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# Synthesis of Alkyl-Ynol-Ethers by "Anti-Michael Addition" of Metal Alkoxides to β-Substituted Alkynylsulfones

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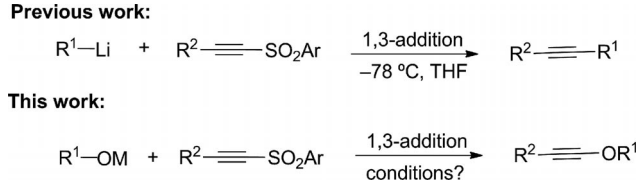
The reaction of metal alkoxides with β-substituted 2-(*p*-tolylsulfonyl)acetylenes, involving an *anti*-Michael addition reaction followed by the in situ elimination of the sulfonyl moiety, provides a direct method for the synthesis of alkyl alkynyl ethers bearing aryl or TIPS groups joined to the triple bond. Arylalkynyl ethers derived from primary alkoxides are in situ hydrolyzed into arylacetic esters.

## Introduction

Ynol ethers are well-known structures in organic synthesis[1] that have seen increased interest in recent years with the publication of interesting new synthetic applications, such as the synthesis of amides in supercritical carbon dioxide,[2] Nazarov reactions with carbonyl compounds,[3] the synthesis of aromatic (1*E*)-α-chloroenol ethers,[4] and cycloaddition reactions,[5] among others.[6] The large synthetic potential of the enolethers could be similar for ynol ethers, therefore it is surprising that ynol ethers are not used extensively in organic synthesis, which can be explained by the limitations of the methods used in their preparation.

There are three classic methods for synthesizing ynol ethers.[7] Two of them have limited scope because they involve the preparation of lithiated terminal *tert*-butoxy[7a] and ethoxy-acetylenes[7b] (other alkoxides cannot be prepared), which are only able to react efficiently with primary halides. The third and most recent method is based on the reaction of diazoketones with alcohols to form alkoxy ketones, which are converted into enol triflates (or phosphates) and subsequently transformed into ynol ethers by treatment with base.[7c] This is the most general method so far reported and allows the preparation of any alkyl- or aryl-substituted acetylene with primary, secondary and tertiary alkoxide groups. However, this methodology requires several steps and the manipulation of potentially explosive diazo compounds. In 2012, Evano et al. described a new method based on coupling reactions mediated by transition metals but is restricted to aryloxy alkynes.[8] Therefore, it would be highly desirable to find new direct and efficient method for the synthesis of ynol ethers.

Our group recently reported[9] the unexpected electrophilic behavior of arylsulfonylacetylenes (**1**) that undergo reactions with nucleophiles such as organolithiums (alkyl, aryl, heteroaryl and alkenyl) through an unusual α-attack (*anti*-Michael addition) followed by elimination of the $ArSO_2^-$ moiety to allow the alkynylation of lithiated $sp^2$ and $sp^3$ carbon atoms (Scheme 1, top). Because the scope of the reaction is quite general and allows the preparation of any dialkyl, alkyl-aryl or diaryl-substituted alkyne, we wondered if less nucleophilic species, such as alkoxides, would also be successful in these reactions. If so, the reaction would create C(sp)–O bonds, thus providing a direct method for the synthesis of ynol ethers (Scheme 1, bottom). In this paper, we describe the scope and limitations of the reaction of β-substituted (alkyl-, aryl-, and silyl-) sulfonylacetylenes with primary, secondary and tertiary metal alkoxides as a general method for the synthesis ynol ethers. A mechanistic proposal to rationalize the results will also be discussed.




Scheme 1. Alkynylation of organolithiums[9] and synthetic proposal for preparing ynol ethers in this paper.

During the preparation of this manuscript, Wilden et al.[10] described a similar protocol starting from alkynyl sulfonamides instead of the more available sulfones based on

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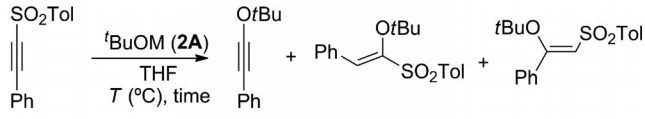
our results from ref.[9] The main differences between both procedures are related to the scope and the mechanistic proposals of the study, which in ref.[10] only concern tertiary alkoxides.

