Pergamon

Tetrahedron Letters, Vol. 37, No. 16, pp. 2731-2734, 1996

0040-4039/96 $15.00 + 0.00

S0040-4039(96)00373-5

Elaboration of a Cyclohexadienyl triflate iron π-Complex by Palladium-catalysed Coupling

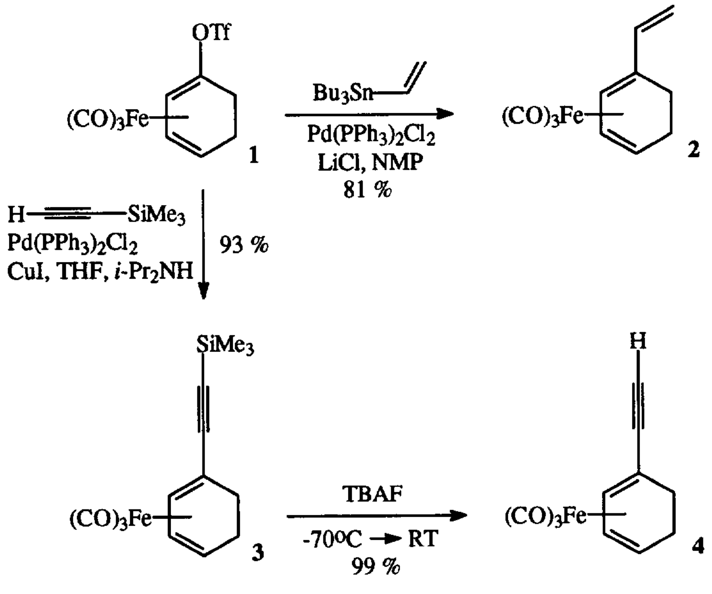
Michael R. Attwood,[b] Tony M. Raynham,[b] Donald G. Smyth,[a] and G. Richard Stephenson[a]*

[a] **School of Chemical Sciences, University of East Anglia, Norwich, NR4 7TJ, U.K.**

[b]**Roche Products Ltd., Research Centre, P.O. Box 8, Welwyn Garden City, Hertfordshire, AL7 3AY, U.K.**

Abstract: Optimisation of Stille coupling between tricarbonyl[1,2,3,4-η-cyclohexadien-1-yl triflate]iron(0) and tributylvinyltin forms the 1-ethenyl-substituted tricarbonyliron complex in up to 81% yield. Coupling with trimethylsilylethyne in the presence of copper(I) iodide afforded, in 93% yield, the corresponding alkyne, which was desilylated with TBAF to give the 1-ethynylcyclohexadiene complex in 99% yield. Copyright © 1996 Elsevier Science Ltd

