Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

A New Method for Synthesis of Methyl Arylpropiolates by Direct Heck Coupling of Aryl Iodide and Methyl Propiolate in Presence of K_2CO_3

Thomas Eckert [a] & Junes Ipaktschi [a]
[a] Institute of Organic Chemistry, Justus-Liebig University, Heinrich-Buff-Ring 58, D-35392, Giessen, Germany

To cite this article: Thomas Eckert & Junes Ipaktschi (1998): A New Method for Synthesis of Methyl Arylpropiolates by Direct Heck Coupling of Aryl Iodide and Methyl Propiolate in Presence of K_2CO_3 , Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 28:2, 327-335

To link to this article: http://dx.doi.org/10.1080/00397919808005726

SYNTHETIC COMMUNICATIONS, 28(2), 327-335 (1998)

A NEW METHOD FOR SYNTHESIS OF METHYL ARYLPROPIOLATES BY DIRECT HECK COUPLING OF ARYL IODIDE AND METHYL PROPIOLATE IN PRESENCE OF K_2CO_3

Thomas Eckert and Junes Ipaktschi*

Institute of Organic Chemistry, Justus-Liebig University, Heinrich-Buff-Ring 58,
D-35392 Giessen, Germany

Abstract: A protocol for the efficient direct cross coupling of esters of propiolic acid and of aryl iodides with a $Pd(PPh_3)_2Cl_2$/copper(I) iodide catalyst system in the presence of K_2CO_3 has been developed.

The palladium-catalyzed coupling of terminal acetylenes with organic halides is a widely used reaction in organic synthesis[1]. Typically this cross coupling reaction proceeds in the presence of catalytic amounts of Palladium complexes such as $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$, a catalytic amount of copper(I) iodide and an organic amine base as solvent[2-4]. It is viewed that the terminal acetylenes containing a

---

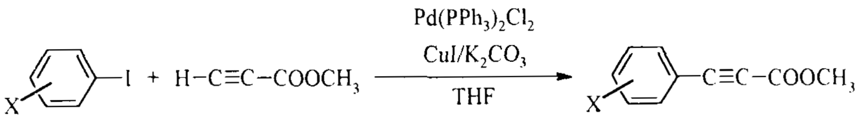
*To whom correspondence should be addressed.

strong electron-withdrawing group directly attached to the ethynyl carbon atom hardly react with aryl halides under these conditions[5]. For example, perfluoroalkylacetylenes failed to give cross coupling products[5] and esters of propiolic acids undergo Michael addition and self-condensation in the presence of amines[6]. In order to avoid these shortcoming in the preparation of esters of arylpropiolates, less sensitive alkynes such as trialkoxy-1-propyne, 2-Alkoxycarbonyl-1-ethynylzinc chloride or alkyl(tributylstanyl)propiolate, which were prepared first from the alkyl propiolate, are coupled with aryl halides[7].

We describe here a high yield heterogeneous direct cross coupling of esters of propliolic acids with aryl iodides in the presence of K_2CO_3 as base.

Results and discussion

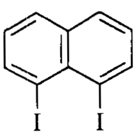
The reaction of iodobenzene **1a** with 4 equivalents of methyl propiolate **2** in THF at 65 °C in the presence of $Pd(PPh_3)_2Cl_2$ (2 mol %), copper(I) iodide (4 mol %) and 4 equivalents K_2CO_3 afforded the ester **3a** in 90 % yield after 6 h. In the presence of Et_2NH as a base, the Michael addition of the amine to methyl propiolate was the dominant reaction, and organic bases such as Et_3N or ethyldiisopropylamine led to self condensation of methyl propiolate. The yield decreased to 20-40% when the cross coupling was carried out with inorganic bases such as Ag_2CO_3, K_3PO_4, CH_3COONa as well as CH_3COOAg. Also the choice of solvent was important. The standard solvent for the Heck-reaction, DMF, brought about very low yields (5%) even using K_2CO_3. THF was the most suitable solvent for the reaction. $Pd(PPh_3)_2Cl_2$ was a preferable catalyst compared to $Pd(PPh_3)_4$, which yields only 10% **3a**.



