A Convenient High Activity Catalyst for the Sonogashira Coupling of Aryl Bromides

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Abstract: A mixture of Na_2PdCl_4, CuI and $(t\text{-Bu})_3PH^+BF_4^-$ (molar ratio 4:3:8) dispersed in $H_2N(i\text{-Pr})_2{}^+Br^-$ can be used as a "single source" pre-catalyst for the Sonogashira coupling of aryl bromides with various aryl- and alkylacetylenes in $HN(i\text{-Pr})_2$ solvent. Arylacetylenes require just 0.005 mol % of Pd catalyst at 80 °C, with TOFs ranging between 3,200 and 10,000 h^{-1}.

Keywords: cross-coupling; homogeneous catalysis; palladium; phosphane ligands; Sonogashira reaction

Introduction

In the last few years various palladium catalyzed cross-coupling reactions for C–C, C–N and C–O bond formation have evolved to powerful synthetic tools due to dramatic progress in the development of catalysts for such reactions.[1] Now that the problems of activating even the formerly difficult substrates such as (sterically demanding and electron-rich) aryl chlorides have essentially been solved,[2,3] new challenges have to be met. In a recent review on palladium-catalyzed alkynylation reactions Negishi and Anastasia have defined the need for significantly more active catalysts in terms of turnover numbers ($>10^3$) and turnover frequencies as the prohibitive costs of active palladium complexes have prevented many of their applications.[4]

The recent advances in catalyst development for cross-coupling reactions have been driven mainly by the development of ever more elaborate phosphines and N-heterocyclic carbenes.[5] Nonetheless, the overall catalyst activity for Sonogashira type reactions is still modest and nowhere near the level realized in the Suzuki coupling reactions.[6] Typically more than 0.5 mol % of catalyst is required to effect quantitative transformation of substrates other than the commercially less attractive aryl iodides.[7] For the latter substrates, excellent TONs have been realized,[8] while the less reactive aryl bromides have proven to be more resilient. Notable in this respect is work from Arques, Molina et al.[9] and Najera et al.[10] In particular, Doucet, Santelli et al. observed excellent turnover numbers for activated aryl bromides at elevated temperatures (130 °C) in the presence of 5 mol % CuI and small amounts of Pd using a palladium-tetraphosphine complex [*cis*,*cis*,*cis*-1,2,3,4-tetrakis(diphenylphosphinomethyl)cyclopentane], which gave excellent results for activated aryl bromides.[11] Comparable results were obtained when using the palladium complex of a novel tridentate ferrocenylphosphine.[12]

We believe that the development of ever new and ever more complex ligands for palladium is only one part of the story. The other, presently somewhat underdeveloped, side is the selection of ideal reaction conditions through the proper choice of reaction solvent, base, palladium source and certain additives. In order to optimize the catalyst performance of Pd-phosphine complexes for Sonogashira coupling of aryl bromides, we have re-evaluated the performance of two established phosphines, $P(t\text{-Bu})_3$ and $(Ad)_2PBn$ (Ad = 1-adamantyl), which have been used for the Sonogashira coupling of aryl bromides at room temperature at catalyst loadings of 0.5–2 mol % and TOFs of below 50 h^{-1}.[13] We want to demonstrate here that apparently simple modifications of the reaction conditions – primarily the use of the right solvent – can lead to a drastic increase in the activity of such catalysts. This is basically one lesson we learned from our studies of cross-coupling reactions under biphasic reaction conditions.[14]

Results and Discussion

In a first round of screening a number of solvents were employed in the Sonogashira coupling of bromobenzene with phenylacetylene at a catalyst loading of 0.1 mol % Na_2PdCl_4, 0.075 mol % CuI and 2 mol % $(1\text{-Ad})_2PBn$ with $HN(i\text{-Pr})_2$ as the base. Significantly improved results were obtained with DME (yield 99%), while dioxane (yield 68%), toluene (yield 35%) and DMSO (yield 28%) are less efficient. Other solvents, like DMF, DMA, acetonitrile, propylene carbonate, methanol, ethanol and halogenated solvents are of limited or no use at all (yield $<<10\%$). A single explanation for this behaviour is less obvious since solvents can influence the catalytic activity in many ways, i.e., through coordination of the active metal center, solvent

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effects on dipolar (Hughes–Ingold rules) and isopolar transitions states, the solubility of the ionic components or special anionic or cationic solvation.[15]