## Results and Discussion

Our initial trial (Table 1, Entry 1), involved the reaction of 2-phenyl sulfonylacetylene (**1a**) with LiO*t*Bu (**2A**) at –78 °C under similar conditions to those reported for alkynylating $sp^2$ and $sp^3$ carbon atoms.[9a–9b] Three products were detected and characterized. Expected ynol ether **3Aa** (resulting from the *anti*-Michael addition/elimination process) and sulfones **4Aa** and **5Aa**, obtained by *anti*-Michael and Michael addition reactions of the LiO*t*Bu, respectively. The (*Z*) configuration of **4Aa**, and therefore of its precursor anion, hinders elimination of the sulfonyl group (presumably requiring an antiperiplanar arrangement[11]), thus justifying its stability. The regioselectivity for the addition step (*anti*-Michel versus Michael products), measured as the (**3Aa** + **4Aa**)/**5Aa** ratio, was only moderate at –78 °C (Table 1, Entry 1) but was improved at higher temperatures (Table 1, Entries 2 and 3), with the best result obtained at room temperature (Table 1, Entry 3). Under these conditions **3Aa** was obtained in 65% isolated yield. Changes in the metal produced significant alterations. The reaction did not work with NaO*t*Bu (Table 1, Entry 4), whereas faster conversions were obtained with KO*t*Bu (Table 1, Entries 5 and 6). Moreover, the regioselectivity was also better with KO*t*Bu than with LiO*t*Bu, with only traces of the Michael addition olefin observed under optimal conditions. With respect to the alkyne/alkene (**3Aa/4Aa**) ratio, the results were not so clear because they were dependent on several factors such as temperature and, mainly, the reaction times. Longer reaction times increased the proportion of alkyne **3Aa** (Table 1, Entries 5 and 6). After studying many conditions, we found that the optimal ones were those indicated in Entry 10 (10 min at –43 °C and then 2 h at room temp.) that gave **3Aa** as a single product. Other interesting effects concerned the increase of the **3Aa/4Aa** ratio when the concentration of the base increased (Table 1, Entries 7, 8 and 9). Finally, it was notable that the presence of 18-crown-6 ether completely inhibited the reaction, despite the presumably increased reactivity of the alkoxide (Table 1, Entry 11), suggesting an essential role of the counterion in the reaction.

Presumably, α-attack of the alkoxides to sulfonylacetylenes is favored by prior association of the metal to the sulfonyl oxygen (as was established in reactions with organolithiums[9b] by theoretical calculations), which would explain the detrimental effect of crown ethers (Table 1, Entry 11). This addition would afford both the (*Z*) and (*E*) vinyl carbanions (Figure 1), with the former easily evolving into ynol ether **3**. The (*E*) vinyl carbanion, stabilized by the chelating potassium, would favor formation of **4** by protonation or regenerate **1** by elimination of the *anti*-OR group, thus opening a route to be equilibrated with the (*Z*)-carbanion. The influence of the reaction time on the **3/4** ratio supports the existence of this equilibrium.

Table 1. Optimization screening of the reaction of **1a** with different metal alkoxides derived from *tert*-butanol.[a]




**1a** **3Aa** **4Aa** **5Aa**

| Entry | M | T [°C] | Time | Conversion [%] | 3Aa/4Aa/5Aa |
|---|---|---|---|---|---|
| 1 | Li | –78 to r.t. | 18 h | 100 | 51:19:30 |
| 2 | Li | –10 | 24 h | 61 | 45:37:18 |
| 3 | Li | r.t. | 3 h | 100 | 73:16:11 |
| 4 | Na | –10 | 48 h | n.r.[b] | – |
| 5 | K | –78 | 15 min | 100 | 57:35:8 |
| 6 | K | –78 | 3 h | 100 | 63: 37:0 |
| 7 | K | –43 | 10 min | 100 | 77:23:0 |
| 8 | K | –43[d] | 10 min | 100 | 84:16:0 |
| 9 | K | –43[e] | 10 min | 100 | 87:13:0 |
| 10 | K | –43 to r.t. | –[c] | 100 | 100:0:0 |
| 11 | K | –43[f] | 10 min | n.r.[b] | – |

[a] Performed in THF (1.0 mL) by using **2A** (0.4 mmol) and **1a** (0.2 mmol). [b] No reaction. [c] 10 min at –43 °C and 2 h at r.t. [d] **2A** (0.8 mmol). [e] **2A** (2.0 mmol). [f] Performed in the presence of 18-crown-6 ether (0.4 mmol).

