Synthesis I. Linder et al. Paper

Reaction of Lithiated Propargyl Ethers with Carbonyl Compounds – A Regioselective Route to Furan Derivatives

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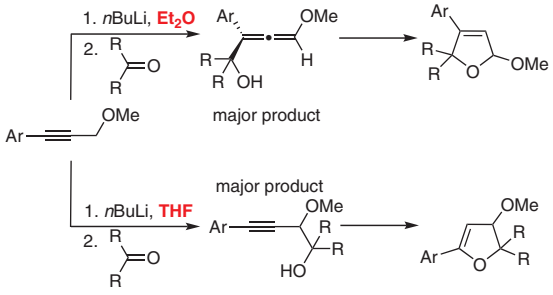

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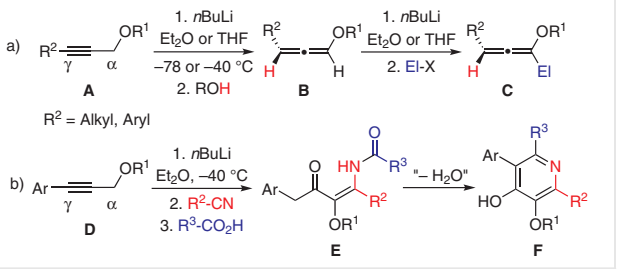
Abstract The deprotonation of 3-aryl-substituted alkyl propargyl ethers with *n*-butyllithium provides an ambident anion that reacts with carbonyl compounds to provide mixtures of γ-substituted products with alkoxyallene substructure and of α-substituted propargyl ethers. The ratio of the two product types strongly depends on the solvent: in diethyl ether the γ-substituted products predominate whereas the more polar tetrahydrofuran favors the α-adducts. The primary addition products undergo 5-*endo-trig* or 5-*endo-dig* cyclizations under various reaction conditions to afford isomeric furan derivatives. The highest selectivity in favor of α-substituted products was achieved by employing a MOM-protected propargyl ether. During the protonation step no evidence for a proton shift leading to an isomeric allenyl anion was found. A brief mechanistic discussion tries to rationalize the observed regioselectivities.

Key words alkoxyallene, alkyne, cyclization, furan, gold catalysis, lithiation, regioselectivity, silver catalysis

Alkoxyallenes and derivatives thereof are versatile building blocks for the synthesis of carbocycles and heterocycles.[1] Of particular value are lithiated alkoxyallenes that react with a large variety of electrophiles and hence lead to many useful product types. The reactivity of simple compounds such as methoxyallene (1-methoxypropa-1,2-diene) and its lithiated intermediates is reasonably well understood and was exploited in many applications,[2] but the corresponding 3-substituted 1-alkoxy-1,2-dienes are not as easily available and as a consequence they are less explored.[3] During our studies on 3-aryl-substituted alkoxyallenes we explored the known route[4] via propargylic ethers **A** which can be deprotonated at the α-position to the alkoxy group with *n*-butyllithium and regioselectively protonated in γ-position to furnish the expected allenes **B** (Scheme 1, equation a). A second deprotonation occurs at the more acidic α-carbon of **B** and electrophiles add to this position to give 1,1,3-trisubstituted alkoxyallenes **C**. This multi-step protocol was employed by our group to prepare a series of dihydrofuran and dihydropyrrole derivatives, including the natural product codonopsinine.[5]



Scheme 1 a) Lithiation of propargyl ethers **A**, regioselective protonation to alkoxyallenes **B**, and transformation into 1,1,3-trisubstituted allenes **C**; b) lithiation of aryl-substituted propargyl ethers **D** and three-component reaction with nitriles and carboxylic acids to β-alkoxy-β-ketoenamides **E**, versatile precursors of functionalized heterocycles such as **F** (all compounds of this report are racemic; nevertheless, we prefer to present geometrically correct allene moieties)

In a three-component reaction, lithiation of aryl-substituted propargylic ethers **D** and treatment with nitriles as electrophiles and subsequently with carboxylic acids unexpectedly provided β-alkoxy-β-ketoenamides **E** as products (Scheme 1, equation b).[6] In this case, the electrophile was connected to the α-position of lithiated **D**. The general mechanism of the formation of β-alkoxy-β-ketoenamides **E** was discussed in earlier publications[7] and as very first step we proposed the addition of a lithiated alkoxyallene to the nitrile. Compounds **E** are excellent precursors for the synthesis of functionalized pyridine, pyrimidine, and oxazole derivatives.[8] In order to understand the mechanisms

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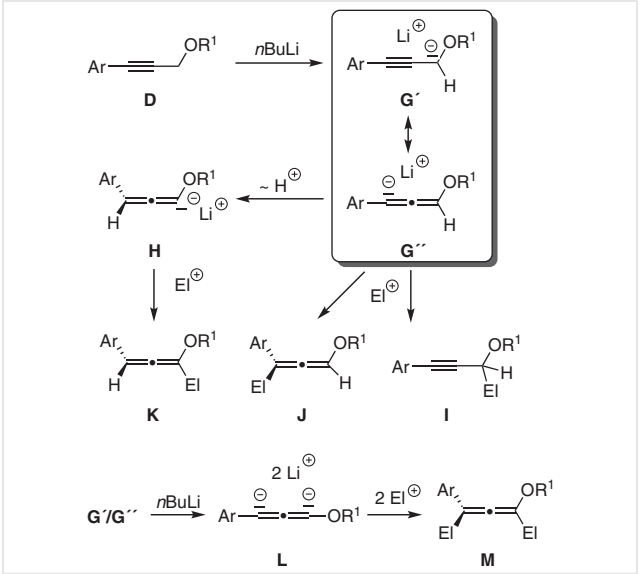
involved in lithiations of aryl-substituted propargylic ethers **D** and their reactions with electrophiles we undertook the investigations described in this report.