Under the conditions determined in the first screen, the concentration of catalyst was reduced successively for the reaction of bromobenzene with phenylacetylene: 0.1 mol % Pd (8 h, yield 97%), 0.05 mol % Pd (20 h, yield 98%) and 0.01 mol % (20 h, yield 74%). It should be noted that the outcome of the reaction is strongly dependent on the quality of the DME; the best results are obtained with scrupulously dried (over potassium) solvent. This motivated us to look for other suitable solvents. Fortunately, a very simple approach was successful. Using $HN(i\text{-}Pr)_2$ not only as a base but also as solvent results in another significant increase of the catalytic activity: 0.05 mol % (5 h, yield 95%), 0.01 mol % (18 h, yield 93%), 0.005 mol % (36 h, 89%, TON 17,800), 0.002 mol % (72 h, yield 56%, TON 28,000). The use of $HN(i\text{-}Pr)_2$ gives excellent yields even with 0.005 mol % of catalyst. We also tested other amines like NEt_3 and $HNEt_2$ as cheap solvent/bases for the Sonogashira coupling. However, the activity of the catalyst in these solvents is only modest, while with Cy_2NH the results are comparable to $(i\text{-}Pr)_2NH$. It is important to note that homocoupling of acetylenes, which is a typical problem in Sonogashira reactions with copper co-catalysts[16] and which has led to the development of numerous copper-free protocols,[17] does not occur to a significant extent with the catalytic system described here.

When dealing with extremely small amounts of highly efficient catalyst, we obviously ran into problems on weighing sub-mg amounts of Na_2PdCl_4, CuI and the respective phosphine. It is obvious that this effort is required for each coupling reaction. Consequently, we were interested in increasing the efficiency of the preparative work and decided to premix all of the three components [Na_2PdCl_4, CuI and $(t\text{-}Bu)_3PH^+BF_4^-$] needed to form the catalyst. The phosphonium salt $(t\text{-}Bu)_3PH^+BF_4^-$ is not sensitive to oxidation, but immediately generates $P(t\text{-}Bu)_3$ in the basic amine solvent.[18] Furthermore, in order to obtain weighable amounts of catalyst, we diluted the mixture of the pre-catalyst with an inert solid. Since all coupling reactions are performed in $(i\text{-}Pr)_2NH$ which acts as the solvent/base and since the respective ammonium salt is a product of all reactions, we decided to use $(i\text{-}Pr)_2NH_2^+Br^-$ as an inert matrix for the catalyst components. In order to prepare a ready-made Sonogashira catalyst we mixed the appropriate amounts of Na_2PdCl_4, CuI and $(t\text{-}Bu)_3P$ and added the nine-fold mass of $(i\text{-}Pr)_2NH_2^+Br^-$. After intimate mixing a pale brownish powder was obtained, consisting of $(i\text{-}Pr)_2NH_2^+Br$- and 10 mass % of catalyst components, which essentially is a "single source" (pre)-catalyst. For small-scale reactions it may be convenient to dilute the active component further to 1% content. This Sonogashira catalyst mixture can be weighed in air and stored under a nitrogen atmosphere for many weeks without loss in activity. It is important to note in this respect that $H_2N(i\text{-}Pr)_2^+Br^-$ is not very hygroscopic.

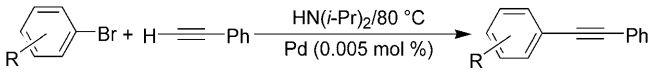
With these two highly active catalysts at hand Sonogashira-type coupling reactions of various aryl bromides and phenylacetylene were performed at catalyst loadings of 0.005 mol % Pd in excellent yields, with $(t\text{-}Bu)_3P$ being superior for most substrate combinations (Table 1).

Activated aryl bromides react within a few hours, while deactivated, electron-rich or sterically hindered aryl bromides couple within less than 20 h at 80 °C. An illustration of the high efficiency of such catalysts is the fact that for the synthesis of 1 mol coupling product (*ca.* 200 g of a 200 Dalton compound), 5 mg Pd are sufficient.[19]

Other acetylenes like trialkylsilylacetylenes, propargylic alcohol and alkylacetylenes are also of great synthetic value.[4] In order to broaden the scope of the catalysts presented here, we investigated the coupling of various aryl bromides with such acetylenes at low catalyst loading. As shown in Table 2 all coupling reactions proceeded smoothly at catalyst concentrations of 0.01 to 0.1 mol %.

