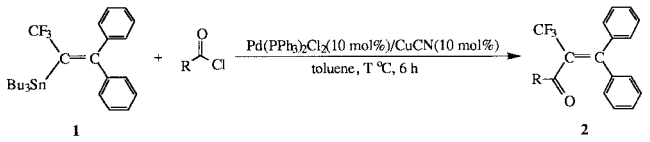
Although a various types of α-(trifluoromethyl)vinylmetal reagents such as lithium[1,2] and zinc[3-6] have been synthesized and utilized previously, the preparation and synthetic utility of α-(trifluoromethyl)vinylstannane reagent have been quite limited. Only a couple of papers described about chemistry of α-(trifluoromethyl)vinylstannane reagent. The α-(trifluoromethyl)vinylstannane reagent bearing only hydrogens at β-position has been synthesized from the reaction of 2-bromotrifluoroisopropene with lithium tributylstannate in the presence of CuI and utilized for the cross-coupling reactions with acyl chlorides in the presence of catalytic amount of $PdCl(Bn)(PPh_3)_2$ in HMPA at 65 °C to give α-(trifluoromethyl)vinyl ketone derivatives.[7] Ichikawa also carried out the reaction of α-(trifluoromethyl)vinylstannane reagent with α,β-unsaturated acyl chlorides in the presence of catalytic amount of $Pd(PPh_3)_2Cl_2$ and CuCN in toluene at 55-75 °C to give the desired NaZarov substrates.[8] Recently, we reported about the preparation of a novel α-(trifluoromethyl)vinylstannane reagent[9] bearing two phenyl groups at β-position and the cross coupling reactions of it with aryl iodides to give trifluoromethylated triphenylethene derivatives which are important framework of many nonsteroidal antiestrogens.[10] As a part of our continuing studies on the synthetic utility of β,β-diphenyl-α-(trifluoromethyl)vinylstannane reagent, we examined palladium-promoted acylation of this reagent with acyl chlorides to give β,β-diphenyl-α-trifluoromethylated enone derivatives which are useful intermediates for the formation of novel 1,3-disubstituted 2-(trifluoromethyl)indene derivatives *via* Friedel-Craft's type of the cyclization. Since nonfluorinated 1,3-disubstituted indene derivative such as Indenestrol A exhibited mammary tumor inhibiting antiestrogen activity,[11,12] it is expected that 1,3-disubstituted 2-(trifluoromethyl)indene derivatives also have a potential similar activity. Herein, we describe the palladium-promoted acylation of β,β-diphenyl-α-(trifluoromethyl)vinylstannane reagent and the formation of 1,3-disubstituted 2-(trifluoromethyl)indene derivatives from the acylated adduct .

A starting material, β,β-diphenyl-α-(trifluoromethyl)vinylstannane reagent **1**, was prepared *via* several steps from 2,3,3,3-tetrafluoro-1-phenyl-1-phenylthiopropene.[9] First of all, the acylation reaction of **1** with acetyl chloride was carried out in the presence of several palladium catalyst. The use of Pd catalyst such as $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ in THF, DMF, toluene or HMPA did not provide any acylated product. However, acylation reaction to give acylated product **2a** was successfully accomplished by using a mixture of 10 mol% $Pd(PPh_3)_2Cl_2$ and 10 mol% CuCN in toluene at 50 °C for 6 h. The higher temperature (80 °C) was needed for the completetion of acylation of **1** with types of benzoyl chlorides. Therefore, starting material **1** underwent the acylation reaction with a various types of acyl chlorides, such as ethyl chloroformate, furoyl chloride, naphthoyl chloride and benzoyl chlorides bearing a bromo, methoxy, methyl, or nitro on the benzene ring, to give the corresponding trifluoromethylated enone derivatives **2** at 80 °C for 6 h. The experimental results of the acylation reactions are summarized in Table 1.

Reduction of **2a** with $LiAlH_4$ (1.5 equiv.) in ether at reflux temperature for 3 h afforded the corresponding allylic alcohols **3a**[13] in 71% yield. The use of $NaBH_4$ did not provide the desired product, whereas the starting material was always recovered. The Fridel-Craft's type of cyclization of **3a** was successfully accomplished to give 2-trifluoromethyl-3-methyl-

Table 1. The acylation reactions of **1** with acyl chlorides



1 2

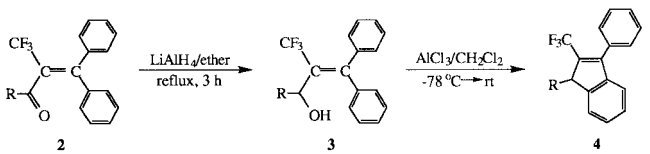
Compound No.	T (°C)	R	Yield (%)[a]
2a	50	CH_3	68
2b	80	C_6H_5	80
2c	80	(*o*-CH_3)-C_6H_4	78
2d	80	(*p*-CH_3)-C_6H_4	88
2e	80	(*p*-OCH_3)-C_6H_4	85
2f	80	(*m*-NO_2)-C_6H_4	72
2g	80	(*m*-CH_3)-C_6H_4	81
2h	80	(*m*-Br)-C_6H_4	77
2i	80	C_2H_5O	62
2j	80	2-furanyl	75
2k	80	2-naphthyl	86

[a] Isolated yields.