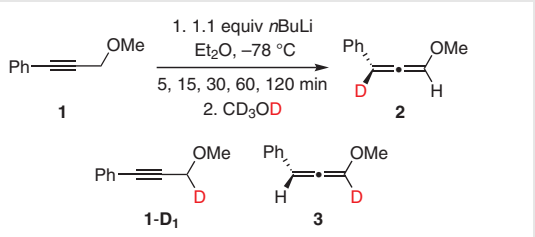
In an accepted scenario, lithiation of **D** with *n*-butyllithium provides the ambident carbanion which is represented by the two mesomeric formulas **G′** and **G″** showing the nucleophilicity of this species in its α- and in γ-position (Scheme 2).[9] Reaction of this carbanion with electrophiles can therefore afford the two isomeric products **I** and **J**. As mentioned above, protonation occurs selectively in γ-position to provide allenes **J**. In literature, the reaction of other electrophiles such as alkyl halides were also reported to give the allenes **J** whereas with carbonyl compounds mixtures of compounds were obtained.[10] For the observed formation of products **E** from **D** (Scheme 1) we proposed an isomerization by a proton shift leading from **G′**/**G″** to the allenyl anion **H**. This proton shift may occur as direct 1,3-shift or more likely by protonation of **G′**/**G″** to **J** (El = H) and deprotonation to **H** which can also be presented in a second mesomeric formula; because of the known predominating reaction to products such as **K** only structure **H** is depicted. Compound **E** could be derived from an in situ formed intermediate **K** (El = R^2–C=NH), which subsequently reacts in a multi-step process with the carboxylic acid.[6,7]



Scheme 2 Lithiation of aryl-substituted propargyl ether **D** to intermediate **G′**/**G″** and its possible reactions to allene **J** and propargyl ether **I**; formation of allene **K** by isomerization to allenyl anion **H**; formation of dilithiated species **L** and reaction to allene **M**

The situation is even more complex since it is also known that the carbanion **G′**/**G″** can be lithiated by an excess of *n*-butyllithium to provide the dianion **L**, which subsequently reacts with electrophiles to give tetrasubstituted alkoxyallenes of type **M**.[11] Despite the demonstrated high synthetic usefulness of alkoxyallenes these easily accessible highly substituted allenes have rarely been employed for further synthetic applications.

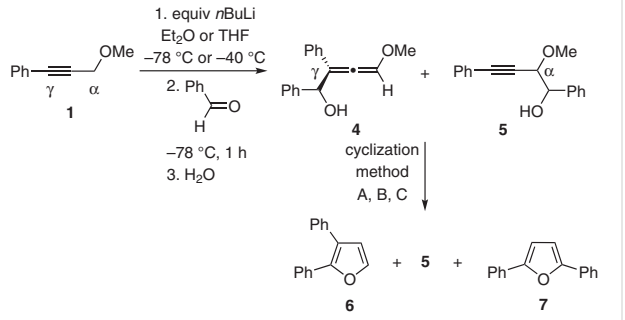
The required starting aryl-substituted methyl propargyl ethers are easily available by Sonogashira–Hagihara coupling of 3-methoxy-1-propyne. We started with phenyl-substituted compound **1** and first studied its deprotonation and deuteration at low temperatures. Compound **1** was lithiated at –78 °C in diethyl ether with a slight excess of *n*-butyllithium and samples were quenched with perdeuterated methanol after certain periods (Scheme 3).[12] Even after 120 minutes at –78 °C only the γ-deuterated allene **2** was detected by ^{1}H NMR analysis. The isomeric compounds with deuterium incorporation in α-position, **1**-$\mathbf{D_1}$ with a propargyl ether structure, and **3** with an allenic structure were not found within the limits of NMR analyses. Similar experiments at –40 °C did not provide clear evidence of an isomerization and formation of compound **3**.[13] At higher temperatures lithiated **1** started to decompose.



Scheme 3 Conversion of phenyl-substituted propargyl ether **1** into 3-deuterated methoxyallene derivative **2**

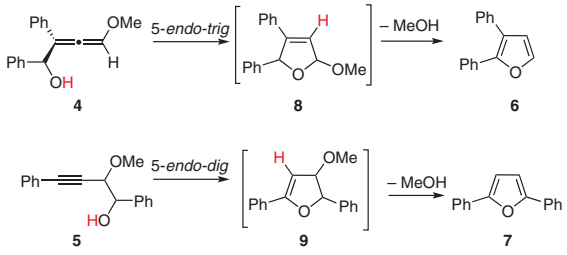
With benzaldehyde as electrophile we investigated the influence of reaction conditions on the regioselectivity of the additions of lithiated **1** in detail (Scheme 4 and Table 1). In most cases the yields were only determined after cyclization of the fairly sensitive primary alkoxyallene **4** to the furan derivative **6**. Conditions similar to the deuteration experiment above were applied in entry 1, which gave a crude product mixture of unconsumed precursor **1**, the expected γ-addition product **4** (diastereomers are very likely formed, but could not be identified in the crude product mixture) and the α-addition product **5** (ca. 2:1 mixture of *syn*/*anti*-diastereomers). After application of catalytic amounts of silver nitrate in the presence of potassium carbonate,[14] 2,3-diphenylfuran (**6**) was isolated in 50% overall yield, whereas substituted propargylic ether **5** was re-isolated unchanged in 5% yield. During these experiments we learned that the analysis and purification of the resulting mixtures is less tedious, when only 0.9 equivalent of *n*-butyllithium were employed as base which led to a higher amount of unconsumed **1**. Entry 2 essentially confirmed the first experiment furnishing a slightly more α-addition product **5**. We repeated the conditions of entry 2, but performed the cyclization under strongly basic conditions with potassium *tert*-butoxide[15] that provided furan derivative **6** in 50% yield (entry 3). Interestingly, these conditions also led to a large extent to a

cyclization of **5** to 2,5-diphenylfuran (**7**) in 10% yield. A complete cyclization of **5** was observed when gold catalysis was applied for the cyclization step (entry 4).[16,17] Now the two furan derivatives **6** and **7** were isolated in 39% and 19% yield, respectively. The deviation of the ratio of γ-product (compound **6**) and α-products (compounds **5** and **7**) are very likely not due to the changed cyclization conditions but to the differing mass balances of the two experiments. The addition of lithiated **1** to benzaldehyde is less selective at –40 °C and it showed a lower mass balance indicating starting decomposition of the carbanion (entry 5).