Even propargylic alcohol, which is normally difficult to activate in Sonogashira reactions can be coupled in excellent yields using only 0.01 mol % Pd. The key to success, i.e., high TON, lies in carefully drying the propargyl alcohol prior to use with anhydrous K_2CO_3. As expected 1-hexyne is the least reactive substrate and therefore requires by far the highest catalyst loading (0.1 mol %). We attribute this to the contamination of commercially available 1-hexyne with 1-bromobutane. The reactions involving 2-methyl-3-butyn-2-ol are useful since the respective coupling products can be con-

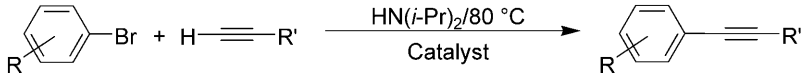
Table 1. Reactions of phenylacetylene and aryl bromides.



R	*T* [h]	Yield [%]/TON[a]	Yield[%]/TON[b]
4-NO_2	5	96/19,200	91/18,200
4-CH_3CO	6	94/18,800	94/18,800
4-COOEt	7	98/19,600	94/18,800
4-Cl	9	93/18,600	92/18,400
3-CF_3	7	93/18,600	89/17,800
2-CF_3	9	94/18,800	88/17,600
H	11	92/18,400	90/18,000
4-Me	11	94/18,800	91/18,200
2-Me	14	90/18,000	88/17,600
2,6-Me_2	20	84/16,800	82/16,400
4-MeO	20	92/18,400	91/18,200
2-MeO	20	87/17,400	86/17,200
4-NMe_2	20	93/18,600	92/18,400

[a] Using $P(t\text{-}Bu)_3$.
[b] Using $(Ad)_2PBn$.

Table 2. Reactions of aryl bromides and various acetylenes.[a]



R	R′	*t* [h]	[Pd] [mol%]	Yield [%]/TON
4-NO_2	TMS	12	0.01	94/9,400
4-CH_3CO	TMS	12	0.01	96/9,600
H	TMS	20	0.01	93/9,300
4-Me	TMS	20	0.01	95/9,500
4-MeO	TMS	20	0.02	92/4,600
4-NO_2	CH_2OH	5	0.01	92/9,200
4-CH_3CO	CH_2OH	6	0.01	93/9,300
H	CH_2OH	12	0.01	90/9,000
4-Me	CH_2OH	14	0.01	93/9,300
4-MeO	CH_2OH	20	0.01	87/8,700
4-Ac	CMe_2OH	20	0.02	97/4,850
4-Cl	CMe_2OH	20	0.02	94/4,700
4-OMe	CMe_2OH	20	0.02	93/4,650
3-NO_2	$CM_{e2}OH$	20	0.02	97/4,850
4-Me	CMe_2OH	20	0.02	94/4,700
4-CH_3CO	*n*-Bu	12	0.1	93/930
H	*n*-Bu	16	0.1	88/880
4-MeO	*n*-Bu	24	0.1	85/850

[a] Catalyst: Na_2PdCl_4, CuI and (*t*-Bu)$_3$P (4:3:8 molar ratio) dispersed in (*i*-Pr)$_2NH_2^+Br^-$.

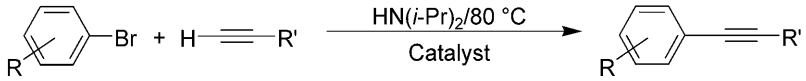
verted into the respective terminal acetylenes by base-induced cleavage of acetone.[20]

Finally, we took a closer look at basic kinetic aspects of the coupling reactions and determined the turnover frequencies (TOF) of the respective catalysts, all of which were resolved on incomplete reaction (20–40% conversion) of the reactants (Table 3).

Again, the coupling of phenylacetylene is the fastest reaction with a TON of close to 10,000 h^{-1} for 4-nitrobromobenzene. Even deactivated 4-bromoanisole reacts at a rate of 3,240 h^{-1} with the (*t*-Bu)$_3$P-based Pd-catalyst, while coupling reactions with (Ad)$_2$PBn as ligand proceed more slowly. Excellent TOFs are also observed for propargylic alcohol and aryl bromides with TOFs ranging from 1,240 h^{-1} to 2,900 h^{-1}.

