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Efficient Method for Propargylation of Aldehydes Promoted by Allenyl Boron Compounds under Microwave Irradiation

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Abstract

The propargylation of aldehydes promoted by microwave irradiation using allenyl boron compounds in a chemo- and regioselective way is described. The corresponding products were obtained in short reaction time, high yield and purity without the need of any solvent when allenyl boronic acid pinacol ester was used, or using a minimal amount of acetone when potassium allenyl trifluoroborate was used.

Keywords

boron compounds; microwave; propargylation; regioselectivity; synthesis

Introduction

The propargylation of carbonyl compounds is widely used in the synthesis of biologically active natural products.[1] Some examples can be found in the synthesis of histrionicotoxin,[2] rhizopodin,[3] bafilomycin,[4] bryostatin,[5] vancosamine,[6] and macrolactin A.[7]

Although there are several stereoselective methods described for the reaction of propargyl or allenyl organometallics with carbonyl compounds,[1,8] the control of the regioselectivity is still a major concern. This is mainly due to the metallotropic rearrangement of propargyl and allenyl organometallics in solution resulting in mixtures of the two reagents.[9] Thus, upon reaction with an aldehyde, mixtures of propargylic and allenic alcohols can be obtained through a chelate transition state (S_E2').

Attempts to improve the regioselectivity of the propargylation reaction by using allenic organometallic species of Zn,[10] Cd,[11] Ga,[12] In,[13] Ti,[14] and Al[15] were described. However, the majority of these methods involve reagents that are difficult to prepare and handle due to the sensitivity to air and moisture.

The use of less reactive species based on tin,[16-18] silicon[19] or boron[20-23] to perform propargylation reactions typically requires catalysis by Lewis acids or bases and although the utility of allenylstannanes is further indicated by the commercial availability of some of them, the toxicity of these compounds makes them inappropriate for the use in pharmaceutical synthesis.[24] Moreover, the removal of tributyltin residues from reaction mixtures is also a major issue.

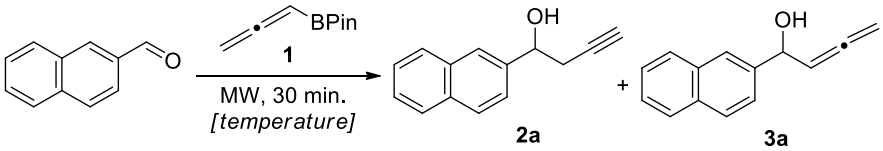
The use of microwave irradiation for the formation of new C-C bonds is nowadays widely used and offers several advantages such as the increment in the product yield, reduction of reaction time and the possibility to perform solvent-free reactions.[25] However, the relative “greenness” of microwave assisted reactions is still a point of discussion. For example the question about the energy efficiency of microwave vs. conventionally heated reactions must, in general, be evaluated with great care on a case-by-case basis. Even so, the search for safer alternatives to current synthetic methodologies avoiding the use of moisture/air-sensitive organometallics and, more important, the development of solvent-free protocols are in accordance with the concept of Environmental Impact Factor (*E* factor).[26]

Within this context, the development of solvent-free methods is highly desirable since the difficult for solvent recycling in academic laboratories and chemical manufacturing plants is universal. In addition, a reliable method for the propargylation reaction which could involve the use of commercially available and stable allenyl- or propargyl compounds without the need of special conditions such as dry solvents or complex catalysts is a subject of great interest.

Results and Discussion

For preliminary optimization of the reaction conditions, 2-naphtaldehyde (1 mmol) and allenylboronic acid pinacol ester, **1** (1.5 mmol) in a capped vial were irradiated in a MW synthesizer for 30 minutes under different temperatures. The results are depicted in Table 1.

Table 1: Propargylation of 2-naphtaldehyde using allenylboronic acid pinacol ester, **1** under different temperatures.[a]



Entry	Temp. (°C)	**2a:3a**[b]	(%)[c]
1	75	97:3	94
2	100	98:2	97
3	125	98:2	81
4	150	98:2	84

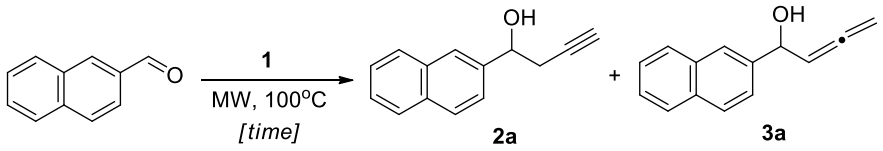
[a]*Reaction conditions:* Reactions were performed with 2-naphtaldehyde (1 mmol), **1** (1.5 mmol) under MW irradiation (300 W) for 30 min. at the temperature indicated. [b]Determined by GC analysis; [c] Isolated yield.

In all cases, the desired propargylic product **2a** was obtained together with a small amount of the corresponding allenic product **3a**. When the reaction was performed at 75^{o}C, good conversions of 2-naphtaldehyde into the corresponding products were observed (Table 1, entry 1). The best result was observed when the temperature was increased to 100^{o}C when the products were obtained in 97% yield in a 98:2 ratio

(Table 1, entry 2). Higher temperatures gave lower yields or the decomposition of the boron reagent, **1** (Table 1, entries 3 and 4).

Next, the shortest time necessary for the formation of the products at 100°C was evaluated. The results are depicted on Table 2. From Table 2, it can be seen that the increment in the reaction time resulted in higher yields without major changes in the ratio of **2a**:**3a**.