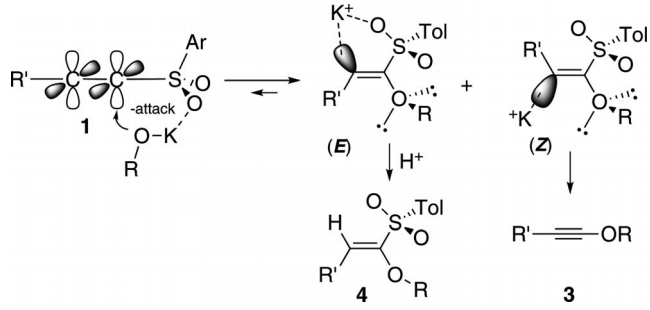


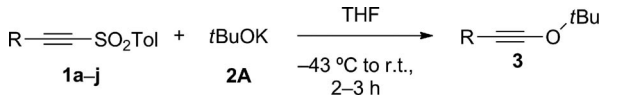

Figure 1. Mechanistic proposal for the reaction of sulfonylacetylenes with KOR.

We then tested the scope of the reaction of *t*BuOK (**2A**) with different sulfonylacetylenes (**1a**–**1j**) under optimized conditions (Table 2). Starting from **1a** (Table 2, Entry 1), **3Aa** was obtained in 84% yield. When this reaction was scaled up to 4.0 mmol, the yield was not significantly affected (Table 2, Entries 1 and 2). These reactions were similarly efficient for aryl derivatives containing electron-withdrawing and electron-donating groups (Table 2, Entries 3–8). Although all of the reactions proceeded to completion (nearly quantitative yield as calculated by NMR), the isolated yields of ynol ethers were clearly lower (likely owing to their volatility).

A different behavior was observed for alkyl-substituted acetylenes and the reaction with **1h** (*n*-butyl derivative; Table 2, Entry 9) did not work. Initially, we attributed this absence of reactivity (which had also been observed in reactions with organolithiums[9j]) to the acidity of the propargylic protons, but the lower basicity of KO*t*Bu suggested that other factors could also contribute to this behavior. A similar lack of reactivity observed for *tert*-butyl derivative **1i** (Table 2, Entry 10), lacking propargylic protons, which had undergone the reaction with organolithiums,[9b] suggested

Table 2. Scope of the reaction: structure of the sulfonylacetylenes.[a]

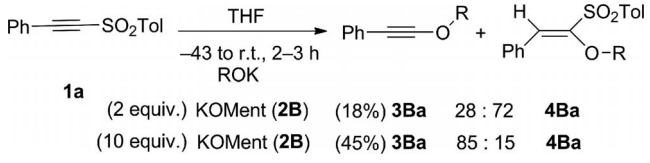



| Entry | R[1] | Yield [%] |
|---|---|---|
| 1 | Ph-**1a** | 84–**3Aa** |
| 2 | Ph-**1a** | 88–**3Aa**[b] |
| 3 | *p*-MeOC$_6$H$_4$-**1b** | 51–**3Ab** |
| 4 | *p*-MeC$_6$H$_4$-**1c** | 70–**3Ac** |
| 5 | 2,4,5-(Me)$_3$C$_6$H$_2$-**1d** | 67–**3Ad** |
| 6 | *o*-ClC$_6$H$_4$-**1e** | 84–**3Ae** |
| 7 | *p*-FC$_6$H$_4$-**1f** | 45–**3Af** |
| 8 | 3,5-(CF$_3$)$_2$C$_6$H$_3$-**1g** | 61–**3Ag** |
| 9 | *n*Bu-**1h** | n.r.[c] |
| 10 | *t*Bu-**1i** | n.r.[c] |
| 11 | TIPS-**1j** | 65–**3Aj** |

[a] Performed under conditions of Table 1, Entry 10. [b] Reaction carried out on a 4.0 mmol scale. [c] No reaction.