Finally, the lack of understanding of when and why a certain Pd catalyst is highly active, highlights the urgent need for a more detailed mechanistic understanding of the Sonogashira reaction. In this respect, a recent study on the Heck coupling by Hills and Fu may shed more light on why amine bases render Pd-based catalysts so much more effective. In contrast to commonly used bases like Cs_2CO_3 or other metal carbonates, amines like Cy_2NMe,[21] appear to be much more efficient in restoring the active PdL_2 species from L_2PdHCl.[22] Even though the mechanistic setup of the Sonogashira reaction is different, especially when it comes to the formal abstraction of HX, the role of the amine is notable and might have implications for the Sonogashira coupling reactions described here.

Table 3. Determination of the TOF [h^{-1}] for several Sonogashira coupling reactions.[a]



R	R′	PR_3	[Pd] [mol%]	TOF [h^{-1}]
4-NO_2	Ph	(Ad)$_2$PBn	0.005	2,990
4-NO_2	Ph	(*t*-Bu)$_3$P	0.005	9,900
H	Ph	(Ad)$_2$PBn	0.005	1,640
H	Ph	(*t*-Bu)$_3$P	0.005	4,860
4-MeO	Ph	(*t*-Bu)$_3$P	0.005	3,240
4-NO_2	CH_2OH	(*t*-Bu)$_3$P	0.01	2,900
4-CH_3CO	CH_2OH	(*t*-Bu)$_3$P	0.01	2,460
H	CH_2OH	(*t*-Bu)$_3$P	0.01	1,240

[a] Catalyst: Na_2PdCl_4, CuI and (*t*-Bu)$_3$P (4:3:8 molar ratio) dispersed in (*i*-Pr)$_2NH_2^+Br^-$.

Conclusions

We have shown here that minor variations in the reaction conditions lead to catalytic systems with drastically increased activity. The advantages of the present approach in the context of Sonogashira coupling reactions are obvious:

- The ready-made Sonogashira catalyst provides a simple and general recipe for the user of the Sonogashira coupling.
- The choice of the best conditions in the well known Sonogashira coupling protocol results in a drastic increase in the activity of the catalyst, such that only 0.005 mol % of Pd are required for the reactions of aryl bromides and phenylacetylene.
- The key to such high activity catalysts with TOFs of up to 10,000 h^{-1} is the use of HN(*i*-Pr)$_2$ as solvent and base.
- It is also important to note that another pertinent problem of Sonogashira coupling reactions, i.e., the formation of homocoupling product does not occur to a significant extent ($<1\%$) and consequently an excess of acetylene is not required.

Experimental Section

General Experimental Procedures

All reactions were carried out under an inert atmosphere of argon using standard Schlenk techniques. Aryl bromides and acetylenes were used as received and deoxygenated prior to the coupling reactions, except for propargylic alcohol which was dried over K_2CO_3, deoxygenated and stored over molecular sieve (4 Å). HN(*i*-Pr)$_2$ was dried over KOH, distilled, deoxygenated and stored over molecular sieve (4 Å). ^{1}H NMR spectroscopy was performed on a Bruker 200 AC at 293 K. Column chromatography was carried out on silica MN60 (63–200 μm), TLC on Merck plates coated with silica gel 60, F254. The identity and purity of all compounds described here was established by ^{1}H NMR (all compounds have been described in the literature previously, references given) and by gas chromatography. GC(/MS): GC-MS Fisons "GC 8000" with integrated MS "MD 800". Carrier gas: He at 50 kPa with a 1:25 split. Injection temperature: 230 °C. Column: Varian "CP-Sil 8 CB", length 15 m, inner diameter 0.25 mm, layer thickness 1 μm. Temperature program: 60 °C for 9 min, heating to 210 °C with 5 °C/min, 210 °C for 9 min, heating to 265 °C at 6 °C/min.

Ready-Made Sonogashira Catalyst

A mixture of CuI (9.5 mg, 0.05 mmol) Na_2PdCl_4 (19.7 mg, 0.067 mmol) and the respective phosphonium salt [(*t*-Bu)$_3$P·HBF$_4$: 38.7 mg, 0.133 mmol or (Ad)$_2$PBn·HBr: 63.0 mg, 0.133 mmol] was finely ground. The molar ratio of Pd:Cu:P is 4:3:8. Subsequently, the nine-fold amount of $H_2N(i\text{-}Pr)_2^+$ Br^- was added and the mixture was intimately mixed. At a 0.005 mol % level, this catalyst mixture is sufficient for the synthesis of 1.3 mol of coupling product.