1-phenylindene (**4a**)[14] by using $AlCl_3$ (1.2 equiv.) in methylene chloride at -78 °C, followed by the slowly warming to room temperature. The use of dilute H_2SO_4 instead of $AlCl_3$ at reflux temperature caused not only to decrease the yield of indene derivatives **4a**, but also to extend the reaction time. The more excess of $AlCl_3$ (2.0 equiv.) was used to carry out the acylation of **3d** and **3f** because of possible coordination of oxygen with $AlCl_3$. Reduction of other types of enone derivatives **2**, followed by treatment with $AlCl_3$ under the same reaction condition also provided the corresponding 1,3-disubstituted 2-(trifluoromethyl)indene derivatives **4** in good yields. The experimental results of reduction and cyclization reactions are summarized in Table 2. Although 2-(trifluoromethyl)indene has been prepared in a previous literature, this method is a lack of generality and provides low yield preparation.[15]

A typical reaction procedure for the preparation of **2a** is as follows. To a toluene (5 mL) solution of acetyl chloride (0.088 g, 1.12 mmol) and β,β-diphenyl-α-(trifluoromethyl)vinylstannane (0.402 g, 0.75 mmol) was added $Pd(PPh_3)_2Cl_2$ (10 mol%) and CuCN (10 mol%), and the reaction mixture was heated at 50 °C for 6 h under argon atmosphere. After the reaction mixture was quenched with water and then washed with 5% KF solution and brine, solution was extracted with ether twice. The ether solution was dried and chromatographed on SiO_2 column. Elution with a mixture of hexane and ethyl acetate (20 : 1) provided 0.145 g of 2-trifluoromethyl-1,1-diphenyl-1-buten-3-one (**2a**) in 68% yield. **2a**: mp 65-66 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 7.41-7.18 (m, 10H), 2.03 (s, 3H); ^{19}F NMR (100 MHz, $CDCl_3$) δ -55.42 (s, 3F); MS, m/z (relative intensity) 290 (M^+, 81), 289 (100), 275 (12), 255 (22), 227 (29), 213 (30), 207 (17), 178 (29), 176 (19), 151 (13), 127 (19), 105 (33), 77 (13), 51 (10); IR (KBr) 3082, 3059, 3028, 2927, 2855, 1704, 1617, 1608, 1492, 1445, 1418, 1357, 1322, 1261, 1216, 1145, 1111, 1078, 1042, 998, 951, 759, 699, 656 cm^{-1}. Anal. Calcd for $C_{17}F_3H_{13}O$: C, 70.32; H, 4.52. Found: C, 70.49; H, 4.60.

Table 2. The synthesis of 1,3-disubstituted 2-trifluoromethylated indene derivatives **4**



2 3 4

Compound No.	R	Yield of **3** (%)[a]	Yield of **4** (%)[a]
3a, 4a	CH_3	71	76
3b, 4b	C_6H_5	74	78
3c, 4c	(*p*-CH_3)-C_6H_4	69	71
3d, 4d	(*p*-OCH_3)-C_6H_4	73	68
3e, 4e	(*m*-Br)-C_6H_4	70	73
3f, 4f	(*m*-NO_2)-C_6H_4	67	66
3g, 4g	2-furanyl	62	63
3h, 4h	2-naphthyl	71	74

[a] Isolated yields.

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13. Spectroscopic data of **3a**: oil; ^{1}H NMR (100 MHz, $CDCl_3$) δ 7.38-7.11 (m, 10H), 4.58 (m, 1H), 1.87 (d, J = 8.0 Hz, 1H), 1.52 (d, J = 7.4 Hz, 3H); ^{19}F NMR (100 MHz, $CDCl_3$) δ -52.64 (s, 3F); MS, m/z (relative intensity) 292 (M^+, 44), 277 (15), 274 (19), 259 (15), 237 (13), 223 (16), 209 (26), 178 (18), 171 (21), 167 (100), 165 (33), 151 (29), 127 (59), 77 (22), 51 (17); IR (neat) 3395, 3059, 3028, 2963, 2932, 1623, 1492, 1445, 1318, 1260, 1130, 1077, 1018, 797, 759, 700 cm^{-1}. Anal. Calcd for $C_{17}F_3H_{15}O$: C, 69.84; H, 5.18. Found: C, 70.01; H, 5.26.
14. Spectroscopic data of **4a**: mp 75-77 °C; ^{1}H NMR (100 MHz, $CDCl_3$) δ 7.41-7.10 (m, 10H), 4.89 (q, J = 7.5 Hz, 1H), 1.76 (d, J = 7.5 Hz, 3H); ^{19}F NMR (100 MHz, $CDCl_3$) δ -52.50 (s, 3F); MS, m/z (relative intensity) 274 (M^+, 39), 233 (41), 205 (100), 203 (36), 196 (52), 190 (15), 177 (24), 127 (14), 101 (20), 91 (18), 77 (19), 51 (15); IR (KBr) 3058, 2929, 2855, 2360, 1598, 1492, 1445, 1320, 1262, 1194, 1137, 1034, 763, 732, 700 cm^{-1}. Anal. Calcd for $C_{17}F_3H_{13}$: C, 74.43; H, 4.78. Found: C, 74.27; H, 4.89.
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