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Palladium-catalysed coupling of terminal alkynes with aryl halides aided by catalytic zinc

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Abstract

The palladium-catalysed coupling of aryl halides with terminal alkynes can be performed using base, zinc chloride and sodium iodide. This protocol represents a convenient method for the generation of nucleophilic acetylides in situ. © 1998 Elsevier Science S.A. All rights reserved.

Keywords: Palladium catalysis; Coupling of oxyhalides with alkynes; Nucleophilic alkynes

1. Introduction

The ability of terminal alkynes to couple with aryl halides using the traditional methodology of a palladium catalyst (either palladium(0) or (II)), a base (frequently a secondary or tertiary amine) and copper iodide (for the generation of the copper acetylide intermediate), has been known for many years [1]. Several recent alternatives have been reported to this general theme and all proceed well in the absence of a copper co-catalyst but with modified reaction conditions. Examples include coupling in the presence of $Pd(PPh_3)_4$ and piperidine or pyrrolidine [2], the use of water soluble phosphine ligands and aqueous solvents [3] and the use of $Pd(OAc)_2$ in aqueous solvents with quaternary ammonium salts [4]. Numerous examples of organometallic acetylide derivatives have been reported including magnesium, zinc and tin and all have been shown to couple efficiently with organic electrophiles in the presence of palladium ([5]a, b). The inherent advantage of the traditional copper acetylides is the ability to catalytically generate the nucleophilic acetylides in situ and avoid the necessity of preparing and storing large quantities of potentially unstable reagents. A potential disadvantage to the use of zinc acetylides is that they have been prepared by the addition of a strong base to a terminal alkyne and $ZnCl_2$ added to effect cation exchange. The resulting solution is air and moisture sensitive and cannot be stored for long periods without deterioration. As aryl alkynes are becoming important intermediates in the synthesis of novel molecular polymers ([6]a, b) and functional molecular devices ([7]a, b), new methodologies for their synthesis under mild conditions are sought. We were interested in establishing a procedure in which the zinc acetylide (or an equivalent nucleophilic species) could be generated in situ, as for the copper acetylides and so provide a more convenient protocol for the use of zinc acetylides in palladium catalysed couplings. In this paper we report a preliminary investigation into the scope and limitations of the use of zinc acetylides (or an equivalent nucleophilic species) generated in situ.

2. Results and discussion

2.1. Activated substrates

An initial treatment of iodobenzene with phenyl-

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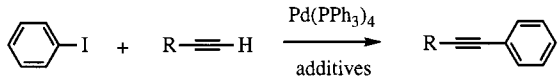
acetylene in the presence of $Pd(PPh_3)_4$, zinc chloride and piperidine at room temperature gave none of the desired diphenylacetylene over a 4-h period (Eq 1). Addition of a small crystal of iodine to the solution gave an immediate reaction as evidenced by the formation of a solid (piperidine hydroiodide) and after 1 h of stirring followed by an extractive workup, diphenylacetylene was isolated in 80% yield (entry 1, Table 1). The yield of diphenylacetylene was not affected by the use of zinc chloride which had not been specifically dried (compare entries 1 and 2, Table 1) showing that the reaction is tolerant of small quantities of water. Only a very slow reaction occurred in the absence of a source of iodide and only a catalytic quantity of either iodine or iodide was necessary to promote the coupling (entries 2 and 3, Table 1). Interestingly, zinc iodide did not promote the conversion as efficiently as a combination of zinc chloride and sodium iodide, so the effect of the iodine or iodide cannot simply be formation of zinc iodide (entry 5, Table 1). Replacing piperidine as the solvent with DMF and adding only 1.5 equivalents of piperidine gave the same yield of product as neat piperidine (entry 6, Table 1). No reaction occurred in the absence of a palladium catalyst (entry 4, Table 1) and no reaction occurred at room temperature when triethylamine replaced piperidine as the solvent (entry 7, Table 1), although a slow conversion did occur at 60°C (entry 8, Table 1), or when *N*,*N*-dimethylaminopyridine (DMAP) was used in addition to the triethylamine at 60°C (entry 9, Table 1).