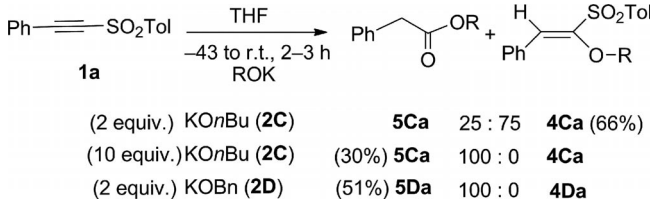
that the stabilization of the vinyl anion resulting from the α-attack is required and is provided by aryl but not for alkyl groups. The good result obtained with triisopropylsilyl (TIPS) derivative **1j** (Table 2, Entry 11) supports this explanation as the silyl atom d orbitals are also capable of providing electron delocalization to the anionic electron pair.

Next, we focused our attention on the preparation of alkoxy acetylenes derived from primary and secondary alcohols with this methodology. Unexpectedly, under the optimal conditions found for KO*t*Bu, the reaction of **1a** with secondary alkoxide **2B** [derived from (–)-menthol] yielded a 28:72 mixture of compound **3Ba** (18% isolated yield) and undesired olefin **4Ba**. All attempts to improve these results by performing the reaction at different temperatures and reaction times were unsuccessful. The lower yield of desired enol-ether **3Ba** can be explained by destabilizing steric interactions of the (*E*)-carbanion (precursor of **4**) with respect to the (*Z*)-one (Figure 1), which is more important for species resulting in the attack of tertiary alkoxide **2A** than secondary alkoxide **2B**. Fortunately, the use of a large excess of nucleophile (10 equiv.) allowed us to obtain a 85:15 mixture of **3Ba** and **4Ba** (calculated from the NMR spectra of the crude reaction mixture; Scheme 2). Under these conditions, **3Ba** was isolated in 45% yield. The excess of alkoxide could favor the transformation of **4** into **1** (E2 process), thus increasing the equilibration between the (*Z*) and (*E*) anions.



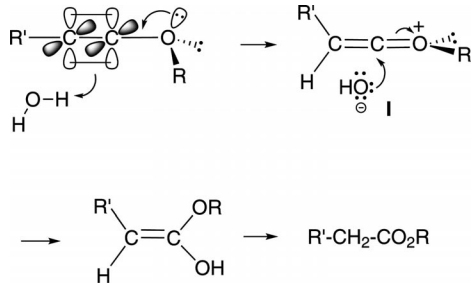

Scheme 2. Reactions of **1a** with secondary alkoxides **2B**.

Finally, we studied the behavior of alkoxides derived from primary alcohols. Despite many attempts, alkoxyacetylene **3Ca** was not obtained by using KO*n*Bu. After 2 h, we observed the formation of a 25:75 mixture of two products (Scheme 3). The major product was olefin **4Ca**, isolated in 66% yield. However, the minor product was identified as *n*-butyl phenyl acetate **5Ca**. It was formed as the only product after 2 h at room temp. by using 10 equiv. of KO*n*Bu (30% isolated yield).[12] Finally, we studied the behavior of primary alkoxide **2D**, derived from benzyl alcohol because of the interest of benzyl as a protecting group. The reaction was very clean yielding only ester **5 Da** in 51% yield (Scheme 3).



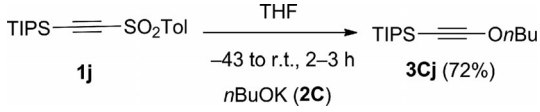

Scheme 3. Reactions of **1a** with primary alkoxydes **2C** and **2D**.

A mechanistic proposal for the formation of esters **5** from ynol ethers **3** is outlined in Scheme 4. Tertiary alkoxy acetylenes are less prone to hydrolysis than primary ones because of the lower stability of intermediate **I**, destabilized by the +I effect of the R group (tertiary > primary).[13]




Scheme 4. Mechanistic proposal for the hydrolysis of ynol ethers.