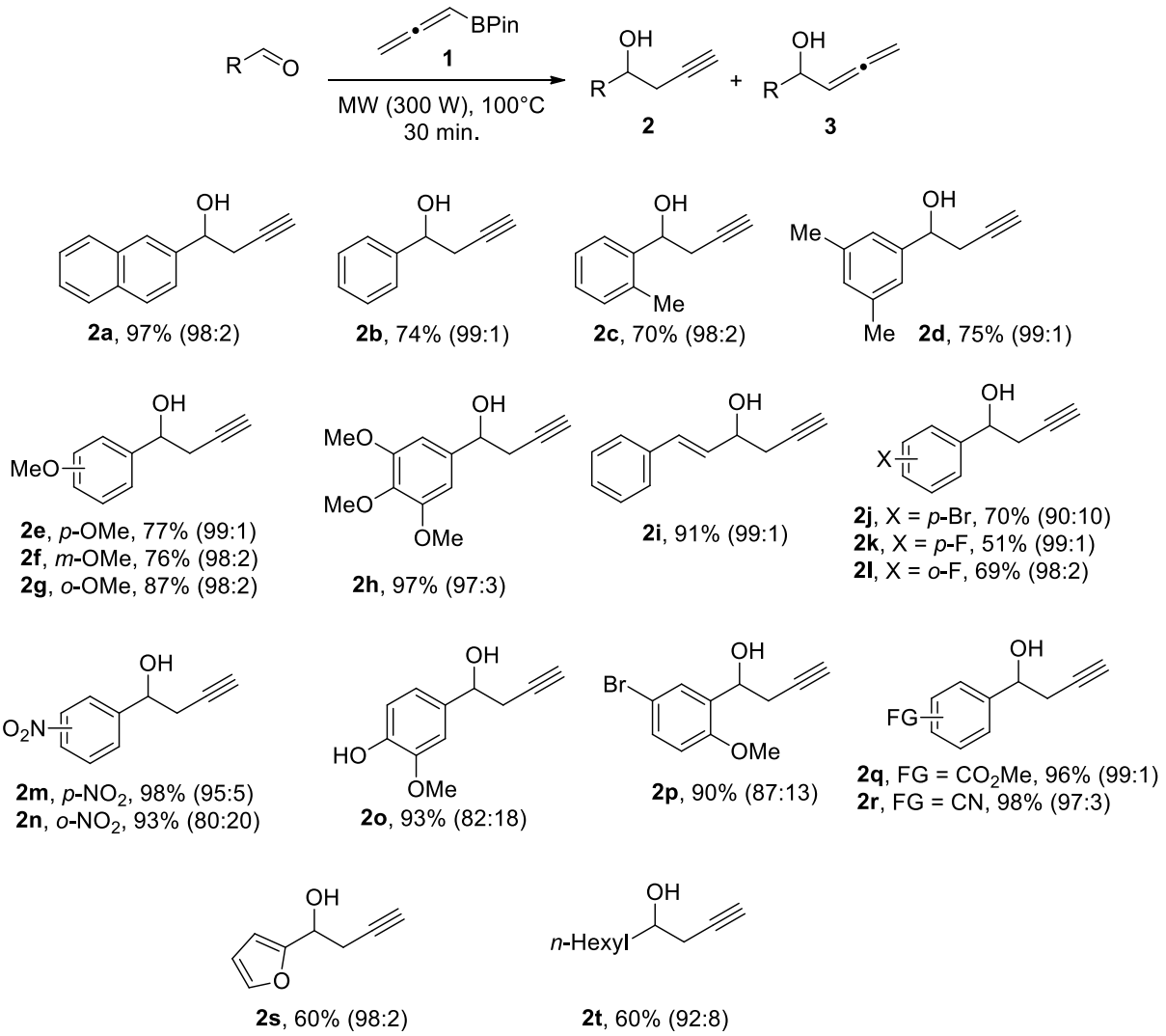
Table 2: Propargylation of 2-naphtaldehyde using allenylboronic acid pinacol ester, **1** using different reaction times.[a]



Entry	Time. (min.)	**2a:3a**[b]	(%)[c]
1	5	98:2	87
2	10	98:2	88
3	15	97:3	88
4	20	98:2	95
5	30	97:3	97

[a]*Reaction conditions:* Reactions were performed with 2-naphtaldehyde (1 mmol), **2** (1.5 mmol) under MW irradiation (300 W) at 100°C for the time indicated. [b]Determined by GC analysis; [c] Isolated yield.

The optimized reaction conditions, namely: 2-naphtaldehyde (1.0 mmol), **1** (1.5 mmol) under 300 W potency microwave irradiation were then applied for the propargylation reaction of aldehydes containing a wide range of functional groups and the results are shown on Scheme 1. In all cases the reaction proceeded smoothly leading to the conversion of aldehydes into the corresponding homopropargylic alcohols **2** in moderate to high yields and in a very regioselective way, while the propargylated product was obtained as the major product in all cases.



Scheme 1: Scope of propargylation reaction. Reactions were performed with the appropriate aldehyde (1 mmol), **1** (1.5 mmol) under microwave irradiation (300 W) at 100°C for 30 min. Isolated yields. The number in parentheses refers to the mixture of propagyl and allenyl regioisomers determined by GC analysis.

Aromatic aldehydes such as benzaldehyde, 2-Me-benzaldehyde and 3,5-Me-benzaldehyde gave the corresponding products **2b**-**d** in good yields in a regioselective way regardless of the position of the substituent on the aromatic ring.

When aldehydes containing electron-donating groups such as 2-, 3- or 4-MeO-benzaldehyde or 3,4,5-trimethoxybenzaldehyde were used, the corresponding products **2e**-**h** were obtained in good yields and regioselectivities. In the same way, aldehydes containing electron-withdrawing groups such as the nitro group also reacted without influence of the substituent location to give the corresponding

homopropargylic alcohols **2m** and **2n** in good yields. It is interesting to note that the nitro group remained intact under the reaction conditions. Usually, this group is sensitive to reduction when methods involving metals are used.