(1)

The traditional copper iodide method gave diphenylacetylene in 100% yield after about 10min at room temperature (entry 10, Table 1), so the zinc chloride/iodide combination effects a slower coupling for this very reactive substrate. Iodide is not the only nucleophile which is capable of promoting the transformation as azide also gave an excellent yield of product (entry 11, Table 1). In order to probe the scope of the reaction further the optimum conditions of piperidine, $ZnCl_2$ and NaI were applied to the coupling of iodobenzene with 1-hexyne, trimethylsilylacetylene, 1,8-octadiyne and 2-propyn-1-ol and each gave an excellent yield of the expected product (entries 12–15, Table 1). The reaction with trimethylsilylacetylene was considerably slower than the other substrates and required 20 h at room temperature whereas all other substrates coupled completely in 1–3 h.

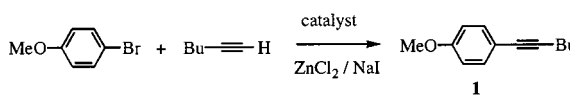
Table 1
Coupling of iodobenzene with terminal alkynes in Eq. 1

Entry	Solvent/base	*R*	Additive	% Yield
1	Piperidine	Ph	$ZnCl_2/I_2$	80[a]
2	Piperidine	Ph	$ZnCl_2^b/I_2$	94
3	Piperidine	Ph	$ZnCl_2^b$/NaI	94
4	Piperidine	Ph	$ZnCl_2^b$/NaI	0[d]
5	Piperidine	Ph	ZnI_2	34
6	Piperidine	Ph	ZnI_2	26[e]
7	NEt_3	Ph	ZnI_2	0
8	NEt_3	Ph	ZnI_2	34[f]
9	NEt_3/DMAP	Ph	$ZnCl_2^c$/NaI	44
10	Piperidine	Ph	CuI	100
11	Piperidine	Ph	$ZnCl_2^c/NaN_3$	100[a]
12	Piperidine	C_4H_9	$ZnCl_2^c$/NaI	94[a]
13	Piperidine	Me_3Si	$ZnCl_2^c$/NaI	100[g]
14	Piperidine	$HC{\equiv}C(CH_2)_4$	$ZnCl_2^c$/NaI	100[a]
15	Piperidine	$HOCH_2$	$ZnCl_2^c$/NaI	100[a]

[a] $Pd(PPh_3)_4$ 5%, base as solvent, room temperature, reaction time <1 h.
[b] $ZnCl_2$ dried under high vacuum.
[c] $ZnCl_2$ used without drying.
[d] Reaction without $Pd(PPh_3)_4$
[e] DMF used as solvent with 3 equivalents of piperidine
[f] Reaction mixture heated at 60°C
[g] Reaction mixture stirred for 18 h.

2.2. Non-activated substrates

The limits of this new protocol for the coupling were then investigated using the non activated 1-hexyne with the less reactive electrophile 4-bromoanisole (Eq 2) and the results are summarised in Table 2. For Table 1 the % yield represented that of the isolated product, whereas in Table 2 the % conversion of 4-bromoanisole to product has been calculated using gas liquid chromatography and an internal standard. No reaction occurred at room temperature as expected for the lower rate of oxidative addition of electron rich aryl bromides to palladium(O) and so all reactions were performed at 60°C.