Scheme 4 Reaction of lithiated propargyl ether **1** with benzaldehyde under different conditions followed by cyclization (for details, see Table 1, Method A: 0.2 equiv $AgNO_3$, 3–5 equiv K_2CO_3, CH_3CN, r.t., 19 h; Method B: 0.3 equiv KO*t*Bu, DMSO, r.t., 19 h; Method C: 0.05 equiv AuCl, 0.15 equiv pyridine, CH_2Cl_2, r.t., 19 h)

The cyclization scenarios are illustrated without mechanistic details in Scheme 5. A 5-*endo-trig* cyclization converts allenyl alcohol **4** into the 2,5-dihydrofuran derivative **8** which undergoes fast 1,4-elimination of methanol to the aromatized heterocycle **6**. This cyclization proceeds with the three methods applied. On the other hand, the isomeric alkynyl alcohol **5** does undergo a 5-*endo-dig* cyclization to



Scheme 5 Cyclization of allene **4** to 2,5-dihydrofuran **8** followed by formation of **6** and cyclization of alkyne **5** to 2,3-dihydrofuran **9** and formation of **7**

2,3-dihydrofuran intermediate **9** under silver(I) catalysis and only slowly under basic conditions. The soft Lewis acid gold(I) smoothly promotes this process generating **9** and after a 1,2-elimination of methanol furan derivative **7**.[17] We could demonstrate the efficiency of this reaction by converting pure compound **5** into **7** in 73% yield.

Next, the influence of the solvent was examined and a 4:1 mixture of diethyl ether and hexanes was employed to decrease the polarity (Table 1, entry 6). After cyclization, 15% of **1** and 40% of 2,3-diphenylfuran (**6**) were isolated. The product of an α-addition **5** was not observed. This result indicates that the polarity of the solvent has a considerable influence on the regioselectivity; since the applied base *n*-butyllithium is delivered in hexanes as solvent the concentration (amount of diethyl ether) certainly has a considerable impact on the outcome of these reactions.[18] This effect was not further studied, but instead we increased the polarity of the applied solvent by using tetrahydrofuran (entries 7–9). In all experiments, the amount of the γ-addition product **4** (respective its subsequent product **6**) was decreased to 15–33%, whereas the α-addition product **5** and/or its cyclization product increased to 50–60%. The best

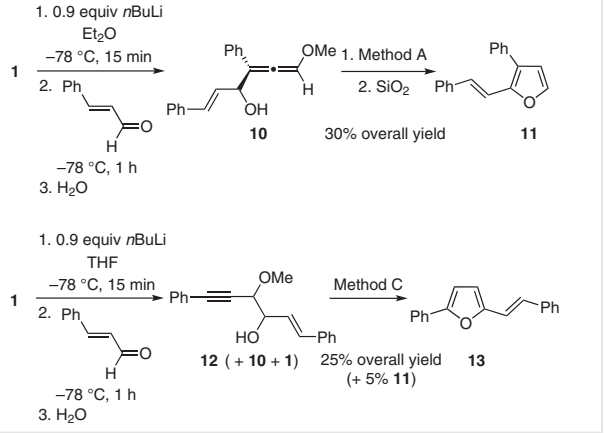
Table 1 Reaction of Lithiated Methyl Propargyl Ether **1** with Benzaldehyde under Different Conditions Followed by Cyclization

Entry	Equiv *n*BuLi	Temperature	Solvent	Cyclization method[a]	Recovered **1**	γ-Product **6**	α-Product **5**	Furan **7**
1	1.2	–78 °C	Et_2O	A	7%	50%	5%	–
2	0.9	–78 °C	Et_2O	A	22%	48%	15%	–
3	0.9	–78 °C	Et_2O	B	27%	50%	5%	10%
4	0.9	–78 °C	Et_2O	C	10%	39%	–	19%
5	0.9	–40 °C	Et_2O	B	12%	23%	20%	–
6	0.9	–78 °C	Et_2O/ hexanes (4:1)	A	15%	40%	–	–
7	0.9	–78 °C	THF	A	–	33%	54%	–
8	0.9	–78 °C	THF	C	2%	24%	7%[b]	51%
9	0.9	–40 °C	THF	C[c]	2%	15%	–	60%

[a] Method A: 0.2 equiv $AgNO_3$, 3–5 equiv K_2CO_3, CH_3CN, r.t., 19 h; Method B: 0.3 equiv KO*t*Bu, DMSO, r.t., 19 h; Method C: 0.05 equiv AuCl, 0.15 equiv pyridine, CH_2Cl_2, r.t., 19 h.
[b] Only *anti*-**5** was re-isolated.
[c] Due to the slow reaction of *anti*-**5** the cyclization protocol was applied twice.

result with respect to the yield of 2,5-diphenylfuran (**7**) is recorded in entry 9 where a reaction temperature of –40 °C was applied. In this experiment, we also observed that the *syn*-diastereomer of **5** isomerized faster and some *anti*-**5** remained unchanged after the first cyclization reaction. Subjecting the crude product again to the cyclization conditions led to complete conversion and isolation of **7** in 60% yield.

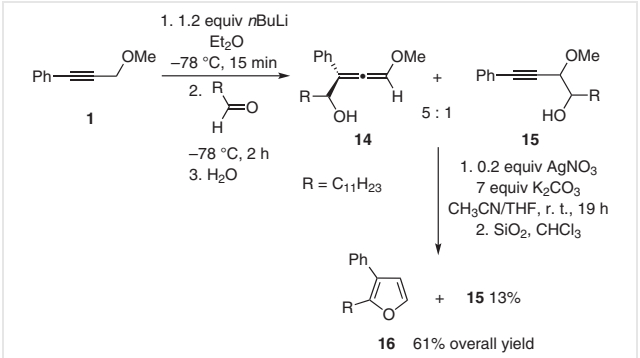
The solvent dependence of the α/γ-regioselectivity was confirmed by experiments employing the α,β-unsaturated cinnamic aldehyde (Scheme 6). Lithiated propargyl ether **1** in diethyl ether and this electrophile furnished γ-adduct **10** which after cyclization/elimination afforded the 2-styryl-substituted furan derivative **11** in moderate yield. On the other hand, the reaction in tetrahydrofuran mainly provided α-addition product **12** which finally provided the 2,5-disubstituted furan derivative in **13** in 25% yield and compound **11** in 5% yield. Although the overall yields are only moderate to low the examples reveal that isomeric furan derivatives are easily available by changing the reaction conditions. Further optimization may increase the efficiency of these simple transformations.