According to this proposal, an increase in the size of R′ would hinder the attack of water to C$_\beta$ thus increasing the stability of the ynol ethers to hydrolysis. Similar consequences could provoke substituents with large electron-donating character, which would decrease the efficiency of the +M effect of the OR. Because the TIPS group has both features, reactions of **1j** with primary alkoxides would provide ynol ethers stable to hydrolysis. Supporting this assumption, reaction of **1j** with KO*n*Bu (**2C**) only gave ynol ether **3Cj** with 72% yield (Scheme 5).




Scheme 5. Reactions of **1j** with primary alkoxide **2C**.

## Conclusions

In conclusion, we have found that the addition of KOR to substituted 2-(*p*-tolylsulfonyl)acetylenes provides a direct method for the synthesis of alkyl alkynyl ethers bearing aryl or TIPS groups joined to the triple bond. Arylalkynyl ethers

derived from primary alkoxide are in situ hydrolyzed into arylacetic esters.

## Experimental Section

**General Methods:** NMR spectroscopic data were acquired with a Bruker 300 spectrometer operating at 300 and 75 MHz for $^1$H and $^{13}$C nuclei, respectively. Chemical shifts ($\delta$) are reported relative to residual solvent signals ($CHCl_3$ 7.26 ppm for $^1$H NMR, and $CDCl_3$, 77.0 ppm for $^{13}$C NMR). $^{13}$C NMR spectra were acquired by using a broadband decoupled mode. Analytical TLC was performed by using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized with ultraviolet irradiation or $KMnO_4$ dip. Purification of reaction products was carried out by using flash chromatography with silica gel Merck-60 or fluorisil® 100–200 mesh. Commercially available alcohols, and solvents were used without further purification. Alkynylsulfones **1a**–**1g**,[14] **1h**–**i**[15] and **1j**[16] were synthesized following reported procedures.

**General Procedure for the Synthesis of Compounds 3Aa–3Aj, 4Aa and 5Aa:** To a cooled (–43 °C) solution of potassium *tert*-butoxide (**2A**, 0.40 mmol) in dry THF (0.5 mL), a solution of sulfone (**1a**–**j**) (0.2 mmol) in THF (0.5 mL) was added. Once the alkynylsulfone has disappeared (followed by TLC), the reaction mixture was warmed to room temperature over 1–2 h. The crude mixture was purified by flash chromatography through a short pad of fluorisil® by using *n*-pentane as solvent. Owing to the volatility of the products any reduced pressures must remain over 300 Torr.

**(*tert*-Butoxyethynyl)benzene (3Aa):** The product was obtained, by following the standard procedure with sulfone **1a**, as colorless oil (84% yield). $^1$H NMR ($CDCl_3$): $\delta$ = 7.26 (d, $J$ = 9.0 Hz, 2 H), 7.20–7.11 (m, 3 H), 1.40 (s, 9 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 131.4, 128.1, 126.2, 124.8, 95.6, 86.7, 42.8, 27.2 ppm. HRMS: calcd. for $C_{12}H_{14}O$ $[M]^+$ 174.1045; found 174.1039.

**1-(*tert*-Butoxyethynyl)-4-methoxybenzene (3Ab):** The product was obtained, by following the standard procedure with sulfone **1b**, as colorless oil (51% yield). $^1$H NMR ($CDCl_3$): $\delta$ = 7.27 (d, $J$ = 9.0 Hz, 2 H), 6.79 (d, $J$ = 9.0 Hz, 2 H), 3.79 (s, 3 H), 1.46 (s, 9 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 158.2, 132.7, 116.8, 113.8, 94.1, 86.4, 55.3, 41.2, 27.2 ppm. HRMS: calcd. for $C_{13}H_{16}O_2$ $[M]^+$ 204.1150; found 204.1160.

**1-(*tert*-Butoxyethynyl)-4-methylbenzene (3Ac):** The product was obtained, by following the standard procedure with sulfone **1c**, as colorless oil (70% yield). $^1$H NMR ($CDCl_3$): $\delta$ = 7.16 (d, $J$ = 9.0 Hz, 2 H), 6.98 (d, $J$ = 6.0 Hz, 2 H), 2.24 (s, 3 H), 1.39 (s, 9 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 136.0, 131.2, 128.8, 94.8, 86.5, 42.6, 27.1, 21.2 ppm. HRMS: calcd. for $C_{13}H_{16}O$ $[M]^+$ 188.1201, found 188.1204.