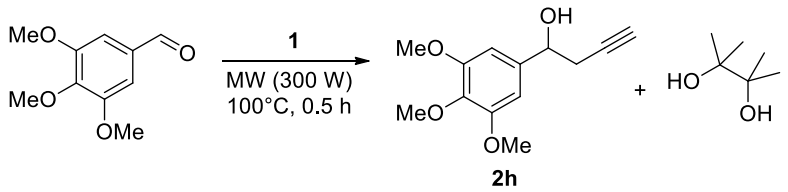
In addition, aldehydes containing halogens **2j**-**l** also gave the corresponding products in moderate yields. These results indicated that the substituent nature, whether electron-donating or electron-withdrawing, have no dramatic influence on the product yields.

When the α,β-unsaturated aldehyde **2i** was used, the corresponding 1,2-addition product was obtained exclusively.

The chemoselectivity of the method was evaluated using aldehydes containing different functionalities. For example, the use of vanillin, an aldehyde containing the acidic phenol group as substituent, gave the corresponding product **2o** in 93% yield in a 82:18 ratio of regioisomers. In the same way, when aldehydes containing an ester or nitrile group were used, the corresponding products **2q** and **2r** were obtained in good yields. The use of a heteroaromatic or an aliphatic aldehyde as substrates under the optimized conditions gave the corresponding homopropargylic alcohols **2s-t** in moderate yields.

The development of a solvent-free protocol for propargylation of aldehydes based on microwave irradiation should take into account not only the reaction itself but also an effective method for the extraction of the obtained products. Despite the excellent results described on Scheme 1, a factor that must be taken into consideration is the removal of the desired alcohols **2a**-**t** from pinacol - the byproduct obtained in the reaction. There are some examples in the literature based on the removal of pinacol by distillation *in vacuo* (50^{o}C/0.05 mbar).[27] However, this technique can only be applied for non-volatile samples. More recently, Aggarwal and coworkers[28] described an efficient method for removal of pinacol based on the formation of an azeotrope with water under moderate vacuum. Thus, a test experiment was performed using compound **2h**. The crude product obtained from the reaction was dissolved in 50% aqueous methanol and the volatile materials were removed using a rotary evaporator. The procedure monitored by gas chromatography and was repeated until the crude mixture displayed less than 1 mol % of pinacol remaining. The results are described on Table 3.

Table 3: Number of cycles to remove pinacol from the crude product.[a]

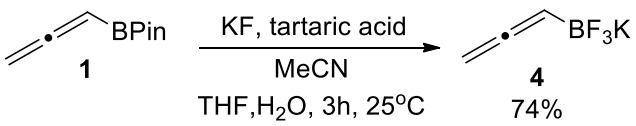


2h

Entry	Cycle	**2h**:**pinacol**(%)[b]
1	1	70:30
2	2	77:23
3	3	84:16
4	4	93:7
5	5	99:1

[a]*Reaction conditions:* Reaction was performed using 3,4,5-trimethoxybenzaldehyde (1 mmol), **1** (1.5 mmol) under microwave irradiation (300 W) at 100°C for 0.5 h. The crude product was dissolved in 50% aqueous methanol (10 mL) and the solvents were removed on a rotary evaporator (45–50°C/25–15 mbar). [b]Determined by GC analysis.

Although the desired products **2a**-**t** having been obtained along with a small proportion of the corresponding regioisomer in some cases, in the development of new synthetic methods, it is desirable that it gives the corresponding product as a single compound. Our group described the synthesis of homopropargylic alcohols using potassium allenyltrifluoroborate as the propargylating agent in a very regioselective way.[29-30] Thus, allenylboronic acid pinacol ester, **1** was converted into the corresponding trifluoroborate using the procedure described by Lloyd-Jones and coworkers.[31] The desired product **4** was obtained in good yield and characterized by ^{1}H, ^{13}C, ^{11}B and ^{19}F NMR[32] (Scheme 2).

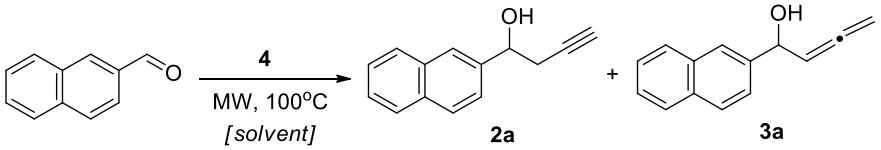


Scheme 2: Synthesis of potassium allenyltrifluoroborate, **4**.

Potassium allenyltrifluoroborate, **4** is a crystalline solid and despite several microwave promoted reactions can be conducted without the use of solvents, the propargylation reaction using 2-naphtaldehyde and **4** under the previously optimized conditions gave the desired product in low conversion (Table 4, entry 1).

In order to find an appropriate and suitable solvent that could be used in small amount to promote the reaction, some commonly solvents were screened and the best result was observed when a small amount of acetone was used, where **2a** was obtained in 92% yield as a single regioisomer (Table 4, entry 2). Low conversions were observed when water or a 1:1 mixture of acetone water was used in the reaction (Table 4, entries 3 and 4). The use of alcohols also gave the desired product in lower yields (Table 4, entries 5 to 7). Finally, when a less polar solvent was used, the observed conversion was only 10% (Table 4, entry 8).