(2)

1

Using piperidine as both the base and solvent with $ZnCl_2$ and NaI as the additives, various metal catalysts were tested for their efficacy in promoting the coupling. Under the standard conditions of $Pd(PPh_3)_4$ as catalyst, 60°C was found to give a reasonable rate of formation of **1** with minimum decomposition of the catalyst, minimum reduction of 4-bromoanisole and minimum formation of alkyne dimer (entry 1, Table 2). Homocoupling of terminal alkynes during traditional copper(I) catalysed heterocoupling reactions has been reported to be an unwanted side reaction when less reactive electrophiles such as electron rich arylbromides

Table 2
Coupling of *p*-methoxybromobenzene with 1-hexyne

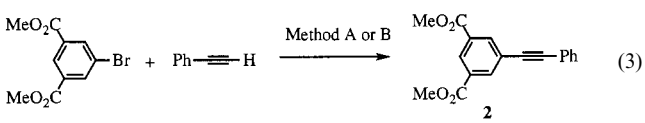
Entry	Solvent/base	Catalyst	Additive	%**1**[a]
1	Piperidine	$Pd(PPh_3)_4$	$ZnCl_2$/NaI	86[b]
2	Piperidine	$PdCl_2P(o\text{-}tolyl_3)_2$	$ZnCl_2$/NaI	67[b]
3	Piperidine	–	$ZnCl_2$/NaI	8[c]
4	Piperidine	$Pd(PPh_3)_4$	CuI	71[b]
5	Piperidine	$PdCl_2(PBu_3)_2$	$ZnCl_2$/NaI	0[c]
6	Piperidine	$PdCl_2(AsPh_3)_2$ /$AsPh_3$	$ZnCl_2$/NaI	15[c]
7	Piperidine	Pd_2dba_3/PPh_3	$ZnCl_2$/NaI	15[c]
8	Piperidine	Pd_2dba_3/dppe	$ZnCl_2$/NaI	19[c]
9	Piperidine	Pd_2dba_3/dppf	$ZnCl_2$/NaI	9[c]
10	Piperidine	$Pd(OAc)_2/PPh_3$	$ZnCl_2$/NaI	47[c]
11	Piperidine	$Niacac_2/PPh_3$	$ZnCl_2$/NaI	0[c]
12	Piperidine	$NiCl_2(PPh_3)_2$	$ZnCl_2$/NaI	0[c]
13	DMF/piperidine	$Pd(PPh_3)_4$	$ZnCl_2$/NaI	76[b]
14	DMSO/piperidine	$Pd(PPh_3)_4$	$ZnCl_2$/NaI	77[b]
15	DMSO/piperidine	$PdCl_2(PPh_3)_2$	$ZnCl_2$/NaI	88[b]
16	DMSO/DBU/NEt_3	$Pd(PPh_3)_4$	$ZnCl_2$/NaI	88[b]
17	DMSO/NMI/NEt_3	$Pd(PPh_3)_4$	$ZnCl_2$/NaI	60[b]
18	DMSO/DBU/NEt_3	$Pd(PPh_3)_4$	Zn dust/NaI	100[d]

[a] % Yield of **1** based on *n*-decane standard and glc analysis of the reaction mixture.
[b] $Pd(PPh_3)_4$ 5%, base as solvent, 60°C, reaction time, 4–8 h.
[c] Reaction time, 12–14 h.
[d] Reaction time, 2–3 h.

or triflates. [9] Reactions were conducted with only 1.2–1.5 equivalents of 1-hexyne in order to determine the extent of competition between homo- and heterocoupling.