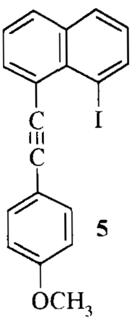
1 **2** **3**

	X
a	H
b	*p*-NO_2
c	*o*-CHO
d	*m*-Br
e	*p*-I
f	*p*-OCH_3

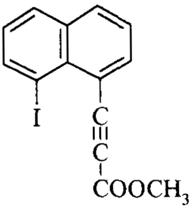
In order to clarify the scope and limitations of this method, we examined the reaction of aryl iodides **1b**-**1f** with the methyl propiolate **2** to the methyl arylpropiolates **3b**-**3f**. Aryl iodides with electron-withdrawing groups (**1b** and **1c**) provided the propiolates (**3b** as well as **3c**) in high yields (99 % and 96 % respectively). With the use of 3-bromoiodobenzene, 1,4-diiodobenzene and *p*-iodoanisole the reaction yield decreased from 33% with **1d**, to only 3% with **1f**. The naphthalene derivatives **4** and **5** showed similar behaviour in the reaction with **2** yielding **6** (35%) and **7** (30%). The results are summarized in table 1.



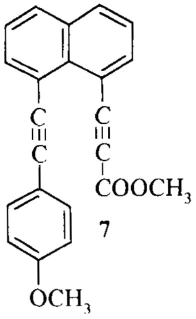
4



5



6



7

Table 1 Reaction of Aryl Iodides **1a-f**, **5** and **6** with Methyl Propiolate **2**

Aryliodide	time (h)	product	yield (%)[a]
1a	6	**3**	92
1b	2	**4**	99
1c	3	**5**	96
1d	9	**6**	33
1e	9	**7**	17
1f	12	**11**	3
5	9	**9**	30
6	9	**10**	35

[a] Isolated yields. [b] All reactions were carried out in THF with K_2CO_3 as base and $Pd(PPh_3)_2Cl_2/CuI$ as catalyst at 65 °C.

Experimental

Elemental analyses were obtained on a Carlo Erba Modell 1104. The IR spectra were recorded on Bruker IFS 25. The UV spectra were measured on Hewlett-Packard 8452A Diode array spectrophotometer. The NMR spectra were recorded on either Bruker AM 400 or Bruker AC 200, J values are given in Hz. Mass spectra were recorded on either Varian MAT 311A. Melting points were determined on a Büchi SMP-20. Methyl propiolate, 4-iodoanisole, and 4-iodonitrobenzene were purchased from Aldrich Chemical Company and 1,4-diiodobenzene from ACROS. Bis(triphenylphosphanyl)palladium(II) chloride was prepared according to the lit.[8], 1,8-diiodonaphthalene according to the lit.[9], 2-iodobenzaldehyde according to the lit.[10] and 4-etynylanisole according to the lit.[11]. All reactions were carried out under argon with dried solvents.