**1-(*tert*-Butoxyethynyl)-2,4,5-trimethylbenzene (3Ad):** The product was obtained following the standard procedure with sulfone **1d**, as colorless oil (67% yield). $^1$H NMR ($CDCl_3$): $\delta$ = 7.11 (s, 1 H), 6.93 (s, 1 H), 2.33 (s, 3 H), 2.20 (s, 3 H), 2.18 (s, 3 H), 1.48 (s, 9 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 136.7, 134.7, 133.4, 132.7, 130.6, 121.5, 98.4, 86.3, 41.6, 27.2, 20.4, 19.4, 19.0 ppm. HRMS: calcd. for $C_{15}H_{20}O$ $[M]^+$ 216.1514; found 216.1311.

**1-(*tert*-Butoxyethynyl)-2-chlorobenzene (3Ae):** The product was obtained, by following the standard procedure with sulfone **1e**, as colorless oil (84% yield). $^1$H NMR ($CDCl_3$): $\delta$ = 7.30–7.25 (m, 2 H), 7.20–7.14 (m, 1 H), 7.06–7.02 (m, 1 H), 1.44 (s, 9 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 135.3, 132.6, 128.9, 127.0, 126.2, 124.7, 100.8, 88.0, 40.7, 27.2 ppm. HRMS: calcd. for $C_{12}H_3OCl$ $[M]^+$ 208.0655; found 208.0645.

**1-(*tert*-Butoxyethynyl)-4-fluorobenzene (3Af):** The product was obtained, by following the standard procedure with sulfone **1f**, as colorless oil (45% yield). $^1$H NMR ($CDCl_3$): $\delta$ = 7.25–7.19 (m, 2 H), 6.86 (t, $J$ = 7.5 Hz, 2 H), 1.40 (s, 9 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 161.4 (d, $J$ = 244.5 Hz, 1 C), 132.9 (d, $J_{C,F}$ = 8.2 Hz, 2 C), 120.7 (d, $J_{C,F}$ = 3.0 Hz, 1 C), 115.2 (d, $J_{C,F}$ = 21.8 Hz, 2 C), 94.9, 86.8, 41.7, 27.2 ppm. HRMS: calcd. for $C_{12}H_3OF$ $[M]^+$ 192.0950; found 192.0942.

**1-(*tert*-Butoxyethynyl)-3,5-bis(trifluoromethyl)benzene (3Ag):** The product was obtained, by following the standard procedure with sulfone **1g**, as colorless oil (61% yield). $^1$H NMR ($CDCl_3$): $\delta$ = 7.72 (s, 2 H), 7.72 (s, 1 H), 1.51 (s, 9 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 138.5, 132.4 ($J_{C,F}$ = 34.0 Hz), 131.2, 121.3 ($J_{C,F}$ = 271.0 Hz), 120.4, 110.6, 88.8, 68.9, 27.3 ppm. HRMS: calcd. for $C_{14}H_{12}F_6O$ $[M]^+$ 310.0792; found 310.0691.

**(*tert*-Butoxyethynyl)triisopropylsilane (3Aj):** The product was obtained, by following the standard procedure with sulfone **1j**, as colorless oil (65% yield). The data for this compound are in agreement with those described in the literature.[17] $^1$H NMR ($CDCl_3$): $\delta$ = 1.46 (s, 9 H), 1.05 (s, 21 H) ppm. HRMS: calcd. for $C_{15}H_{30}OSi$ $[M]^+$ 254.2066; found 254.1999.

**(*E*)-1-{[1-(*tert*-Butoxy)-2-phenylvinyl]sulfonyl}-4-methylbenzene (4Aa):** The product was obtained, by following the standard procedure with sulfone **1a**, as colorless oil. The *E* geometry was determined by means of NOESY experiments (see Supporting Information, page S16). $^1$H NMR ($CDCl_3$): $\delta$ = 7.81 (d, $J$ = 9.0 Hz, 2 H), 7.58 (dd, $J$ = 9.0, 3.0 Hz, 2 H), 7.41 (s, 1 H), 7.36–7.21 (m, 5 H), 2.44 (s, 3 H), 1.39 (s, 9 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 151.1, 144.1, 136.6, 132.8, 129.8, 129.6, 129.0, 128.5, 128.4, 125.5, 87.9, 29.2, 21.6 ppm. HRMS: calcd. for $C_{19}H_{22}O_3SNa$ $[M + Na]^+$ 353.1181; found 353.1184.