Scheme 6 Reaction of lithiated propargyl ether **1** with cinnamic aldehyde in diethyl ether or in tetrahydrofuran leading after cyclization to 2,3- and 2,5-disubstituted furan derivatives **11** and **13**, respectively (Method A: 0.2 equiv $AgNO_3$, 3–5 equiv K_2CO_3, CH_3CN, r.t., 19 h; Method C: 0.05 equiv AuCl, 0.15 equiv pyridine, CH_2Cl_2, r.t., 19 h).

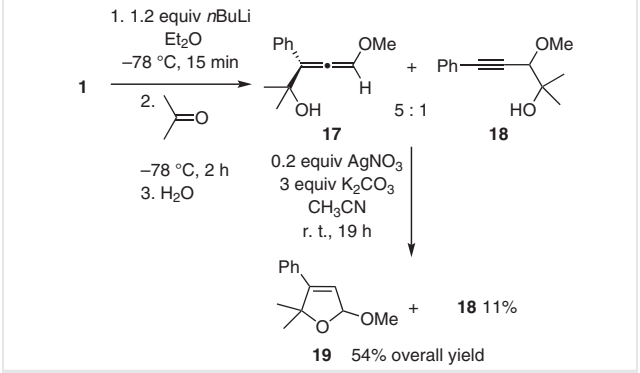
As representative of an aliphatic aldehyde dodecanal was examined as electrophile and after its reaction with lithiated **1** under standard conditions in diethyl ether, a mixture of the primary products **14** and **15** (ratio ca. 5:1) was obtained (Scheme 7). The crude product mixture was subjected to the silver nitrate cyclization method and the oxygen sensitive 2-alkyl-3-aryl-substituted furan derivative **16** was isolated in 61% overall yield; a second fraction provided 13% of pure **15**.

The reaction of lithiated **1** with aliphatic or cyclic ketones provided similar results. Under the standard reaction conditions in diethyl ether as solvent, acetone furnished a



Scheme 7 Reaction of lithiated propargyl ether **1** with dodecanal followed by silver-promoted cyclization to furan derivative **16**

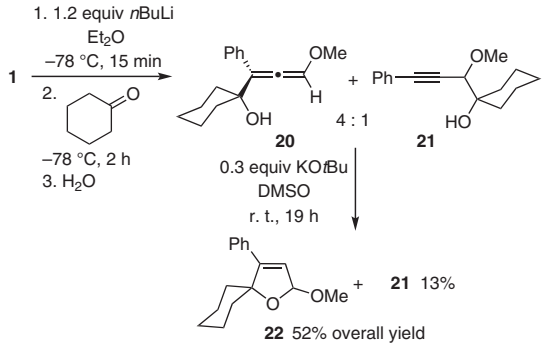
5:1 mixture of the primary γ- and α-addition products **17** and **18** (Scheme 8). Silver-catalyzed isomerization of allene **17** gave 2,5-dihydrofuran derivative **19** in 54% overall yield and unchanged **18** was isolated in 11% yield. The aromatization to furan derivatives is not possible in this case due to the dimethyl substitution at C-2 of **19**. Application of the standard reaction conditions but addition of HMPA as highly polar co-solvent inverted the ratio of **17**:**18** to ca. 1:9. Unfortunately the crude product was not sufficiently pure to allow full purification and isolation of defined compounds, but this experiment confirms that higher polarity of the solvent shifts the regioselectivity to α-addition.



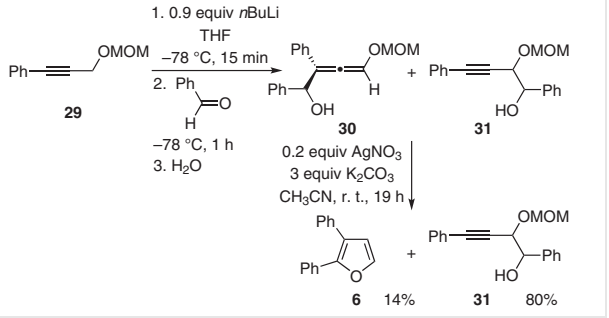
Scheme 8 Reaction of lithiated propargyl ether **1** with acetone followed by silver-catalyzed cyclization to dihydrofuran derivative **19** as major product

Comparable results were obtained by combining lithiated propargyl ether **1** with cyclohexanone (Scheme 9). The crude product mixture of **20** and **21** (ratio ca. 4:1) was treated under basic conditions to give the 2,2-dialkyl-substituted dihydrofuran derivative **22** in 52% overall yield. Unchanged alkynyl alcohol **21** was isolated in 13% yield.

The results obtained with phenyl-substituted methyl propargyl ether **1** were confirmed with precursors bearing an electron-donating methoxy or a fluorine substituent in *para*-position of the aryl group (Scheme 10). In both cases,

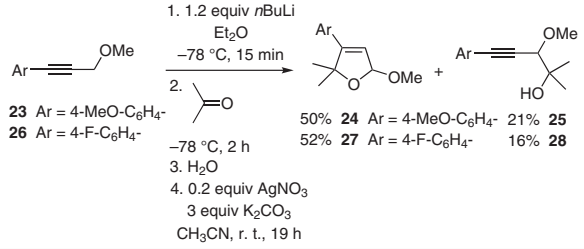


Scheme 9 Reaction of lithiated propargyl ether **1** with cyclohexanone followed by base-promoted cyclization to spiro compound **22** as major product



Scheme 11 Reaction of lithiated propargyl ether **29** with benzaldehyde leading to alkynyl alcohol **31** as major product

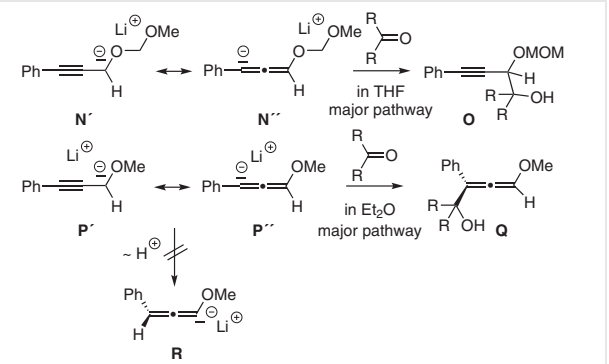
lithiation under standard conditions, reaction with acetone and silver-catalyzed isomerization provided mixtures of the dihydrofuran derivatives **24** or **27** with the alkynyl alcohols **25** or **28**, respectively. The ratio of γ- and α-products is slightly lower (ca. 2.5:1 or 3:1) compared with the parent compound **1**. It is pure speculation to attribute this lower selectivity to the electron-donating effect of the aryl group and a higher electron density in α-position of the ambident anion (see intermediate **G′** in Scheme 2 and discussion below).