Table 4: Propargylation of 2-naphtaldehyde using potassium allenyltrifluoroborate, **4** using different solvents[a]



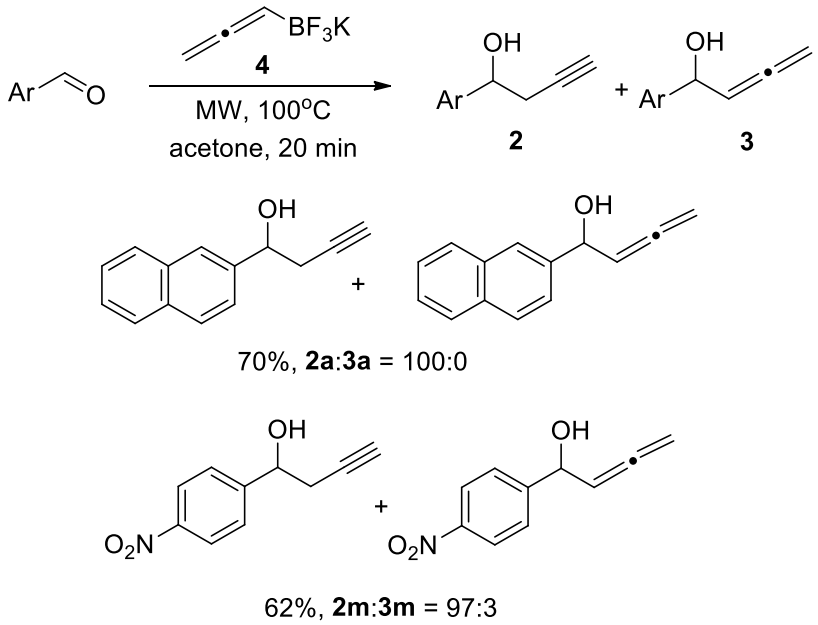
Entry	Solvent	Time (min)	(**2a**:**3a**)[b]	(%)[c]
1	-	-	-	6
2	acetone	30	100:0	92
3	water	30	100:0	3
4	acetone:water	30	100:0	10
5	ethylene glycol	20	100:0	45
6	ethanol	20	100:0	45
7	methanol	20	100:0	30
8	dichloromethane	20	100:0	10

[a]*Reaction conditions:* Reactions were performed with 2-naphtaldehyde (1 mmol), **4** (1.5 mmol) under MW irradiation (300 W) at 100°C for the time indicated using the appropriate solvent (500 μL). [b]Determined by GC analysis; [c]Isolated yield.

Two factors must be taken into consideration by using a boron specie in the reaction. The first is that the atomic efficiency[33] using potassium allenyltrifluoroborate, **4**

(62%) or allenylboronic acid pinacol ester, **1** (58%) is higher when compared to the commercially available allenyltributyltin (22%) for similar reactions.

The second refers to the regioselectivity of the reaction. Despite the reaction using 2-naphtaldehyde led only to the propargyl isomer **2a**, when the same reaction conditions were applied to 4-nitro-benzaldehyde, the desired product **2m** was once again obtained with a small amount of the corresponding regioisomer **3m** in a 97:3 ratio (Scheme 3). These facts indicated that the control of the regioselectivity of the reaction is governed by other effects in addition to the nature of the boron reagent.



Scheme 3: Propargylation of aldehydes using potassium allenyltrifluoroborate, **4**.

Conclusion

In summary, we have shown an efficient method for the propargylation of aldehydes promoted by microwave irradiation using allenyl boron compounds in a chemo- and regioselective way. The corresponding products were obtained in a short reaction time, high yield and purity without the need of a solvent when allenyl boronic acid pinacol ester was used, or using a minimal amount of acetone when potassium allenyl trifluoroborate was used. The method is simple, fast and general allowing further applications in the synthesis of more complex compounds.

Experimental

Materials and Methods

All reagents and solvents used were previously purified and dried in agreement with the literature.[34] The aldehydes and allenylboronic acid pinacol ester, **1** were purchased from Aldrich Chemical Co. and used as received. Reactions were monitored by thin-layer chromatography on 0.25 mm E. Merck silica gel 60 plates (F_{254}) using UV light, vanillin and *p*-anisaldehyde as visualizing agents. ^{1}H NMR and ^{13}C NMR data were recorded in $CDCl_3$ or DMSO-d_6. The chemical shifts are reported as delta (δ) units in parts per million (ppm) relative to the solvent residual peak as the internal reference. ^{11}B (128 MHz) and ^{19}F NMR (376 MHz) spectra were obtained in DMSO-d_6. Spectra were calibrated using BF_3•Et_2O (0.0 ppm) as external reference in the case of ^{11}B NMR and chemical shifts were referenced to external CF_3CO_2H (0.0 ppm) in the case of ^{19}F NMR. Coupling constants (*J*) for all spectra are reported in Hertz (Hz).

General procedure for the propargylation of aldehydes using allenylboronic acid pinacol ester, 1 promoted by microwave irradiation: A vial containing the appropriate aldehyde (1 mmol) and allenylboronic acid pinacol ester, **1** (1.5 mmol, 250 mg) was irradiated at 300 W at 100^{o}C for 30 minutes. The vial contents were diluted with EtOAc (10 mL) and washed with water (2 x 15 mL). The combined organic phase was dried over $MgSO_4$, filtered, and the solvent was removed *in vacuo* followed by purification by a flash column chromatography [hexanes:EtOAc (8:2)] to yield **2a**-**t**.