Substitution of $P(o\text{-tolyl})_3$ for PPh_3 gave a reasonable yield of **1** although the reaction was noticeably slower and required 12 h for completion in contrast to 4–6 h for $Pd(PPh_3)_4$ (entry 4, Table 2). Very little conversion was effected without the presence of a metal catalyst (entry 3, Table 2). The traditional copper iodide method gave **1** in similar yield and at a similar rate to the $ZnCl_2$ and NaI method when $Pd(PPh_3)_4$ was the catalyst (entry 4, Table 2). Substituting the electron rich tertiary phosphine PBu_3 for PPh_3 gave no product after 24 h (entry 5, Table 2) and a $AsPh_3$ substituted catalyst gave a poor conversion to **1** due to premature catalyst decomposition at 60°C (entry 6, Table 2). Reducing the ratio of phosphine ligand to palladium from 4:1 to 2:1 for monodentate and 1:1 for bidentate ligands gave low conversions of 4-bromoanisole and catalysts which decomposed after 4–5 h (entries 7–9, Table 2). These catalysts gave very little dimer formation from homocoupling of 1-hexyne but significant reduction of 4-bromoanisole. The combination of $Pd(OAc)_2$ and PPh_3 gave an initial rapid conversion but the catalyst decomposed after 4 h and no further conversion took place (entry 10, Table 2). Dimer formation and reduction of 4-bromoanisole were major side reactions under these conditions. Nickel catalysts gave no product, no dimer formation and no reduction under these conditions (entries 11–12, Table 2). Since $Pd(PPh_3)_4$ appeared to be a suitable catalyst the effect of changing the solvent and base was investigated. The polar aprotic solvent DMF with 1.5 equivalents of piperidine gave a good conversion to **1** within 5 h (entry 13, Table 2). Increasing the solvent polarity by using DMSO with 1.5 equivalents of piperidine gave a faster reaction with fewer side products, as did the combination of DMSO with $PdCl_2(PPh_3)_2$ (entries 14–15, Table 2). The most efficacious combination was DMSO with 1.5 equivalents of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) and 1.5 equivalents of NEt_3 (entry 16, Table 2). Nucleophilic bases are necessary for this coupling protocol and this would imply a coordination of the base to the zinc intermediate which either stabilizers and/or activates the nucleophile. The use of *N*-methyl imidazole gave a reasonable yield of product in DMSO but the reaction was not as efficient as with DBU (entry 17, Table 2). The most efficient protocol was the use of DBU in DMSO with zinc dust instead of zinc chloride and this gave the most rapid reaction with minimal reduction and dimer formation (entry 18, Table 2).

The coupling of phenylacetylene with dimethyl 5-bromoisophthalate was examined and showed that the ester functional group is not affected by the reaction conditions with the product **2** being isolated in 70 and 75% yield under two different sets of conditions (Eq. 3 and Section 3).



2 (3)

In conclusion, an alternative protocol has been developed for the palladium catalysed coupling of terminal alkynes with aryl halides. This method appears to be as efficient as the traditional methodology using copper iodide and base to generate nucleophilic acetylides in situ. It offers a distinct advantage over the use of zinc acetylides which are prepared using a strong base and strictly anhydrous conditions. The nature of the active nucleophile in this protocol is not clear at this stage. It would seem unlikely that the active nucleophile is identical to that formed from a terminal alkyne, a strong base and $ZnCl_2$. The requirement for a nucleophilc base suggests a coordination to the zinc either before or after the activation of the terminal alkyne. We are presently investigating the nature of the nucleophilic species and the mechanism of the coupling and these results will be reported in due course.

3. Experimental

^{1}H-NMR spectra were recorded at 300 MHz on a Varian Gemini NMR spectrometer (75.47 MHz for 13C) or at 200 MHz on a Varian Gemini spectrometer (50.28 MHz for 13C), using a dual 5-mm ^{13}C/^{1}H probe. All spectra were recorded as dilute solutions in deuteriochloroform using tetramethylsilane as an internal standard. Melting points were determined on a Kofler hot-stage micro-melting point apparatus equipped with a Reichart microscope and are uncorrected. Electron impact mass spectra were recorded at 70 eV on a Vacuum Generators ZAB 2HF mass spectrometer. Thin layer chromatography (TLC) was carried out using Merck Silica gel (Kieselgel) $60F_{254}$ on aluminium backed plates. TLC plates were visualised using 253 nm ultraviolet light and/or by an acidic solution of 10% ammonium molybdate or 1% potassium permanganate solution. Flash and squat column chromatography was carried out using Merck Silica gel 60 (particle size 0.040–0.063mm).