Scheme 10 Reaction of lithiated propargyl ethers **23** and **26** with acetone followed by silver-catalyzed cyclization to dihydrofuran derivatives **24** and **27** and alkynyl ethers **25** and **28**

Finally, the influence of the alkoxy group was briefly investigated. MOM-Protected propargyl ether **29**[19] bearing the methoxymethly instead of a methyl substituent was lithiated in tetrahydrofuran as solvent and after addition of benzaldehyde the two primary products **30** and **31** were formed with the latter clearly being the dominating component (Scheme 11). Silver-promoted cyclization of the crude product gave 2,3-diphenylfuran (**6**) in 14% yield and unchanged alkynyl alcohol **31** was isolated in 80% yield. By using the more polar solvent tetrahydrofuran and the stronger complexing alkoxy substituent a reasonably and high yielding access to α-addition products of type **31** could be achieved.

Our mechanistic explanation is based on the plausible assumption that the regioselectivity of the overall process is decided by the addition of the lithiated propargyl ethers to the carbonyl compounds. The simplified interpretation (Scheme 12) regards the ambident anions as ion pairs with relatively weak interaction with the lithium cation (see ref. 9). The result with the MOM-protected compound **29** suggests that a larger distance between the anion **N′**/**N″** and the counter ion preferentially leads to α-substitution product **O**. A similar effect is operating when THF is employed as solvent which is a better ligand for the lithium cation and may lead to a solvent separated ion pair. On the other hand, a shorter distance and stronger interaction of the lithium cation as depicted in **P′**/**P″** in the less polar solvent diethyl ether (possibly a contact ion pair) leads to the favored formation of the γ-addition product **Q**. The γ-position of **P′**/**P″** is also the preferred position of attack of other electrophiles (proton, deuteron and alkyl halides[4]).[20] In none of our experiments we gained evidence that a proton shift of the lithiated propargyl ethers **P′**/**P″** to an isomeric allenyl species such as **R** occurs. For a sound mechanistic explanation of the formation of products such as **E** (Scheme 1) additional experiments are required.



Scheme 12 Mechanistic interpretation of the observed regioselectivities of ambident anion **N′**/**N″** (solvent separated ion pair) and **P′**/**P″** (contact ion pair)

In summary, this study shows that the deprotonation of alkyl propargyl ethers with *n*-butyllithium provides an ambident anion which reacts with carbonyl compounds to give

mixtures of the expected γ-addition and α-addition products. The observed regioselectivity depends on the solvent employed: in diethyl ether the γ-adducts are favored and in THF the α-adducts predominate. After cyclization either under silver or gold catalysis, γ-adducts such as benzaldehyde-derived allenyl alcohol **4** provided 2,3-disubstituted furans like **6**. On the other hand, the regioisomeric 2,5-disubstituted furan **7** was smoothly obtained by the gold-catalyzed isomerization of α-addition product **5**. The regioselective reactions of lithiated propargyl ethers with ketones as electrophile provide the corresponding 2,5-dihydrofuran derivatives, for instance spiro-compound **22**. These products contain a ketal moiety at C-5 of the 2,5-dihydrofuran ring which should allow subsequent Lewis acid-promoted substitution reactions. Although the methods reported here were not optimized they show an interesting regiodivergent approach to specifically substituted furan and dihydrofuran derivatives.[21]

Reactions were generally performed under argon in flame-dried flasks, and the components were added by syringe. Unless otherwise stated, yields refer to analytically pure samples.

The solvents (THF, CH_2Cl_2, CH_3CN, and Et_2O) were dried with the solvent system SPS-800 (M. Braun GmbH). Hexanes (mixture of isomers) and EtOAc were dried with CaH_2 or K_2CO_3, respectively, and distilled of before use. Et_3N and pyridine were distilled from CaH_2 and stored under an argon atmosphere. The concentration of *n*BuLi (ca. 2.4 M in hexanes, Acros) was determined by the diphenylacetic acid method. Reagents were purchased and used without further purification. KO*t*Bu was freshly sublimed in vacuo before use. TLC was performed with silica gel 60 F254 plates (Merck), column chromatography was performed with silica gel 60 (230–400 mesh, 40–63 μm, Merck or Fluka).

^{1}H NMR [$CHCl_3$ (δ = 7.26 ppm), TMS (δ = 0.00 ppm) as internal standard] and ^{13}C NMR spectra [$CDCl_3$ (δ = 77.0 ppm) as internal standard] were recorded in $CDCl_3$ solutions with Bruker AC 250, EXC 400 instruments or a Joel Eclipse 500 instrument. Integrals are in accordance with assignments; coupling constants are given in Hz. Multiplicities refer to: $C_{quart.}$ (s), CH (d), CH_2 (t), CH_3 (q). ^{1}H/^{13}C-correlated spectra (HSQC, HMBC) and ^{1}H/^{1}H-correlated spectra (COSY, NOESY) were recorded for assignments. IR spectra were measured with Nicolet 5 SXC FTIR or Nicolet 205 FTIR spectrometers. MS analyses were performed with Aligent 6210 (ESI-TOF, 4 kV), Ionspec QFT-7 (ESI-FT-ICR), CH-5 (FAB), Varian, and with MAT 711 (EI, 80 eV, 8 kV), Finigan. The elemental analyses were recorded with Vario El, III (Elementar).

General Procedure for Lithiation of the Propargylic Ethers (GP1)

Under an atmosphere of dry argon, the corresponding propargylic ether (1.0 equiv) was dissolved in Et_2O (4 mL/mmol), cooled to –40 °C or –78 °C and a solution of *n*BuLi (0.9–1.2 equiv) was added. After stirring for the indicated time and temperature, the corresponding electrophile was added. After the indicated time, the mixture was quenched with saturated aqueous $NaHCO_3$ solution (10 mL/mmol). The phases were separated and the aqueous phase was extracted with Et_2O (2 × 10 mL/mmol). The combined organic phases were dried (Na_2SO_4), filtered and evaporated in vacuo to provide the crude product.