(**2a**) *1-(naphth-2-yl)but-3-yn-1-ol:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79-7.75 (m, 4H, $H_{naphthyl}$), 7.44-7.39 (m, 2H, $H_{naphthyl}$), 7.18 (s, 1H, $H_{naphthyl}$), 4.98 (t, *J*= 6.4 Hz, 1H, OC*H*CH_2), 2.68-2.65 (m, 2H, OCHC*H*$_2$), 2.01 (t, *J*= 2.8 Hz, 1H, C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.8, 133.2, 133.1, 128.3, 128.0, 127.7, 126.2, 126.0, 124.6, 123.7, 80.6, 72.4, 71.1, 29.4. The data match with the previously described compound.[35]

(**2b**) *1-phenyl-3-butyn-1-ol:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42-7.32 (m, 5H, H_{aryl}), 4.90 (t, *J*= 6.3 Hz, 1H, OC*H*CH_2), 2.67-2.65 (m, 2H, OCHC*H*$_2$), 2.10 (t, *J*= 2.8 Hz, 1H,

C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.5, 128.4, 127.9, 125.7, 80.7, 72.2, 70.9, 29.4. The data match with the previously described compound.[35]

(**2c**) *1-(o-tolyl)but-3-yn-1-ol:* ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53-7.50 (m, 1H, H_{aryl}), 7.28-7.13 (m, 3H, H_{aryl}), 5.12 (dd, *J*= 6.0 and 5.7 Hz, 1H, OC*H*CH_2), 2.69-2.54 (m, 2H, OCHC*H*$_2$), 2.37 (s, 3H, C*H*$_3$), 2.12 (br s, 1H, O*H*), 2.09 (t, *J*= 2.4 Hz, 1H, C≡CH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 140.4, 134.6, 130.4, 127.7, 126.3, 125.0, 80.9, 70.7, 68.8, 28.2, 19.0. The data match with the previously described compound.[19]

(**2d**) *1-(2,5-dimethylphenyl)but-3-yn-1-ol:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 (s, 1H, H_{aryl}), 7.06-7.01 (m, 2H, H_{aryl}), 5.12-5.08 (m, 1H, OC*H*CH_2), 2.66-2.55 (m, 2H, OCHC*H*$_2$), 2.34 (s, 3H, C*H*$_3$), 2.33 (s, 3H, C*H*$_3$), 2.10 (t, *J*= 2.8 Hz, 1H, C≡CH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.2, 135.8, 131.4, 130.4, 128.4, 125.6, 80.0, 70.6, 68.9, 28.3, 21.1, 18.6.

(**2e**) *1-(p-methoxyphenyl)but-3-yn-1-ol:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (d, *J*= 8.0 Hz, 2H, H_{aryl}), 6.91 (d, *J*= 8.8 Hz, 2H, H_{aryl}), 4.85 (t, *J*= 6.4 Hz, 1H, OC*H*CH_2), 3.82 (s, 3H, OC*H*$_3$), 2.65-2.63 (m, 2H, OCHC*H*$_2$), 2.08 (t, *J*= 2.4 Hz, 1H, C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.3, 134.6, 127.0, 113.9, 80.8, 72.0, 70.9, 55.3, 29.4. The data match with the previously described compound.[35]

(**2f**) *1-(m-methoxyphenyl)but-3-yn-1-ol:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.23-7.18 (m, 1H, H_{aryl}), 6.90-6.88 (m, 2H, H_{aryl}), 6.79-6.76 (m, 1H, H_{aryl}), 4.78 (t, *J* = 6.4 Hz, 1H, OC*H*CH_2), 3.75 (s, 3H, OC*H*$_3$), 2.58-2.56 (m, 2H, OCHC*H*$_2$), 2.00 (t, *J*= 2.8 Hz, 1H, C≡CH); ^{13}C NMR ($CDCl_3$,100 MHz) δ 159.7, 144.1, 129.5, 118.0, 113.4, 111.2, 80.6, 72.2, 70.9, 55.2, 29.4. The data match with the previously described compound.[35]

(**2g**) *1-(o-methoxyphenyl)but-3-yn-1-ol:* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, *J*= 7.6, 1.6 Hz, 1H, H_{aryl}), 7.31-7.26 (m, 1H, H_{aryl}), 6.99 (dt, *J*= 7.6, 0.8 Hz, 1H, H_{aryl}), 6.90 (d, *J*= 8.4 Hz, 1H, H_{aryl}), 5.10 (dd, *J*= 7.6, 5.2 Hz, 1H, OC*H*CH_2), 3.87 (s, 3H, OC*H*$_3$), 2.78 (ddd, *J*= 16.8, 5.2, 2.8 Hz, 1H, OCHC*H*$_2$), 2.65 (ddd, *J*= 16.8, 7.2, 2.8 Hz, 1H, OCHC*H*$_2$), 2.06 (t, *J* = 2.8 Hz, 1H, C≡CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 130.2, 128.7, 126.8, 120.7, 110.4, 81.3, 70.4, 68.9, 55.2, 27.4. The data match with the previously described compound.[19]

(**2h**) *1-(3,4,5-trimethoxyphenyl)but-3-yn-1-ol:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.64 (s, 2H, H_{aryl}), 4.83 (dt, *J*= 6.4 and 2.8 Hz, 1H, OC*H*CH_2), 3.88 (s, 6H, OC*H*$_3$), 3.85 (s, 3H, OC*H*$_3$), 2.68-2.59 (m, 2H, OCHC*H*$_2$), 2.41 (d, *J*= 3.2 Hz, 1H, OH), 2.11 (t, *J*= 2.8 Hz,

1H, C≡CH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.4, 138.2, 137.6, 102.7, 80.7, 72.5, 71.1, 60.8, 56.1, 29.6. The data match with the previously described compound.[36]

(**2i**) *(E)-1-phenylhex-1-en-5-yn-3-ol:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41 (d, *J*= 7,6 Hz, 2H, H_{aryl}), 7.34 (t, *J*= 8.0 Hz, 1H, H_{aryl}), 7.28-7.24 (m, 2H, H_{aryl}), 6.68 (d, *J*= 16.0 Hz, 1H, C*H*=CH), 6.30 (dd, *J*= 16.0 and 6.0 Hz, 1H, CH=C*H*), 4.52-4.47 (m, 1H, OC*H*CH_2), 2.61 (ddd, *J*=16.8, 5.6 and 2.8 Hz, 1H, OCHCH_2), 2.54 (ddd, *J*= 16.8, 6.0, 2.4 Hz, 1H, OCHCH_2), 2.10 (t, *J*= 2.4 Hz, 1H, C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.3, 131.4, 129.9, 128.6, 127.9, 126.6, 80.2, 71.1, 70.7, 27.7. The data match with the previously described compound.[35]