Preparation of 1-(4-Anisylethynyl)-8-iodonaphthalene 5

To a solution of 1,8-diiodonaphthalene **4** (3.8 g, 10 mmol) and of 4-ethynylanisole (1.6 g, 12 mmol) in triethylamine (20 ml) were added $Pd(PPh_3)_2Cl_2$ (140 mg, 2 mol %) and CuI (76 mg, 4 mol %). The obtained mixture was stired 24 h. Subsequently the triethylamine was evaporated and the residual was extracted with diethyl ether. The crude product was purified by silca gel column chromatography [diethyl ether/pentane (2:1)]. Yield 2.0 g (56%); colorless crystals; mp 89.5 °C (Found: C, 59.3; H, 3.3. Calc. for $C_{19}H_{13}IO$: C, 59.4; H, 3.4%); $\tilde{\nu}_{max}$(KBr)/cm^{-1} 3009, 2954, 2831, 2202, 1603, 1568, 1508 and 1249; λ_{max} (EtOH)/nm 240 (log ε/dm^3 mol^{-1} cm^{-1} 4.26), 272 (3.80), 342 (4.01) and 356 (3.95); δ_H(400 MHz; $CDCl_3$) 3.83 (3 H, s, OCH_3), 6.83-6.88 (2 H, m, aryl-H), 7.05-7.09 (1 H, m, aryl-H), 7.40-7.45 (1 H, m, aryl-H), 7.55-7.61 (2 H, m, aryl-H), 7.78 (1 H, d *J* 8.2, aryl-H), 7.82 (1 H, d *J* 8.2, aryl-H) and 7.90 (1 H, dd *J* 1.0 and 7.3, aryl-H); δ_C(100 MHz; $CDCl_3$) 55.32 (OCH_3), 87.94 (C), 92.94 (C), 100.96 (C), 114.14 (2 x CH), 116.25 (C), 123.17 (C), 125.45 (CH), 127.01 (CH), 130.00 (CH), 130.10 (CH), 131.84 (C), 132.27 (2 x CH), 134.92 (C), 135.60 (CH), 142.56 (CH) and 159.83 (C).

General Procedure for the Preparation of the Methyl arylpropiolates 3a-3f, 6 and 7 from the corresponding Aryl iodides 1a-1f, 4 and 5 and the Methyl propiolat 2

To a solution of aryl iodide **1a-1f**, **4** resp. **5** (10 mmol) and of methyl propiolat **2** (3.4 g, 40 mmol) in THF (30 ml) were added $Pd(PPh_3)_2Cl_2$ (140 mg, 2 mol %), CuI (76 mg, 4 mol %) and K_2CO_3 (2.8 g, 20 mmol). The obtained mixture was stired at 65 °C between 1 and 12 h (table 1). Subsequently the THF was evaporated at vacuum and the residual was extracted with diethyl ether. The crude products were purified by silca gel column chromatography.

Methyl phenylpropiolate 3a from compond 1a. Yield 1.4 g (90%); light yellow crystals after destillation at 100 °C and 5 Torr; mp 25 °C (lit.[12] mp 25 °C).

Methyl (4-nitrophenyl)propiolate 3b from compound 1b. Yield 2.0 g (99%); light yellow crystals after silca gel column chromatography [pentane/dichlormethane (1:1)]; mp 110 °C (lit.[13] mp 110 °C).

Methyl (2-formylphenyl)propiolate 3c from compound 1c. Yield 1.8 g (96%); light yellow crystals after silca gel column chromatography (dichlormethane); mp 42°C (Found: C, 70.05; H, 4.0 Calc. for $C_{11}H_8O_3$: C, 70.2; H, 4.3%); $\tilde{\nu}$(film)/cm^{-1} 3065, 2999, 2842, 2224, 1701, 1640, 1592, 1466, 1435 and 1289; λ_{max}(CH_2Cl_2)/nm 258 (log ε/dm^3 mol^{-1} cm^{-1} 4.09), 270 (3.87), 274 (3.88) and 302 (3.77); δ_H(400 MHz; $CDCl_3$) 3.89 (3 H, s, OCH_3), 7.58-7.67 (2 H, m, aryl-H), 7.71 (1 H, d *J* 7.7, aryl-H) 7.99 (1 H, d *J* 8.8, aryl-H) and 10.51 (1 H, s, O=C-H); δ_C(100 MHz; $CDCl_3$) 53.01 (OCH_3), 81.51 (C), 86.12 (C), 122.46 (C), 127.87 (CH), 130.94 (CH), 133.78 (CH), 134.51 (CH), 137.26 (C), 153.81 (C=O) and 190.17 (C=O).