General Procedure for the Sonogashira Coupling of Aryl Bromides and Acetylenes

A solution of the aryl bromide (10 mmol) and the respective acetylene (10.3 mmol) in HN(*i*-Pr)$_2$ (10 mL) was carefully degassed (freeze and thaw). After addition of the ready-made Sonogashira catalyst (0.005–0.1 mol %) the mixture was heated to 80 °C with vigorous stirring. Precipitation of $H_2N(i\text{-}Pr)_2^+$ Br^- indicated the start of the reaction and stirring was continued for the given time. After cooling to room temperature, the reaction mixture was filtered and the precipitate washed with HN(*i*-Pr)$_2$ (25 mL) or Ef_2O. The volatiles were removed under vacuum and the residue was purified by flash column chromatography on silica (heptane or cyclohexane/ethyl acetate).

^{1}H NMR Spectra (200 MHz, $CDCl_3$) of the Coupling Products

4-(Phenylethynyl)nitrobenzene:[23] δ = 8.19 (m, 2H), 7.64 (m, 2H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.41–7.32 (m, 3H).

Phenyl-(2-trifluoromethylphenyl)acetylene:[24] δ = 7.61 (d, *J* = 7.6 Hz, 2H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.41 (dd, *J* = 7.6 and 7.4 Hz, 1H), 7.35–7.28 (m, 4H).

Phenyl-(3-trifluoromethylphenyl)acetylene:[24] δ = 7.78 (s, 1H), 7.62 (m, 1 H), 7.56–7.42 (m, 4H), 7.36 (m, 2 H), 7.29 (m, 1 H).

4-(Phenylethynyl)acetophenone:[24] δ = 7.90 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.54 (m, 2H), 7.33 (m, 3H), 2.56 (s, 3H).

4-(Phenylethynyl)chlorobenzene:[25] δ = 7.54–7.43 (m, 4H,), 7.36–7.31 (m, 5H).

Diphenylacetylene:[11c] δ = 7.51–7.46 (m, 4H,), 7.34–7.30 (m, 6H).

Ethyl 4-(phenylethynyl)benzoate:[23] δ = 8.03 (d, *J* = 8.1 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.56–7.51 (m, 2H), 7.41–7.32 (m, 3H), 4.39 (q, *J* = 7.2 Hz, 2H), 1.41 (t, *J* = 7.2 Hz, 3H).

4-(Phenylethynyl)toluene:[10] δ = 7.54–7.31 (m, 7H), 7.15 (d, *J* = 7.8 Hz, 2H), 2.34 (s, 3H).

2-(Phenylethynyl)toluene:[10] δ = 7.53–7.49 (m, 2H), 7.46 (d, *J* = 8.7 Hz, 2H), 7.32 (m, 3H), 6.86 (d, *J* = 8.7 Hz, 2H), 3.81 (s, 3H).

2,6-Dimethylpheny-phenylacetylene:[13a] δ = 7.59 (m, 2H), 7.44–7.28 (m, 3H), 7.19 (m, 3H), 2.56, (s, 6H).

4-(Phenylethynyl)anisole:[25] δ = 7.53–7.49 (m, 2H), 7.46 (d, *J* = 8.7 Hz, 2H), 7.32 (m, 3H), 6.86 (d, *J* = 8.7 Hz, 2H), 3.81 (s, 3H).

2-(Phenylethynyl)anisole:[26] δ = 7.94–6.73 (m, 9H), 3.81 (s, 3H).

4-(Phenylethynyl)-N,N-*dimethylaminobenzene:*[13a] δ = 7.55 (m, 2H), 7.42 (m, 2H), 7.33 (m, 2H), 6.42 (m, 3H), 3.01 (s, 6H).

2-(4-Nitrophenyl)-1-ethynyl(trimethyl)silane:[27] δ = 8.21 (d, *J* = 10.3 Hz, 2H), 7.52 (d, *J* = 10.3 Hz, 2H) 0.12 (s, 9H).

2-(4-Acetylphenyl)-1-ethynyl(trimethyl)silane:[27] δ = 7.87 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 2.57 (s, 3H) 0.09 (s, 9H).