Solvents were purified and dried using standard laboratory procedures [8]. All organic extracts were dried over anhydrous magnesium sulphate. All solvents for palladium catalysed coupling reactions were degassed by the freeze-pump-thaw method and kept under an atmosphere of nitrogen.

The following compounds were purchased from Aldrich: $NiCl_2(PPh_3)_2$, $Ni(acac)_2$, $PdCl_2(PBu_3)_2$, $PdCl_2(PPh_3)_2$ $PdCl_2$dppe and $Pd(OAc)_2$. The following compounds were prepared from literature procedures: $PdCl_2[P(o\text{-tolyl})_3]_2$ [10], $PdCl_2(AsPh_3)_2$ [10], Pd_2dba_3 [11] and $Pd[PPh_3]_4$ [12]. Reactions were performed under an atmosphere of nitrogen unless otherwise mentioned.

3.1. Diphenylacetylene

To a solution of iodobenzene (0.20 ml, 1.78 mmol) in degassed piperidine (3 ml) was added $Pd(PPh_3)_4$ (105 mg, 8.93×10^{-5} mol), phenylacetylene (0.20 ml, 1.82 mmol), zinc chloride (not dried) (50 mg, 3.67×10^{-4} mol) and sodium iodide (27 mg, 1.78×10^{-4} mol). The resulting suspension was then stirred under nitrogen at room temperature for 45 min. The reaction mixture was then added to dichloromethane (40 ml), washed with saturated ammonium chloride (40 ml) and the aqueous layer extracted with an additional portion of dichloromethane (40 ml). The organic layers were combined, dried and the solvent removed. The resulting oil was passed down a short squat column of silica (5:1 hexane:dichloromethane) and the solid obtained was recrystallised from an ethanol/water mixture to give tolan as colourless plates (272 mg, 86%). Mp. 58.5–60° (Mp. lit. 59–61°). [13] C-NMR: 89.4 (C≡C), 123.4, 128.2, 128.3, 131.6; m/z: 178 (M+, 100%), 152 (7), 126 (4).

3.2. 1-(1-Hexynyl)benzene

To a solution of iodobenzene (0.25 ml, 2.23 mmol) in piperidine (3 ml) was added $Pd(PPh_3)_4$ (129 mg, 1.12×10^{-4} mol), 1-hexyne (0.28 ml, 2.46 mmol), $ZnCl_2$ (not dried, 61 mg, 4.47×10^{-4} mol) and a crystal of iodine. The resulting suspension was then stirred at room temperature for 2 h. The reaction mixture was then added to CH_2Cl_2 (40 ml), washed with saturated NH_4Cl (40 ml) and the aqueous layer re-extracted with another portion of CH_2Cl_2 (40 ml). The organic layers were combined, dried and the solvent removed. The crude product was passed through a squat column of silica (eluant:- hexane:dichloromethane 3:1 (v/v)) to give the title compound as a golden oil (333 mg, 94%). ^{1}H-NMR:0.87 (t, 2H, J 7 Hz), 1.51 (m, 4H), 2.40 (t, 2H, J 7Hz), 7.26 (m, 3H), 7.39 (m, 2H); ^{13}C-NMR: 13.4, 19.0, 21.9, 30.8, 80.6 (C≡C), 90.4 (C≡C), 124.2, 127.4, 128.2, 131.6; m/z: 158 (M+, 41%), 143 (65), 129 (69), 115 (100); Ir (neat) (ν_{max}, cm^{-1}) 2231 (C≡C).