Palladium-catalysed cross-coupling offers an attractive method for carbon-carbon bond-formation at an sp^2 centre and now is regarded as a routine synthetic step that can be applied with confidence in a wide variety of situations. Aryl, alkenyl and alkynyl substituents are easily introduced in this way, and the reaction has found widespread application in organic synthesis. Less common, however, are coupling reactions performed at sp^2 carbon atoms within the η^n metal-bound moiety of a stoichiometric π-complex though even in this situation, examples of cross-coupling reactions are known. Most fully explored are couplings to aryl halides and triflates bound to the tricarbonylchromium group. A variety of substituents have been introduced[1,2] in this way to the metal-bound aromatic ring, and, since the tricarbonylchromium group can be retained within the product, the procedure can give access to elaborated organochromium complexes which are versatile intermediates in asymmetric synthesis. The Stille reaction[3] between aryl or vinyl triflates and organostannanes is one of the most popular and widely applied cross-coupling procedures. This process begins by oxidative addition of the palladium catalyst to the carbon-oxygen bond of the vinyl triflate. Examples with organochromium-bound aromatic substrates[2] indicate that oxidative addition proceeds, even when the carbon atom is covalently attached to chromium. Besides (η^6-arene)tricarbonylchromium complexes, the η^4-diene complexes of the tricarbonyliron group are also widely employed as intermediates in organic synthesis. In this case, however, the only reported examples of palladium-catalysed coupling concerns a case where the alkenylstannane portion is bound to iron and the coupling partner is an acid chloride.[4] In this paper, we describe the use of iron-bound alkenyl triflates in the optimisation of synthetic routes to ethenyl and ethynyl tricarbonyliron complexes by palladium-catalysed cross-coupling. Attempted Stille coupling of tributylvinyltin (1.1 equivalents) with the η^4-cyclohexadienyl triflate iron complex (**1**)[5] in THF, with a catalyst prepared from Pd(OAc)$_2$/PPh$_3$, in the presence of lithium chloride gave no product at room temperature. However, after heating at reflux for 48 hours the expected product (**2**) was obtained in 19% yield (Table 1, entry 1). The catalyst *tris*(dibenzylideneacetone)dipalladium(0)/triphenylphosphine (entry 2) similarly afforded **1** in low yield. However, when THF was replaced with 1-methyl-2-pyrrolidinone (NMP) (a solvent recommended by Farina[6,7]) the yield of the reaction was doubled to 38% (entry 3). Since Farina reports that NMP is the best solvent for the Stille reaction (the rate of coupling increases in the order: $CHCl_3$ < THF < CH_3CN < DMF < NMP[7]), we selected NMP as the solvent of choice for the remainder of our investigation of Stille coupling with **1**. The ligands present during the coupling process are crucial to the success of the reaction since they must readily dissociate to allow the oxidative addition and transmetallation steps of the catalytic cycle to proceed. Farina[6,7] has commented that trifurylphosphine has the correct electronic properties to sufficiently stabilise the palladium(0) species, while allowing facile ligand dissociation and so promoting efficient catalysis. We examined the use of both trifuryl- (entry 4) and trithienyl- (entry 5) phosphines in place of triphenylphosphine, and were rewarded by a further improvement in the efficiency in the coupling with **1**, with the product **2** now formed in 47-50% yield. A range of phosphines with 4-substituted aromatic rings are commercially available and offer a further means to examine the effect of variation of phosphine-basicity on reaction efficiency. Methyl-, methoxy-, chloro- and fluoro-substituted triarylphosphines have been studied in our work (entries 6-9) and all proved more efficient than triphenylphosphine, with the best result being obtained with the tri-p-tolylphosphine. The palladium(0) complex $Pd(dppe)_2$ was also examined, to avoid the need for a redox stage prior to the introduction of the reactants. In this case (entry 10), however, the product **2** was obtained in only 50% yield. Other sources of the palladium catalyst have been studied (entries 11-13) with the best results being obtained by the use of 5 mol% of *bis*(triphenylphosphine)palladium(II) dichloride in NMP in the absence of an added phosphine ligand (entry 13).



Scheme 1

The experiments (summarised in Table 1) demonstrate not only that palladium coupling is possible at an iron-bound carbon atom, but that through judicious choice of catalyst, ligand, and solvent systems, considerable optimisation of the efficiency of the reaction can be achieved, giving access (Scheme 1) to the vinyl-substituted tricarbonyliron complex **2** in a most acceptable 81% yield.

TABLE 1. Optimisation of cross-coupling between **1** and $H_2C{=}CH\text{-}SnBu_3$ to form **2**.

Entry	Catalyst (5 mol%)	Phosphine	Solvent	Yield (%)
1	$Pd(OAc)_2$	PPh_3[a]	THF[c]	19
2	$Pd_2(dba)_3$	PPh_3[b]	THF[c]	16
3	$Pd_2(dba)_3$	PPh_3[b]	NMP[d]	38
4	$Pd_2(dba)_3$	$P(C_4H_3O)_3$[b]	NMP[d]	50
5	$Pd_2(dba)_3$	$P(C_4H_3S)_3$[b]	NMP[d]	47
6	$Pd_2(dba)_3$	$P(C_6H_4OMe)_3$[b]	NMP[d]	51
7	$Pd_2(dba)_3$	$P(C_6H_4F)_3$[b]	NMP[d]	63
8	$Pd_2(dba)_3$	$P(C_6H_4Cl)_3$[b]	NMP[d]	65
9	$Pd_2(dba)_3$	$P(C_6H_4Me)_3$[b]	NMP[d]	68
10	$Pd(dppe)_2$[g]	-	NMP[d,e]	50
11	$Pd(MeCN)_2Cl_2$	-	NMP[d]	70
12	$Pd(dppf)Cl_2$[h]	-	NMP[d]	78
13	$Pd(PPh_3)_2Cl_2$	-	NMP[d]	81