2-Phenyl-1-ethynyl(trimethyl)silane:[27] δ = 7.53–7.42 (m, 2H,), 7.37–7.31 (m, 3H), −0.01 (s, 9H).

2-(4-Methylphenyl)-1-ethynyl(trimethyl)silane:[27] δ = 7.41 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 2.35 (s, 3H,), 0.07 (s, 9H).

2-(4-Methoxyphenyl)-1-ethynyl(trimethyl)silane:[25] δ = 7.40 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 3.79 (s, 3H,), 0.08 (s, 9H).

3-(4-Nitrophenyl)prop-2-yn-1-ol:[28] δ = 8.14 (d, *J* = 10.5 Hz, 2H), 7.55 (d, *J* = 10.5 Hz, 2H), 4.47 (d, *J* = 6.2 Hz, 2H), 1.67 (t, *J* = 6.2 Hz, 1H).

3-(4-Acetylphenyl)prop-2-yn-1-ol:[30] δ = 7.87 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 4.63 (s, 2H), 2.58 (s, 3H), 2.21 (s, 1H).

3-(Phenyl)prop-2-yn-1-ol:[29] δ = 7.51–7.46 (m, 2H), 7.34–7.30 (m, 3H), 4.37 (d, *J* = 6.0 Hz, 2H), 1.73 (t, *J* = 6.0 Hz, 1H).

3-(4-Methylphenyl)prop-2-yn-1-ol:[30] δ = 7.37 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 4.73 (d, *J* = 6.0 Hz, 2H), 2.36 (s, 3H), 1.94 (t, *J* = 6.0 Hz, 1H).

3-(4-Methoxyphenyl)prop-2-yn-1-ol:[30] δ = 7.41 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 4.67 (d, *J* = 6.1 Hz, 2H), 3.82 (s, 3H), 1.81 (t, *J* = 6.1 Hz, 1H).

4-(1-Hexyn-1-yl)acetophenone:[31] δ = 7.83 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 2.58 (s, 3H), 2.43 (t, *J* = 7.0 Hz, 2H,), 1.53–1.17 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H).

1-Hexyn-1-yl)benzene:[31] δ = 7.62–7.49 (m, 2H), 7.38–7.29 (m, 3H), 2.45 (t, *J* = 6.9 Hz, 2H,), 1.56–1.21 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H).

4-(1-Hexyn-1-yl)anisole:[31] δ = 7.45 (d, *J* = 8.3 Hz, 2H), 6.81 (d, *J* = 8.3 Hz, 2H), 3.79 (s, 3H), 2.39 (t, *J* = 7.1 Hz, 2H,), 1.54–1.20 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H).

4-(4-Methoxyphenyl)-2-methyl-but-3-in-2-ol:[13a] δ = 7.35 (d, *J* = 7.1 Hz, 2H), 6.82 (d, *J* = 8.9 Hz, 2H,), 3.78 (s, 3H), 2.02 (s, 1H), 1.58 (s, 6H).

4-(4-Acetylphenyl)-2-methyl-but-3-in-2-ol:[13a] δ = 7.88 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 2.57 (s, 3H) 2.20 (s, 1H), 1.60 (s, 6H).

4-(4-Methylphenyl)-2-methyl-but-3-in-2-ol:[32] δ = 7.31 (d, *J* = 8.05 Hz, 2H, ArH-2), 7.10 (d, *J* = 7.95 Hz, 2H, ArH-3), 2.31 (s, 3H), 2.20 (s, 1H), 1.59 (s, 6H).

4-(3-Nitrophenyl)-2-methyl-but-3-in-2-ol:[33] δ = 8.23 (s, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.50 (dd, *J* = 7.9 Hz, 7.8 Hz, 1H), 2.27 (s, b, 1H), 1.61 (s, 6H).

4-Methoxyphenyl acetylene:[32] δ = 7.43 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 3H), 2.98 (s, 1H).

4-Chlorophenylacetylene:[32] δ = 7.30 (d, *J* = 8.6 Hz, 2H), 7.18 (d, *J* = 8.6 Hz, 2H), 2.96 (s, 1H).

4-Methylphenyl acetylene:[32] δ = 7.26 (d, *J* = 7.6 Hz, 2H), 7.00 (d, *J* = 7.6 Hz, 2H), 2.88 (s, 1H), 2.21 (s, 3H).

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