3.3. Trimethyl(2-phenyl-1-ethynyl)silane

The procedure was analogous to that for diphenylacetylene except that the solution was stirred for 20 h. The crude product was passed through a squat column of silica (eluant:-hexane:dichloromethane 5:1 (v/v)) to give the title compound as a colourless oil (quantitative). ^{1}H-NMR: 0.25 (s, 9H), 7.30 (m, 3H), 7.47 (m, 2H); ^{13}C-NMR: −0.1, 93.9 (C≡C), 105.2 (C≡C), 123.2, 128.2, 128.5, 131.9; Ir (neat) (ν_{max}, cm^{-1}) 2160 (C≡C).

3.4. 1,8-Diphenyl-1,7-octadiyne

The procedure was analogous to that for diphenylacetylene except that the solution was stirred for 3 h. The crude product was passed through a squat column of silica (eluant:-hexane:dichloromethane 4:1 (v/v)) and then further purified by flash chromatography (eluant:-hexane:dichloromethane 3:1 (v/v), R_f 0.43) to give the title compound as a colourless oil (quantitative). ^{1}H-NMR: 1.86 (m, 4H), 2.55 (m, 4H), 7.33 (m, 6H), 7.51 (m, 4H); ^{13}C-NMR: 18.8, 27.7, 80.9 (C≡C), 89.7 (C≡C), 123.9, 127.5, 128.1, 131.5; m/z 258 (M+, 100%), 230 (79); Ir (neat) (ν_{max}, cm^{-1}) 2230 (C≡C).

3.5. 3-Phenyl-2-propyn-1-ol

The procedure was analogous to that for diphenylacetylene. The crude product was purified by flash chromatography (eluant:- dichloromethane:ethyl acetate 10:1 (v/v), R_f 0.57) to give the title compound as a golden oil (quantitative). ^{1}H-NMR (δ, ppm): 4.49 (br s, 2H), 7.26 (m, 3H), 7.43 (m, 2H); ^{13}C-NMR (δ, ppm): 51.0, 85.3 (C≡C), 87.3 (C≡C), 122.5 (q), 128.2, 128.3, 131.6; m/z 132 (M+, 6%), 131 (9), 115 (4); ir (neat) (ν_{max}, cm^{-1}) 2238 (C≡C, stretching).

3.6. 1-(1-Hexynyl)-4-methoxybenzene (1)

To a solution of 4-bromoanisole (0.30 ml, 2.39 mmol) in piperidine (3 ml) was added $Pd(PPh_3)_4$ (138 mg, 1.20×10^{-4} mol), 1-hexyne (0.30 ml, 2.64 mmol), wet $ZnCl_2$ (65 mg, 4.79×10^{-4} mol) and NaI (72 mg, 4.79×10^{-4} mol). The resulting suspension was then stirred at 50°C for 16 h. The reaction mixture was then added to CH_2Cl_2 (40 ml), washed with saturated NH_4Cl (40 ml) and the aqueous layer re-extracted with another portion of CH_2Cl_2 (40 ml). The organic layers were combined, dried and the solvent removed. The crude product was passed through a squat column of silica (eluant:- hexane:dichloromethane 5:1 (v/v), R_f 0.40) and then further purified by flash chromatography, with the same solvent system, to give the title compound as a colourless oil (412 mg, 92%). ^{1}H-NMR: 0.94 (t, 2H, *J* 7 Hz), 1.50 (m, 4H), 2.39 (t, 2H, *J* 7 Hz), 3.79 (s, 3H), 6.80 (d, 2H, *J* 9 Hz), 7.30 (d, 2H, *J* 9 Hz); ^{13}C-NMR: 13.5, 19.0, 21.9, 30.9, 55.0, 80.2 (C≡C), 88.6 (C≡C), 113.8, 132.2, 132.8, 159.0; *m/z*: 188 (M+, 84%), 173 (41), 159 (29), 145 (100), 115 (27); Ir (neat) (ν_{max}, cm^{-1}) 2535 (C≡C).