[a] 15 mole%; [b] 10 mole%; [c] 48 h at reflux; [d] 16 h at ambient temp.; [e] then 4 h at 100°C; [f] Although entries 10-13 show that catalysis can proceed without added phosphines, with $Pd_2(dba)_3$, the presence of a phosphine is essential. When the reaction was attempted without addition of a phosphine, none of the product **2** was obtained; [g] dppe = 1,2-*bis*(diphenylphosphino)ethane; [h] dppf = 1.1'-*bis*(diphenylphoshino)ferrocene.

Cross-coupling of alkynes with alkenyl triflates was reported by Stille[8] in 1985. Typical conditions employed *bis*(triphenylphosphine)palladium(II) dichloride in DMF and triethylamine at 75°C. A year later, the procedure was modified by Cacchi[9] by including a copper(I) species which allowed the reaction to be carried out at room temperature. In his work, Cacchi used DMF/diethylamine as solvent, but subsequently Brückner and Suffert reported that coupling could be effected at room temperature using a 3:1 mixture of THF and diisopropylamine,[10] obviating the need to use DMF. We have employed the Brückner and Suffert version of the reaction to examine the cross-coupling of our η^4-cyclohexadienyl triflate iron complex **1** with trimethylsilylethyne in the presence of CuI. In our case heating was necessary and the coupling product **3** was obtained in 93% yield. Desilylation with tetrabutylammonium fluoride (TBAF) in THF at 0°C proved relatively inefficient (33%), but by the simple expedient of adding TBAF to a stirred solution of the complex **3** at -70°C, and then allowing the reaction mixture to warm slowly to room temperature, efficient conversion of **3** into **4** was achieved in 99% yield.

Conclusions. The reaction sequences presented in Scheme 1 allow efficient conversion of the η^4-cyclohexadienyl triflate iron complex **1** into either the ethenyl- (**2**)[11] or ethynyl- (**4**)[12] substituted products in greater than 80% yield. In both cases, *bis*(triphenylphosphine)palladium(II) dichloride proved to be a suitable catalyst for the coupling step.

Acknowledgements. DGS thanks the EPSRC (SERC) for a CASE award.