General Procedure for Silver(I)-Catalyzed Cyclizations (GP2)

Under exclusion of light, the crude addition product, silver nitrate (0.2 equiv) and potassium carbonate (5 equiv) were put into a flask which was evacuated and flushed with argon. The mixture was dissolved in acetonitrile (5 or 10 mL), stirred for 19 h at room temperature and filtered through a pad of Celite. After washing with ethyl acetate and evaporation of the filtrate, the crude product was purified by column chromatography.

General Procedure for Gold(I)-Catalyzed Cyclizations (GP3)

In a flame-dried flask under argon, to a solution of the crude addition product in dichloromethane (10 mL) were added pyridine (0.15 equiv) and gold(I) chloride (0.05 equiv) and the mixture was stirred for 19 h at room temperature. Dichloromethane (5 mL), saturated aqueous sodium $NaHCO_3$ solution (5 mL) and water (5 mL) were added and the aqueous phase was extracted with dichloromethane (3 × 10 mL/mmol). The combined organic phases were dried with $MgSO_4$, concentrated in vacuo and purified by column chromatography.

Deuteration Experiments

According to **GP1**, propargyl ether **1** (100 mg, 0.68 mmol) in diethyl ether (3 mL) was treated with *n*BuLi (0.3 mL, 0.75 mmol, 1.2 equiv) at –78 °C. Small samples of the mixture were taken via syringe and quenched with methanol-D_4 within the syringe (slight warming before deuteration cannot be excluded). Samples were taken after 5, 15, 30, 45, 60 und 120 min. Without purification, the resulting product mixture was analyzed by ^{1}H NMR spectroscopy.

Data of deuterated compound 2

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.45 (s, 3 H, OMe), 7.08 (s, 1 H, =CH), 7.30–7.35, 7.38–7.43 (2 m, 3 H, 2 H, Ph).

2,3-Diphenylfuran (6)

According to **GP1** (Table 1, entry 1), propargyl ether **1** (205 mg, 1.40 mmol) in Et_2O (10 mL) was treated with *n*BuLi (0.71 mL, 1.68 mmol) for 15 min at –78 °C. Benzaldehyde (164 mg, 1.54 mmol) was added and the mixture was quenched after 1 h with water. Work-up provided the crude product (595 mg) as a mixture of compounds **4** and **5**.

According to **GP2**, the crude product mixture was stirred with $AgNO_3$ (48 mg, 0.28 mmol), K_2CO_3 (966 mg, 7.00 mmol) in acetonitrile (10 mL) for 19 h at room temperature. Purification by chromatography (silica gel, hexanes/EtOAc 50:1 to 20:1) furnished **1** (14 mg, 7%), **6** (138 mg, 50%) and **5** (18 mg, 5%, ratio of diastereomers: *syn*/*anti* ≈ 2:1) as yellow oils.

2,3-Diphenylfuran (6)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.55 (d, *J* = 1.8 Hz, 1 H, 4-H), 7.26–7.43 (m, 8 H, Ph), 7.49 (d, *J* = 1.8 Hz, 1 H, 5-H), 7.50–7.54 (m, 2 H, Ph).

The data agree with those of the literature.[17c]

syn-2-Methoxy-1,4-diphenylbut-3-yn-1-ol (5)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.50 (s, 3 H, OMe), 4.37 (d, *J* = 4.3 Hz, 1 H, 2-H), 4.96 (d, *J* = 4.2 Hz, 1 H, 1-H), 7.26–7.41, 7.46–7.52 (2 m, 8 H, 2 H, Ph); the signal of OH could not be detected.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 57.3 (q, OMe), 75.4, 77.2 (2 d, C-1, C-2), 84.4, 88.7 (2 s, C-3, C-4), 122.5, 127.0, 128.2, 128.4, 128.4, 128.7, 131.9, 139.5 (s, 6 d, s, Ph).

***anti*-2-Methoxy-1,4-diphenylbut-3-yn-1-ol (5)**

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.58 (s, 3 H, OMe), 4.16 (d, *J* = 8.0 Hz, 1 H, 2-H), 4.80 (d, *J* = 8.0 Hz, 1 H, 1-H), 7.26–7.40, 7.46–7.52 (2 m, 8 H, 2 H, Ph); the signal of OH could not be detected.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 57.1 (q, OMe), 76.5, 77.2 (2 d, C-1, C-2), 84.7, 88.5 (2 s, C-3, C-4), 122.4, 127.5, 128.1, 128.2, 128.4, 128.7, 131.8, 139.2 (s, 6 d, s, Ph).

Data of both isomers

IR (ATR): 3450 (O-H), 3060–2820 (=C-H, C-H), 2225 (C≡C), 1605 (C=C) cm^{-1}.

HRMS (ESI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{16}O_2Na$: 275.1043; found: 275.1045.

2,5-Diphenylfuran (7)

According to **GP1** but using THF (Table 1, entry 9), propargyl ether **1** (197 mg, 1.35 mmol) in THF (10 mL) was treated with *n*BuLi (0.54 mL, 1.21 mmol) for 1 h at –40 °C. Benzaldehyde (158 mg, 1.48 mmol) was added and the mixture was quenched after 1.5 h with water. Work-up provided the crude product (546 mg) as a mixture of compounds.

According to **GP3**, the crude product mixture was stirred with AuCl (14 mg, 0.06 mmol), pyridine (15 µL, 0.18 mmol) in CH_2Cl_2 (10 mL) for 19 h at room temperature. The received crude product still contained compound *anti*-**5** and therefore the procedure was repeated. Purification by chromatography (silica gel, hexanes/EtOAc 50:1 to 20:1) furnished **1** (4 mg, 2%) and a 20:80 mixture of **6** and **7** (200 mg, 75%); the calculated yields of **6** and **7** are 15% and 60%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.74 (s, 2 H, 3-H, 4-H), 7.28, 7.37–7.44, 7.72–7.77 (m_c, 2 m, 2 H, 4 H, 4 H, Ph).