Methyl (3-bromophenyl)propiolate 3d from compound 1d. Yield 0.8 g (33%); light yellow crystals after silca gel column chromatography [pentane/dichlormethane (1:1)]; mp 50 °C (Found: C, 50.2; H, 2.5 Calc. for $C_{10}H_7BrO_2$: C, 50.2; H, 2.9%); $\tilde{\nu}$(KBr)/cm^{-1} 3061, 2960, 2231, 1716 and 1201; λ_{max}(EtOH)/nm 254 (log ε/dm^3 mol^{-1} cm^{-1} 4.10); δ_H(400 MHz; $CDCl_3$) 3.85 (3 H, s, OCH_3), 7.20-7.30 (1 H, m, aryl-H), 7.52 (1 H, ddd *J* 1.1, 1.2 and 7.7, aryl-H) 7.58 (1 H, ddd *J* 1.1, 1.2 and 8.8, aryl-H) and 7.73 (1 H, m, aryl-H); δ_C(100 MHz; $CDCl_3$) 52.77 (OCH_3), 81.31 (C), 84.39 (C), 121.71 (C), 122.41 (C), 130.01 (CH), 131.41 (CH), 133.63 (CH), 135.54 (CH) and 154.04 (C=O); *m/z* (EI) 237.9602 (M^+. $C_{10}H_7BrO_2$ requires 237.9630).

Methyl (4-iodophenyl)propiolate 3e from compound 1e. Yield 0.5 g (17%); colorless crystals after silca gel column chromatography [pentane/dichlormethane (1:1)]; mp 110 °C (Found: C, 41.6; H, 2.3 Calc. for $C_{10}H_7IO_2$: C, 42.0; H, 2.5%.); $\tilde{\nu}$(KBr)/cm^{-1} 2959-2859, 2226, 1720 and 1292; λ_{max}(EtOH)/nm 277 (log ε/dm^3 mol^{-1} cm^{-1} 3.90); δ_H(400 MHz; $CDCl_3$) 3.81 (3 H, s, OCH_3), 7.22 (2 H, d *J* 8.3, aryl-H) and 7.68 (2 H, d *J* 8.3, aryl-H); δ_C(100 MHz; $CDCl_3$) 52.87 (OCH_3), 81.47 (C), 85.34 (C), 97.54 (C), 119.01 (C), 134.17 (2 x CH), 137.91 (2 x CH) and 154.25 (C=O); *m/z* (EI) 285.9476 (M^+. $C_{10}H_7IO_2$ requires 285.9491).

Methyl (4-anisyl)propiolate 3f from compound 1f. Yield 0.1 g (5%); light yellow crystals after silca gel column chromatography [pentane/dichlormethane (1:1)]; mp 41 °C (lit.[14] mp 42 °C).

1-Iod-8-methylpropynatnaphthalene 6 from compound 4. Yield 1.2 g (35%), light yellow crystals after silca gel column chromatography [pentane/diethyl ether (10:1)]; mp 57.5 °C (Found: C, 49.9; H, 2.6 Calc. for $C_{14}H_9IO_2$: C, 50.0; H, 2.7%); $\tilde{\nu}$(KBr)/cm^{-1} 3070, 2991, 2210, 1719, 1294 and 1216; λ_{max}(EtOH)/nm 228 (log ε/dm^3 mol^{-1} cm^{-1} 4.32) and 332 (3.82); δ_H(400 MHz; $CDCl_3$) 3.86 (3 H, s, OCH_3), 7.11-7.17 (1 H, m, aryl-H), 7.42-7.48 (1 H, m, aryl-H), 7.84 (1 H, d *J* 8.0, aryl-H), 7.90 (1 H, dd *J* 1.0 and 8.1, aryl-H), 7.98 (1 H, dd *J* 1.3 and 7.3, aryl-H) and 8.30 (1 H, dd *J* 1.0 and 7.4, aryl-H); δ_C(100 MHz; $CDCl_3$) 52.67 (OCH_3), 85.92 (C), 92.02 (C), 92.66 (C), 119.34 (C), 125.32 (CH), 127.55 (CH), 130.21 (CH), 132.78 (C), 132.95 (CH), 134.81 (C), 138.72 (CH), 143.22 (CH) and 155.00 (C=O).