3.7. Dimethyl 5-(2-phenyl-1-ethynyl)isophthalate (2)

3.7.1. Method A

To a solution of dimethyl 5-bromoisophthalate (200 mg, 7.33×10^{-4} mol) in DMF (3 ml) was added $Pd(PPh_3)_4$ (42 mg, 3.66×10^{-5} mol), phenylacetylene (0.09 ml, 8.21×10^{-4} mol), triethylamine (0.20 ml, 2.76×10^{-3} mol), $ZnCl_2$ (not dried, 20 mg, 1.47×10^{-4} mol), NaI (22 mg, 1.47×10^{-4} mol) and imidazole (10 mg, 1.47×10^{-4} mol). The resulting suspension was then stirred at 60° for 16 h. The reaction mixture was then added to CH_2Cl_2 (40 ml), washed with saturated NH_4Cl (40 ml) and the aqueous layer re-extracted with another portion of CH_2Cl_2 (40 ml). The organic layers were combined, dried and the solvent removed. The crude product was then passed through a short column of silica (eluant:-dichloromethane) to give a fawn solid. Recrystallisation from hexane gave the title compound as fine colourless needles (160 mg, 75%). Mp 115-116°; Anal. Cald for $C_{18}H_{14}O_4$: C, 73.46; H, 4.79. Found: C, 73.59; H, 4.57; ^{1}H-NMR: 3.97 (s, 6H), 7.37 (m, 3H), 7.54 (m, 2H), 8.36 (d, 2H, *J* 2 Hz), 8.63 (t, 1H, *J* 2 Hz); ^{13}C-NMR: 52.4, 87.3 (C≡C), 91.2 (C≡C), 122.5, 124.4, 128.5, 128.9, 130.0, 130.9, 131.8, 136.5, 165.7 (C=O); *m/z* 294 (M+, 89), 263 (44), 235 (14), 220 (21), 176 (61); Ir (nujol mull) (ν_{max}, cm^{-1}) 1722, 1736 (C = O), 2231 (C≡C).

3.7.2. Method B

To a solution of dimethyl 5-bromoisophthalate (200 mg, 7.33×10^{-4} mol) in DMF (3 ml) was added $Pd(PPh_3)_4$ (42 mg, 3.66×10^{-5} mol), phenylacetylene (0.09 ml, 8.21×10^{-4} mol), DBU (0.20 ml, 1.34×10^{-3} mol), $ZnCl_2$ (not dried, 20 mg, 1.47×10^{-4} mol) and NaI (22 mg, 1.47×10^{-4} mol). The resulting suspension was then stirred at 60° for 3 h. The reaction mixture was then added to CH_2Cl_2 (20 ml), washed with saturated NH_4Cl (20 ml) and the aqueous layer re-extracted with another portion of CH_2Cl_2 (20 ml). The organic layers were combined, washed once with water (40 ml), dried and the solvent removed. The crude product was purified by flash chromatography (eluant:-dichloromethane:hexane 2:1 (v/v), R_f 0.37) and then recrystallised from hexane to give colourless needles (150 mg, 70%).

3.8. GLC experiments

A standard protocol was used for all of the results summarised in Table 2. To a solution of 4-bromoanisole (0.2 ml, 1.6 mmol) in solvent (3 ml) which had been degassed by the freeze thaw method was added the metal catalyst (0.054 mmol), 1-hexyne (0.22 ml, 1.92 mmol), $ZnCl_2$ (not dried, 45 mg, 0.32 mmol), NaI (24 mg, 0.16 mol) and *n*-decane as an internal standard (0.05 ml, 0.26 mmol). The resulting solution was then stirred at 60°C and at regular intervals a sample was withdrawn from the mixture, added to a vial containing 0.5 ml of 5% HCl solution and 0.5 ml of diethyl ether and shaken. The ether layer was subjected to glc analysis on a 30 m × 0.53 mm DB1 Megabore column and the % conversion of 4-bromoanisole to **1** was determined by the relative integrations of **1** versus the total integrations for **1** and 4-bromoanisole relative to the *n*-decane standard.

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