(**2j**) *1-(p-bromophenyl)but-3-yn-1-ol:* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J*= 8.4 Hz, 2H, H_{aryl}), 7.29 (d, *J*= 8.4 Hz, 2H, H_{aryl}), 4.86 (t, *J*= 6.4 Hz, 1H, OC*H*CH_2), 2.68–2.57 (m, 2H, OCHCH_2), 2.09 (t, *J*= 2.8 Hz, 1H, C≡CH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 131.6, 127.5, 121.8, 80.1, 71.6, 71.3, 29.4. The data match with the previously described compound.[19]

(**2k**) *1-(p-fluorophenyl)but-3-yn-1-ol:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40-7.36 (m, 2H, H_{aryl}), 7.08-7.04 (m, 2H, H_{aryl}), 4.88 (t, *J*= 6.4, 1H, OC*H*CH_2), 2.65-2.62 (m, 2H, OCHCH_2), 2.09 (t, *J*= 2.8 Hz, 1H, C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.4 (d, *J*= 244.7 Hz), 138.1 (d, *J*= 3.1 Hz), 127.4 (d, *J* = 8.5 Hz), 115.3 (d, *J*= 21.7 Hz), 80.3, 71.7, 71.2, 29.6. The data match with the previously described compound.[35]

(**2l**) *1-(o-fluorophenyl)but-3-yn-1-ol:* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (t, *J*= 7.6 Hz, 1H, Ar), 7.22-7.19 (m, 1H, Ar), 7.10 (t, *J*= 7.6 Hz, 1H, Ar), 6.97 (t, *J*= 9.2 Hz, 1H, Ar), 5.13 (br, 1H, OC*H* CH_2), 2.71-2.67 (m, 1H, OCHCH_2), 2.59-2.54 (m, 1H, OCHCH_2), 2.00 (m, 1H, ≡CH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.6 (d, *J* = 244.8 Hz), 129.3 (d, *J*= 8.0 Hz), 127.2, 124.3, 115.3 (d, *J*= 22.0 Hz), 80.2, 71.1, 66.4, 28.3. The data match with the previously described compound.[19]

(**2m**) *1-(p-nitrophenyl)but-3-yn-1-ol:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.23 (d, *J*= 8,8 Hz, 2H, H_{aryl}), 7.58 (d, *J*= 8,8 Hz, 2H, H_{aryl}), 4.99 (dd, 1H, *J*= 6.8 and 5,6 Hz, 1H, OC*H*CH_2), 2.70 (ddd, *J*= 16.8, 5.6, 2.4 Hz, 1H, OCHCH_2), 2.63 (ddd, *J*= 16.8, 6.8, 2.8 Hz, 1H, OCHCH_2), 2.11 (dd, *J*= 2.8 and 2.4, 1H, C≡CH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.4, 147.5, 126.6, 123.7, 79.3, 72.0, 71.3, 29.5. The data match with the previously described compound.[35]

(**2n**) *1-(o-nitrophenyl)but-3-yn-1-ol:* ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (dd, *J*= 8.1 and 1.2 Hz, 1H, H_{aryl}), 7.90 (dd, *J*= 8.4 and 1.2 Hz, 1H, H_{aryl}), 7.69 (dt, *J*= 7.8 and 1.2 Hz, 1H, H_{aryl}), 7.48 (dt, *J* = 7.2 and 1.2 Hz, 1H, H_{aryl}), 5.48 (dd, *J* = 7.2 and 4.8 Hz, 1H, OC*H*CH_2), 2.92 (ddd, *J* = 16.5, 4.8 and 3.0 Hz, 1H, OCHC*H*$_2$), 2.68 (ddd, *J*= 3.0, 7.5, 16.5 Hz, 1H, OCHC*H*$_2$), 2.12 (t, *J* = 3.0 Hz, 1H, ≡CH). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 147.6, 137.7, 133.6, 128.6, 128.2, 124.5, 79.7, 71.8, 67.4, 28.5. The data match with the previously described compound.[19]

(**2o**) *4-(1-hydroxybut-3-ynyl)-2-methoxyphenol:* ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (d, *J*= 2.0 Hz, 1H, H_{aryl}), 6.88 (d, *J*= 8.2 Hz, H_{aryl}), 6.85 (dd, *J*= 8.2 and 1.6 Hz, 1H, H_{aryl}), 5.67 (br s, 1H, PhO*H*), 4.81 (t, *J* = 6.4 Hz, 1H, OC*H*CH_2), 3.89 (s, 3H, C*H*$_3$), 2.68-2.59 (m, 2H, OCHC*H*$_2$), 2.44 (br s, 1H, CHO*H*), 2.08 (t, *J* = 2.8 Hz, 1H, ≡CH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.5, 145.3, 134.5, 118.8, 114.1, 108.2, 80.8, 72.2, 70.9, 55.9, 29.4. The data match with the previously described compound.[37]

(**2p**) *1-(5-bromo-2-methoxyphenyl)but-3-yn-1-ol:* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J*= 2.4 Hz, 2 H_{aryl}), 7.36 (dd, *J*= 8.4, 2.4 Hz, 1 H_{aryl}), 6.75 (d, *J*= 8.8 Hz, 1 H_{aryl}), 5.06 (dd, *J*= 7.6, 4.8 Hz, 1 H, OC*H*CH_2), 3.83 (s, 3 H, C*H*$_3$), 2.75 (ddd, *J*= 16.8, 7.2, 2.8 Hz, 1 H, OCHC*H*$_2$), 2.56 (ddd, *J*= 16.8, 7.6, 2.4 Hz, 1 H, OCHC*H*$_2$), 2.08 (t, *J*= 2.8 Hz, 1 H, C≡C*H*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 132.5, 131.2, 129.6, 113.1, 112.0, 80.7, 70.9, 67.7, 55.5, 27.4.