**(*Z*)-1-{[2-(*tert*-Butoxy)-2-phenylvinyl]sulfonyl}-4-methylbenzene (5Aa):** The product was obtained, by following the standard procedure with sulfone **1a**, as colorless oil. The *Z* geometry was determined by means of NOESY experiments (see Supporting Information, page S18). $^1$H NMR ($CDCl_3$): $\delta$ = 7.89 (d, $J$ = 6.0 Hz, 2 H), 7.40–7.26 (m, 7 H), 6.03 (s, 1 H), 2.43 (s, 3 H), 1.33 (s, 9 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 165.8, 143.4, 136.9, 132.7, 130.3, 129.3, 128.4, 128.1, 127.4, 118.2, 84.8, 29.3, 21.5 ppm. HRMS: calcd. for $C_{19}H_{22}O_3SNa$ $[M + Na]^+$ 353.1205; found 353.1195.

**General Procedure for the Synthesis of Compounds 3Ba, 4Ba, 5Ca, 4Ca and 3Cj:** A solution of corresponding alcohol (0.4 mmol) in THF (0.5 mL) is added to a solution of potassium hydride (0.4 mmol) in THF (0.5 mL) at room temperature. After 10 min the reaction is cooled to –43 °C and the solution of corresponding sulfone (0.2 mmol) in THF (0.5 mL) is added. Once the alkynylsulfone had reacted (followed by TLC), the reaction mixture was warmed to room temperature over 1–2 h. The crude reaction was purified by flash chromatography through a short pad of fluorisil® by using *n*-pentane as solvent. Owing to the volatility of the products any reduced pressures must remain over 300 Torr.

**({[(1*R*,2*S*,4*S*)-2-Isopropyl-4-methylcyclohexyl]oxy}ethynyl)benzene (3Ba):** The product was obtained, by following the standard procedure with sulfone **1a**, as colorless oil (18% yield when 2 equiv. of alkoxide was used and 45% yield when 10 equiv. were used). $^1$H NMR ($CDCl_3$): $\delta$ = 7.36–7.32 (m, 2 H), 7.28–7.24 (m, 2 H), 7.24–7.22 (m, 1 H), 3.95 (dt, $J$ = 6.0, 4.0 Hz, 1 H), 2.38–2.18 (m, 2 H), 1.73–1.68 (m, 3 H), 1.67–1.64 (m, 2 H), 1.43–1.26 (m, 1 H), 1.22–1.20 (m, 1 H), 0.99 (d, $J$ = 7.0 Hz, 3 H), 0.94 (d, $J$ = 5.3 Hz, 3 H), 0.87 (d, $J$ = 5.3 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 131.4, 128.1, 126.3, 124.5, 97.7, 88.7, 68.0, 47.0, 40.8, 39.8, 34.1, 31.7, 26.0, 22.1, 20.6, 16.4 ppm.

**1-[((*E*)-1-{[(1*R*,2*S*,4*S*)-2-Isopropyl-4-methylcyclohexyl]oxy}-2-phenylvinyl)sulfonyl]-4-methylbenzene (4Ba):** The product was obtained, by following the standard procedure with sulfone **1a**, as colorless oil (67% yield when 3 equiv. of alkoxide was used). $^1$H NMR ($CDCl_3$): $\delta$ = 7.81 (d, $J$ = 9.0 Hz, 2 H), 7.68 (d, $J$ = 9.0 Hz, 2 H), 7.37–7.30 (m, 5 H), 7.25 (s, 1 H), 4.51 (td, $J$ = 10.8, 4.2 Hz, 1 H), 2.43 (s, 3 H), 2.12–2.08 (m, 2 H), 1.67–1.57 (m, 2 H), 1.49–1.42 (m, 1 H), 1.28–1.22 (m, 2 H), 1.10–0.98 (m, 1 H), 0.87 (d, $J$ = 7.0 Hz, 3 H), 0.79 (d, $J$ = 5.3 Hz, 3 H), 0.75 (d, $J$ = 5.3 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 150.1, 144.3, 131.4 (2 C), 129.2, 128.1 (2 C), 126.4, 124.5, 83.2, 48.8, 39.1, 34.1, 23.3, 26.0, 25.0, 23.4, 22.1, 20.6, 16.4 ppm. HRMS: calcd. for $C_{25}H_{32}O_3SNa$ $[M + Na]^+$ 435.1964; found 435.1977.