1-(4-Anisylethynyl)-8-methylpropinatnaphthalene 7 from compound 5. Yield 1.0 g (30%); light yellow oil after silca gel column chromatography [pentane/ diethyl ether (10:1)] (Found: C, 81.1; H, 4.7 Calc. for $C_{23}H_{16}O_3$: C, 81.2; H, 4.7%); $\tilde{\nu}$(film)/cm^{-1} 3070, 2990, 2850, 2209, 1710, 1289, 1250 and 1218; λ_{max}(EtOH)/nm 231 (log ε/dm^3 mol^{-1} cm^{-1} 4.03), 288 (3.76), 300 (3.58), 318 (3.56) and 340 (3.55); δ_H(400 MHz; $CDCl_3$) 3.50 (3 H, s, OCH_3), 3.83 (3 H, s, OCH_3), 6.85-8.91 (2 H, m, aryl-H), 7.42-7.49 (2 H, m, aryl-H), 7.51-7.57 (2 H, m, aryl-H), 7.79-7.86 (2 H, m, aryl-H) and 7.88-7.93 (2 H, m, aryl-H); δ_C(100 MHz; $CDCl_3$) 52.24 (OCH_3), 55.30 (OCH_3), 86.82 (C), 86.87 (C), 87.54 (C), 97.43 (C), 113.78 (2 x CH), 115.94 (C), 117.22 (C), 120.92 (C), 125.36 (CH), 126.06 (CH), 129.31 (CH), 131.75 (C), 131.83 (CH), 133.08 (2 x CH), 133.87 (C), 134.71 (CH), 136.87 (CH), 154.70 (C=O) and 159.66 (C).

Acknowledgements

We thank the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie* for support.

References

1 Sonogashira K., in *Comprehensive Organic Synthesis*, eds. Trost B. M. and Fleming I., Pergamon Press, Oxford, **1991**, vol. 3, ch. 2.4, p. 521-549.

2 Cassar L. *J. Organometal. Chem.* **1975**, *93*, 253-257.

3 Dieck H. A. and Heck F. R. *J. Organometal. Chem.* **1975**, *93*, 259-263.

4 Sonogashira K., Thoda Y. and Hagihara N. *Tetrahedron Lett.* **1975**, *50*, 4467-4470.

5 Yoneo N., Matsuoka S., Miyaura N., Fukuhara T. and Suzuki A. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2124-2126.

6 Wenkert E., Adams K. A. H. and Leicht C. L. *Can. J. Chem.* **1963**, *41*, 1844-1846.

7 Sakamoto T., Shiga F., Yasuhara A., Uchiyama D., Kondo Y. and Yamanyka H. *Synthesis* **1992**, 746-748.

8 Heck R. F. "Palladium Reagents in Organic Synthese," Academic Press, London, **1985,** pp. 18.

9 House H. O., Koepsell D. G. and Campbell W. J. *J. Org. Chem.* **1972**, *37*, 1003-1011.

10 Larock R. C. and Doty M. J. *J. Org. Chem.* **1993**, *58*, 4579-4583.

11 Crisp G. T. and Flynn B. L. *J. Org. Chem.* **1993**, *58*, 6614-6619.

12 Takeuchi R., Tsuji Y., Fujita M., Kondo T. and Watanabe Y. *J. Org. Chem.* **1989**, *54*, 1831-1836.

13 Sharf S. M., Al-Sadany S. K., Hamed E. A. and Youssef A-H. A. *Can. J. Chem.* **1991**, *69*, 1445-1449.

14 Morris J. and Wishka D. G. *Synthesis*, **1994**, 43-46.

(Received in The Netherlands 11 August 1997)