(**2q**) *methyl 4-(1-Hydroxybut-3-ynyl)benzoate:*^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (d, *J*= 8.4 Hz, 2H, H_{aryl}), 7.46 (d, *J*= 8.0 Hz, 2H, H_{aryl}), 4.95-4.92 (m, 1H, OC*H*CH_2), 3.91 (s, 3H, C*H*$_3$), 2.71-2.59 (m, 2H, OCHC*H*$_2$), 2.59 (d, *J*= 3.6 Hz, 1H, OH), 2.08 (t, *J*= 2.8 Hz, 1H, C≡CH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.8, 147.4, 129.7, 129.7, 125.7, 80.0, 71.8, 71.4, 52.1, 29.4. The data match with the previously described compound.[38]

(**2r**) *4-(1-hydroxybut-3-yn-yl)benzonitrile:* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (d, *J*= 8.0 Hz, 2H, H_{aryl}), 7.52 (d, *J*= 8.0 Hz, 2H, H_{aryl}), 4.95 (dd, *J*= 7.8, 1.8 Hz, 1H, OC*H*CH_2), 2.73-2.57 (m, 2H, OCHC*H*$_2$), 2.11 (t, *J*= 2.8 Hz, 1H, C≡CH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.5, 132.3, 126.5, 118.7, 111.8, 79.4, 71.9, 71.4, 29.4. The data match with the previously described compound.[38]

(**2s**) *1-(2-furyl)but-3-yn-1-ol:* ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.39 (t, *J*= 1.2 Hz, 1H H_{furyl}), 6.34 (d, 2H, *J*= 1.2 Hz, 1H, H_{furyl}), 4.88 (t, *J*= 6.0 Hz, 1H, OC*H*CH_2), 2.77 (dd, *J*= 6.0 and 2.4 Hz, 2H, OCHC*H*$_2$), 2.33 (s, 1H, OH), 2.07 (t, *J*= 2.4 Hz, 1H, C≡CH);

^{13}C NMR ($CDCl_3$, 75 MHz) δ 154.6, 142.3, 110.3, 106.6, 79.8, 71.2, 66.1, 26.1. The data match with the previously described compound.[35]

(**2t**) *dec-1-yn-4-ol:* ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.80–3.72 (m, 1H, OC*H*CH_2), 2.44 (ddd, *J*= 16.5, 4.8 and 3.0 Hz, 1H, OCHC*H*$_2$), 2.31 (ddd, *J*= 16.5, 6.3 and 3.0 Hz, 1H, OCHC*H*$_2$), 2.06 (t, *J*= 3,0 Hz, 1H, C≡CH), 1.56-1.51 (m, 2H, C*H*$_2$), 1.36–1.29 (m, 8H, (C*H*$_2$)$_4$), 0,88 (t, *J*= 6.3 Hz, 3H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 80.9, 70.7, 69.9, 36.2, 31.7, 29.2, 27.3, 25.5, 22.6, 14.0. The data match with the previously described compound.[39]

Representative procedure for propargylation of 2-naphtaldehyde using potassium allenyltrifluoroborate, 4 promoted by microwave irradiation: A vial containing 2-naphtaldehyde (1 mmol, 156 mg) and potassium allenyltrifluoroborate, **4** (1.5 mmol, 250 mg) in acetone (500 μL) was irradiated at 300 W at 100ºC for 20 minutes. The vial contents were diluted with EtOAc (10 mL) and washed with water (2 x 15 mL). The organic phase was dried over $MgSO_4$ and filtered. The solvents were removed *in vacuo* to yield **2a** (137 mg, 70%) as a single isomer.

Supporting Information

Supporting Information File 1:
Additional experimental procedures and ^{1}H, ^{13}C, ^{11}B and ^{19}F NMR spectra for all synthesized compounds.
File Name: Text

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References

1. Ding, C.-H.; Hou, X-L. *Chem. Rev.*, **2011**, *111*, 1914-1937. doi: 10.1021/cr100284m.
2. Adachi, Y.; Kamei, N.; Yokoshima, S.; Fukuyama, T. *Org. Lett.*, **2011**, *13*, 4446-4449. doi: 10.1021/ol2018032.

3. Pulukuri, K. K.; Chakraborty, T. K. *Org. Lett.*, **2014**, *16*, 2284-2287. doi: 10.1021/ol5008179.

4. Marshall, J. A.; Adams, N. D. *Org. Lett.*, **2000**, *2*, 2897-2900. doi: 10.1021/ol006344b.

5. Trost, B. M.; Dong, G. *Nature*, **2008**, *456*, 485-488. doi: 10.1038/nature07543.

6. Parker, K. A.; Chang, W.; *Org. Lett.*, **2003**, *5*, 3891-3893. doi: 10.1021/ol035479.

7. Marino, J. P.; McClure, M. S.; Holub, D. P.; Comasseto, J. V.; Tucci, F. C. *J. Am. Chem. Soc.*, **2002**, *124*, 1664-1668. doi: 10.1021/ja017177t.

8. Wisniewska, H. M.; Jarvo, E. R. *J. Org. Chem.*, **2013**, *78*, 11629-11636. doi: 10.1021/jo4019107.

9. Yamashita, Y.; Cui, Y.; Xie, P.; Kobayashi, S. *Org. Lett.*, **2015**, *17*, 6042-6045. doi: 10.1021/acs.orglett.5b03045.