REFERENCES AND NOTES

1. Uemura, M.; Nishimura, H.; Kamikawa, K.; Nakayama, K.; Hayashi, Y. *Tetrahedron Lett.* **1994**, *35*, 1909; Umeura, M.; Kamikawa, K. *J. Chem. Soc., Chem. Commun.* **1994**, 2697; Caldirola, P.; Chowdhury, R.; Johansson, A. M.; Hacksell, U. *Organometallics* **1995**, *14*, 3897; Uemura, M.; Kamikawa, K.; Watanabe, T. *Synlett* **1995**, 1040.
2. Gilbert, A. M.; Wulff, W.D. *J. Am. Chem. Soc.* **1994**, *116*, 7449.
3. Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033.
4. Colson, P. J.; Franck-Neuman, M.; Sedrati, M. *Tetrahedron Lett.* **1989**, *30*, 2393.
5. Tricarbonyl[1,2,3,4-η-cyclohexadien-1-yl triflate]iron(0) was prepared in two steps as follows: Trifluoromethanesulfonic anhydride (0.158 mL, 0.94 mmol) was added to a stirred solution of tricarbonyl(cyclohexa-2,4-dien-1-one)iron(0)[13] (0.2 g, 0.855 mmol) in dichloromethane at room temperature, instantly resulting in the formation of a precipitate. On addition of tetrafluoroboric acid (0.28 g, 1.71 mmol) the precipitate dissolved to produce a dark solution which was stirred for 30 min. Addition to diethyl ether (50 mL) afforded a yellow precipitate which was collected by filtration, washed with dry ether, and added at once to stirred solution of lithium tri-*tert*-butoxyaluminohydride (0.94 mL, 1M, 0.94 mmol) in THF (15 mL) at -100°C to afford complex **1** in 70% overall yield. (Found M^+ 367.9259; $C_{10}H_7F_3SO_6Fe$ (M^+) requires 367.9264). ν_{max} (CH_2Cl_2)/cm^{-1} 2063, 1989 and 1563; δH (270 MHz; $CDCl_3$; Me_4Si) 5.64 (1H, d, *J* 5, 3-H), 5.13 (1H, t, *J* 5, 3-H), 3.2 (1H, m. 4-H), 2.3-1.9 (4H, m, 5-H and 6-H). For a related preparation of the 1-AcO analogue, see: Stephenson, G. R.; Howard, P. W.; Owen, D. A.; Whitehouse, A. J. *J. Chem. Soc., Chem. Commun.* **1991**, 641.
6. Farina, V.; Roth, G. P. *Tetrahedron Lett.* **1991**, *32*, 4243.
7. Farina, V.; Krishman, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.
8. Scott, W. J.; Pena, M. R.; Stille, J. K. *J. Org. Chem.* **1985**, *50*, 2302.
9. Cacchi, S. *Synthesis* **1986**, 320.
10. Brückner, R.; Suffert, J. *Tetrahedron Lett.* **1991**, *32*, 1453.
11. *Bis*(triphenylphosphine)palladium(II) dichloride (5 mol%, 19 mg, 0.027 mmol) was added to a stirred solution of lithium chloride (68 mg, 1.6 mmol) and **1** (0.2 g, 0.54 mmol) in NMP (3 mL). Tributylvinyltin (0.17 mL, 0.6 mmol) was added, and the reaction mixture was stirred at room temperature for 16 hours. The reaction mixture was transferred directly onto a silica column and eluted with hexane to afford **2** in 81% yield. (Found: C, 53.7; H, 4.1. $C_{11}H_{10}FeO_3$ requires C, 53.65; H, 4.1%); ν_{max} (CH_2Cl_2)/cm^{-1} 2039, 1963 and 1618; δH (270 MHz; $CDCl_3$; Me_4Si) 6.0 (1H, dd, *J* 10 and 17, 1'-H), 5.3-5.1 (4H, m. 3-H, 2-H and 2'-H), 3.2 (1H, m. 4-H), 2.15 (1H, t, *J* 15, 6β-H) 1.9 (1H, t, *J* 15 5β-H), 1.7 (1H, m, 6α-H) and 1.5 (1H, m, 5α-H).
12. Copper(I) iodide (3 mg, 0.016 mmol, 4 mol%) and *bis*(triphenylphosphine)palladium(II) dichloride (5.6 mg, 0.008 mmol, 2 mol%) were added to a solution of **1** (0.147 g, 0.4 mmol), trimethylsilylethyne (2.15 g, 22 mmol) and diisopropylamine (2 mL) in THF (6 mL), and the resulting mixture was heated at reflux for 6 h. After cooling, the reaction mixture was diluted with distilled water and extracted with dichloromethane, and the product purified by column chromatography (silica/hexane) to afford **3** in 93% yield. Tetrabutylammonium fluoride (0.372 mmol) was added as a 1M solution in THF to a stirred solution of **3** in THF (2 mL) at -70°C. The reaction was allowed to warm slowly to room temperature, diluted with distilled water and extracted with dichloromethane to afford **4** in 99% yield after column chromatography (silica/hexane). (Found: C, 54.2; H, 3.32. $C_{11}H_8FeO_3$ requires C, 54.1; H, 3.3%); ν_{max} (CH_2Cl_2)/cm^{-1} 3277, 2050 and 1982; δH (270 MHz; $CDCl_3$; Me_4Si) 5.56 (1H, d, *J* 4, 2-H), 5.23 (1H, dd, *J* 4 and 5, 3-H), 3.25 (1H, m, 4-H), 2.66 (1H, s, 2'-H), 1.9 (2H, m, 5β-H and 6β-H) and 1.7 (2H, m, 5α-H and 6α-H).
13. Birch, A. J.; Cross, P. E.; Lewis, J.; White, D. A.; Wild, S. B. *J. Chem. Soc. (A)* **1968**, 332.

(*Received in USA* 22 *January* 1996; *revised* 2 *February* 1996; *accepted* 14 *February* 1996)