The data agree with those of the literature.[22]

Synthesis of 7 Starting with Pure Compound 5

According to **GP3**, alkynyl alcohol **5** (140 mg, 0.56 mmol) was stirred with AuCl (6.5 mg, 0.03 mmol) and pyridine (6.7 µL, 0.08 mmol) in CH_2Cl_2 (9 mL) for 19 h at room temperature. The received crude product was dissolved in $CHCl_3$ and stirred with silica gel to complete the elimination of methanol. Purification by chromatography (silica gel, hexanes/EtOAc 20:1) furnished **7** (90 mg, 73%) as solid.

(*E*)-3-Phenyl-2-styrylfuran (11)

According to **GP1**, propargyl ether **1** (200 mg, 1.37 mmol) in Et_2O (10 mL) was treated with *n*BuLi (0.53 mL, 1.23 mmol) for 15 min at –78 °C. Cinnamic aldehyde (181 mg, 1.37 mmol) was added and the mixture was quenched after 1 h with water. Work-up provided the crude product (600 mg) as a mixture of compounds **10** and **1**.

According to **GP2**, the crude product mixture was stirred with $AgNO_3$ (42 mg, 0.25 mmol), K_2CO_3 (846 mg, 6.15 mmol) in acetonitrile (10 mL) for 19 h at room temperature. To complete the elimination, the crude product was dissolved in $CHCl_3$ (10 mL) and stirred under argon with silica gel for 10 h at room temperature. Purification by chromatography (silica gel, hexanes/EtOAc 50:1 to 20:1) furnished **11** (90 mg, 30%) as yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.62 (d, *J* = 1.9 Hz, 1 H, 4-H), 7.12, 7.22 (2 d, *J* = 16.1 Hz, 1 H each, HC=CH), 7.24–7.29, 7.33–7.39 (2 m, 2 H, 3 H, Ph), 7.46 (d, *J* = 1.9 Hz, 1 H, 5-H), 7.47–7.52 (m, 5 H, Ph).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 112.8, 115.4 (2 d, Furan-CH, C=CH), 124.7, 126.5, 127.2, 127.7, 128.2, 128.5, 128.8, 128.9 (3 d, s, 4 d, Furan-C, Ph, C=CH), 133.7, 137.3 (2 s, Ph), 142.0 (d, Furan-CH), 148.6 (s, Furan-C).

The data agree with those of the literature.[23]

(*E*)-2-Phenyl-5-styrylfuran (13)

According to **GP1** but using THF, propargyl ether **1** (200 mg, 1.37 mmol) in THF (10 mL) was treated with *n*BuLi (0.55 mL, 1.23 mmol) for 1 h at –78 °C. Cinnamic aldehyde (189 mg, 1.50 mmol) was added and the mixture was quenched after 1 h with water. Work-up provided the crude product (330 mg) as a mixture of compounds **10**, **12** and **1**.

According to **GP3**, the crude product mixture was stirred with AuCl (14 mg, 0.06 mmol), pyridine (15 µL, 0.18 mmol) in CH_2Cl_2 (10 mL) for 19 h at room temperature. Purification by chromatography (silica gel, hexanes/EtOAc 50:1 to 20:1) furnished **13** (75 mg, 25%), **11** (15 mg, 5%) and precursor **1** (45 mg, 25%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.44, 6.70 (2 d, *J* = 3.4 Hz, 1 H each, 3-H, 4-H), 6.92, 7.14 (2 d, *J* = 16.2 Hz, 1 H each, HC=CH), 7.19–7.53, 7.74 (m, m_c, 9 H, 1 H, Ph).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 107.5, 111.2, 116.5 (3 d, Furan-CH, C=CH), 124.0, 126.5, 127.1, 127.6, 127.7, 128.9 (6 d, Ph, Furan-CH), 130.8, 137.2, 153.0, 153.6 (4 s, Ph, Furan-C).

The data agree with those of the literature.[22]

3-Phenyl-2-undecylfuran (16)

According to **GP1**, propargyl ether **1** (200 mg, 1.37 mmol) in Et_2O (10 mL) was treated with *n*BuLi (0.66 mL, 1.64 mmol) for 15 min at –78 °C. Dodecanal (252 mg, 1.37 mmol) was added and the mixture was quenched after 2 h with water. Work-up provided a mixture of crude product **14** and **15** (ratio ca. 5:1, 815 mg).

According to **GP2**, the crude product mixture was stirred with $AgNO_3$ (46 mg, 0.27 mmol), K_2CO_3 (945 mg, 9.84 mmol) in acetonitrile (10 mL) and THF (10 mL) for 19 h at room temperature. To complete the elimination, the crude product was dissolved in $CHCl_3$ (10 mL) and stirred under argon with silica gel for 10 h at room temperature. Purification by chromatography (silica gel, alumina, hexanes/EtOAc 20:1 to 4:1) furnished **16** (376 mg, 61%) as yellow oil, a 4:1 mixture of **15** and **16** (20 mg, 4%) and pure compound **15** (65 mg, 13%, ratio of diastereomers *syn*/*anti* ≈ 2.1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 6.8 Hz, 3 H, Me), 1.22–1.37, 1.71 (m, m_c, 16 H, 2 H, CH_2), 2.79 (t, *J* = 7.5 Hz, 2 H, 2-CH_2), 6.51 (d, *J* = 1.6 Hz, 1 H, 4-H), 7.25–7.31 (m, 1 H, Ph), 7.36 (dd, *J* = 0.5, 1.6 Hz, 1 H, 5-H), 7.38–7.43 (m, 4 H, Ph).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 14.2 (q, Me), 22.8, 27.0, 28.6, 29.45, 29.46*, 29.67, 29.74, 29.75, 32.0 (9 t, CH_2), 111.3 (d, C-4), 120.8 (s, C-3), 126.4, 127.9, 128.6, 134.5 (3 d, s, Ph), 140.4 (d, C-5), 152.2 (s, C-2); * signal with higher intensity.

***syn*-3-Methoxy-1-phenylpentadec-1-yn-4-ol (15)**

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.9 Hz, 3 H, Me), 1.13–1.38, 2.12–2.19 (2 m, 18 H, 2 H, CH_2), 2.60 (br s, 1 H, OH), 3.52 (s, 3 H, OMe), 3.77–3.84 (m, 1 H, 4-H), 4.17 (d, *J* = 3.9 Hz, 1 H, 3-H), 7.28–7.36, 7.40–7.49 (2 m, 2 H, 3 H, Ph).