10. Zheng, Y.; Bao, W.; Zhang, Y. *Synth. Comm.,* **2000**, *30*, 3517-3521. doi: 10.1080/00397910008087264.

11. Lee, P. H.; Kim, H.; Lee, K. *Adv. Synth. Catal.*, **2005**, *347*, 1219-1222. doi: 10.1002/adsc.200505046.

12. Lin, M-J.; Loh, T-P. *J. Am. Chem. Soc.*, **2003**, *125*, 13042-13043. doi: 10.1021/ja037410i.

13. Millan, A.; Cienfuegos, L. A.; Martin-Lasanta, A.; Campana, A. G.; Cuerva, J. M.; *Adv. Synth. Catal.*, **2011**, *353*, 73-78. doi: 10.1002/adsc.201000655.

14. Guo, L. N.; Gao, H. J.; Mayer, P.; Knochel, P. *Chem. Eur. J.*, **2010**, *16*, 9829-9834. doi: 10.1002/chem.201000523.

15. Kobayashi, S.; Kitanosono, T.; Ueno, M. *Synlett*, **2010**, *13*, 2033-2036, doi: 10.1055/s-0030-1258485.

16. Keck, G. E.; Krishnamurthy, D.; Chen, X. *Tetrahedron Lett.*, **1994**, *35,* 8323-8324. doi: 10.1016/S0040-4039(00)74397-8.

17. Yu, C.-M.; Kim, J.-M.; Shin, M.-S.; Cho, D. *Tetrahedron Lett.*, **2003**, *44*, 5487-5490. doi: 10.1016/S0040-4039(03)01033-5.

18. Yu, C.-M.; Yoon, S. K.; Baek, K.; Lee, J.-Y. *Angew. Chem., Int. Ed.*, **1998**, *37*, 2392-2395. doi: 10.1002/(SICI)1521-3773(19980918)37:17<2392::AID-ANIE2392>3.0.CO;2-D.

19. Chen, J.; Captain, B.; Takenaka, N. *Org. Lett.*, **2011**, *13*, 1654-1657. doi: 10.1021/ol200102c.

20. Grayson, M. N.; Goodman, J. M. *J. Org. Chem.*, **2013**, *78*, 8796-8801, doi: 10.1021/jo401611q.

21. Grayson, M. N.; Goodman, J. M. *J. Am. Chem. Soc.*, **2013**, *135*, 6142-6148. doi: 10.1021/ja3122137.

22. Reddy, L. R. *Org. Lett.*, **2012**, *14*, 1142-1145. doi: 10.1021/ol300075n.

23. Wang, M.; Khan, S.; Miliordos, E.; Chen, M. *Org. Lett.* **2018**, *13*, 3810-3814. doi: 10.1021/acs.orglett.8b01399.

24. Tri-n-butyltin compounds [MAK Value Documentation, 1990]. The MAK Collection for Occupational Health and Safety (2012) 316.

25. Kappe, C. O. *Angew. Chem. Int. Ed.*, **2004**, *43*, 6250-6284. doi:10.1002/anie.200400655.

26. Sheldon, R. A. *Green Chem.*, **2017**,*19*, 18-43. doi: 10.1039/C6GC02157C.

27. Murphy, J. M.; Tzschucke, C. C.; Hartwig, J. F. *Org. Lett.*, **2007**, *9*, 757-760. doi: 10.1021/ol062903o.

28. Bagutski, V.; Ros, A.; Aggarwal, V. K.; *Tetrahedron*, **2009**, *65*, 9956-9960. doi: 10.1016/j.tet.2009.10.002.

29. Freitas, J. J. R.; Couto, T. R.; Cavalcanti, I. H.; Freitas, J. C. R.; Barbosa, Q. P. S.; Oliveira, R. A. *Tetrahedron Lett.*, **2016**, *57*, 760-765, doi: 10.1016/j.tetlet.2016.01.017.

30. Couto, T. R.; Freitas, J. J. R.; Freitas, J. C. R.; Cavalcanti, I. H.; Menezes, P. H; Oliveira, R. A. *Synthesis*, **2015**, *47*, 71-78. doi: 10.1055/s-0034-1379163.

31. Lennox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.*, **2012**, *51*, 9385-9388. doi: 10.1002/anie.201203930.

32. Oliveira, R. A.; Silva, R. O.; Molander, G. A.; Menezes, P. H. *Magn. Res. Chem.*, **2009**, *47*, 873-878. doi: 10.1002/mrc.2467.

33. Trost, B. M. *Science*, **1991**, *254*, 1471-1477. doi: 10.1126/science.1962206.

34. D. D. Perrin, W. L. F. Armarego, in *Purification of Laboratory Chemicals*, **1980**, Pergamon: Oxford.

35. Li, Q. R.; Gu, C. Z.; Yin, H. Chin. J. Chem., **2006**, *24*, 72-78. doi: 10.1002/cjoc.200690024.

36. Justicia, J.; Sancho-Sanz, I.; Álvarez-Manzaneda, E.; Oltra, J. E.; Cuerva, J. M. *Adv. Synth. Catal.*, **2009**, *351*, 2295-2300. doi: 10.1002/adsc.200900479.

37. Wu, S.; Huang, B.; Gao, X. *Synth. Commun.*, **1990**, *20*, 1279-1286. doi: 10.1080/00397919008052838.

38. Guo, L. N.; Gao, H. J.; Mayer, P.; Knochel, P. *Chem. Eur. J.*, **2010**, *16*, 9829-9834. doi: 10.1002/chem.201000523.

39. Ma, X.; Wang, J. X.; Li, S.; Wang, K. H.; Huang, D. *Tetrahedron*, **2009**, *65*, 8683-8689. doi: 10.1016/j.tet.2009.08.051.