**(*E*)-1-[(1-Butoxy-2-phenylvinyl)sulfonyl]-4-methylbenzene (4Ca):**[4] The product was obtained, by following the standard procedure with sulfone **1a**, as colorless oil (66% yield). $^1$H NMR ($CDCl_3$): $\delta$ = 7.54 (d, $J$ = 9.0 Hz, 2 H), 7.35–7.30 (m, 2 H), 7.06–6.99 (m, 5 H), 6.90 (s, 1 H), 3.77 (t, $J$ = 9.0 Hz, 2 H), 2.28 (s, 3 H), 1.42–1.25 (m, 2 H), 1.12–1.00 (m, 2 H), 0.61 (t, $J$ = 6.1 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 152.8, 144.5, 136.1, 131.8, 129.7, 129.2, 128.7, 128.5, 126.7, 121.9, 74.4, 41.4, 21.6, 18.9, 13.7 ppm. HRMS: calcd. for $C_{19}H_{23}O_3S$ $[M + H]^+$ 331.1362; found 331.1389.

**Butyl 2-Phenylacetate (5Ca):**[5] The product was obtained, by following the standard procedure with sulfone **1a**, as yellow oil (64% yield). Data for **5Ca** are in agreement with those described in the literature.[18] $^1$H NMR ($CDCl_3$): $\delta$ = 7.37–7.26 (m, 5 H), 4.11 (t, $J$ = 6.0 Hz, 2 H), 3.64 (s, 2 H), 1.62–1.59 (m, 2 H), 1.41–1.30 (m, 2 H), 0.93 (t, $J$ = 6.0 Hz, 3 H) ppm.

**Benzyl 2-Phenylacetate (5Da):** The product was obtained, by following the standard procedure with sulfone **1a**, as yellow oil (51% yield). Data for **5Da** are in agreement with those described in the literature.[19] $^1$H NMR ($CDCl_3$): $\delta$ = 7.41–7.28 (m, 10 H), 5.15 (s, 2 H), 3.69 (s, 2 H) ppm.

**(Butoxyethynyl)triisopropylsilane (3Cj):** The product was obtained, by following the standard procedure with sulfone **1j**, as colorless oil (72% yield). $^1$H NMR ($CDCl_3$): $\delta$ = 3.61 (t, $J$ = 9.2 Hz, 2 H), 1.35–1.32 (m, 2 H), 1.23–1.25 (m, 1 H), 1.16–1.11 (m, 2 H), 0.98 (d, $J$ = 3.3 Hz, 18 H), 0.85 (t, $J$ = 9.1 Hz, 3 H) ppm. $^{13}$C NMR ($CDCl_3$): $\delta$ = 104.5, 63.2, 35.1, 25.2, 19.2, 18.2, 17.7, 13.9, 12.6 ppm.

**Supporting Information** (see footnote on the first page of this article): Spectroscopic data for compounds **3Aa**–**3Aj**, **4Aa**, **4Ca**, **4Da**, **5Aa**, **5Ca**, **5Da**.

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[12] We followed the reaction in $[D_8]$THF by NMR spectroscopy and observed the formation of corresponding benzyl-ynol-ethers **3Da**, indicating that the aqueous media used in the workup procedure is responsible of the hydrolysis to ether **5Da**.

[13] Taking into account that the approach of the nucleophile ($H_2O$) must take place as indicated in Scheme 4 (the opposite face is occupied by the lone electron pair at oxygen interacting with the enriched π bond at the triple bond), the steric hindrance of the R group (tertiary > secondary > primary) could also explain the higher stability of the tertiary ynol ethers.

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