***anti*-3-Methoxy-1-phenylpentadec-1-yn-4-ol (15)**

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 6.9 Hz, 3 H, Me), 1.13–1.38, 1.83–1.89 (2 m, 18 H, 2 H, CH_2), 2.60 (br s, 1 H, OH), 3.52 (s, 3 H, OMe), 3.69–3.74 (m, 1 H, 4-H), 3.97 (d, *J* = 7.7 Hz, 1 H, 3-H), 7.28–7.36, 7.41–7.51 (2 m, 2 H, 3 H, Ph).

The sensitive compounds **16** and **15** decomposed by oxidation before further characterization.

5-Methoxy-2,2-dimethyl-3-phenyl-2,5-dihydrofuran (19)

According to **GP1**, propargyl ether **1** (200 mg, 1.37 mmol) in Et_2O (5 mL) was treated with *n*BuLi (0.66 mL, 1.64 mmol) for 15 min at –78 °C. Acetone (0.30 mL, 235 mg, 4.10 mmol) was added and the mixture was quenched after 2 h with water. Work-up provided the crude product (280 mg) as a 5:1 mixture of compounds **17** and **18**.

According to **GP2**, the crude product mixture was stirred with $AgNO_3$ (47 mg, 0.27 mmol), K_2CO_3 (568 mg, 4.11 mmol) in acetonitrile (5 mL) for 19 h at room temperature. Purification by chromatography (alumina, hexanes/EtOAc 20:1 to 4:1) furnished **19** (152 mg, 54%) and **18** (31 mg, 11%) as yellow oils.

IR (ATR): 3060–2870 (=C-H, C-H), 1600 (C=C) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.48, 1.57 (2 s, 3 H each, Me), 3.45 (s, 3 H, OMe), 5.69 (d, *J* = 1.2 Hz, 1 H, 5-H), 5.86 (d, *J* = 1.2 Hz, 1 H, 4-H), 7.30–7.36, 7.38–7.41 (2 m, 3 H, 2 H, Ph).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.0, 29.0 (2 q, Me), 54.4 (q, OMe), 88.4 (s, C-2), 106.6 (d, C-5), 121.8 (d, C-4), 127.4, 128.3, 128.5, 133.5 (3 d, s, Ph), 152.8 (s, C-3).

HRMS (pos. ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{16}O_2Na$: 227.1043; found: 227.1043.

Anal. Calcd for $C_{13}H_{16}O_2$ (204.3): C, 76.44; H, 7.90. Found: C, 76.40; H, 7.07.

3-Methoxy-2-methyl-5-phenylpent-4-yn-2-ol (18)

IR (ATR): 3455 (O-H), 2990–2835 (=C-H, C-H), 2225 (C≡C), 1605 (C=C) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.350, 1.354 (2 s, 3 H each, Me), 3.53 (s, 3 H, OMe), 3.97 (s, 1 H, 3-H), 7.30–7.34, 7.44–7.48 (2 m, 3 H, 2 H, Ph); the signal of OH could not be detected.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 24.5, 25.6 (2 q, Me), 57.6 (q, OMe), 73.0 (s, C-2), 79.9 (d, C-3), 85.6, 87.4 (2 s, C-4, C-5), 122.5, 128.4, 128.7, 131.9 (s, 3 d, Ph).

HRMS (pos. ESI): *m*/*z* for [M +Na]$^+$ calcd for $C_{13}H_{16}O_2Na$: 227.1043; found: 227.1049.

2-Methoxy-4-phenyl-1-oxaspiro[4.5]dec-3-ene (22)

According to **GP1**, propargyl ether **1** (230 mg, 1.57 mmol) in Et_2O (5 mL) was treated with *n*BuLi (0.76 mL, 1.89 mmol) for 15 min at –78 °C. Cyclohexanone (462 mg, 4.71 mmol) was added and the mixture was quenched after 2 h with water. Work-up provided the crude product (603 mg, ratio of **20**/**21** ≈ 4:1).

The crude product was stirred with KO*t*Bu (53 mg, 0.47 mmol) in DMSO (5 mL) for 19 h at room temperature. After quenching with saturated aqueous $NaHCO_3$ solution (4 mL) the aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic phases were dried with Na_2SO_4. After evaporation the crude product (395 mg) was purified by chromatography (alumina, hexanes/EtOAc 20:1 to 10:1) to provide **22** (201 mg, 52%) and **21** (49 mg, 13%) as yellow oils.

IR (ATR): 3080–2820 (=C-H, C-H), 1595 (C=C) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13 (qt, *J* = 12.9, 3.4 Hz, 1 H, CH_2), 1.59–1.84 (m, 9 H, CH_2), 3.47 (s, 3 H, OMe), 5.70 (d, *J* = 1.2 Hz, 1 H, 2-H), 5.78 (d, *J* = 1.2 Hz, 1 H, 3-H), 7.30–7.35 (m, 5 H, Ph).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 22.4, 22.7, 25.2, 35.8, 36.8 (5 t, CH_2), 54.2 (q, OMe), 89.9 (s, C-5), 106.5 (d, C-2), 122.53 (d, C-3), 127.9, 128.3, 128.5, 134.4 (3 d, s, Ph), 153.7 (s, C-4).

HRMS (pos. ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{20}O_2Na$: 267.1356; found: 267.1362.

Anal. Calcd for $C_{16}H_{20}O_2$ (244.3): C, 78.65; H, 8.25. Found: C, 78.58; H, 8.14.

1-(1′-Methoxy-3′-phenylprop-2′-ynyl)cyclohexanol (21)

IR (ATR): 3455 (O-H), 3080–2820 (=C-H, C-H), 2220 (C≡C), 1595 (C=C) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83–0.92 (m, 1 H, CH_2), 1.52–1.77 (m, 9 H, CH_2), 3.52 (s, 3 H, OMe), 3.95 (s, 1 H, 1′-H), 7.28–7.35, 7.45–7.49 (2 m, 3 H, 2 H, Ph); the signal of OH could not be detected.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 21.5, 21.6, 26.0, 32.5, 33.4 (5 t, CH_2), 57.7 (q, OMe), 73.6 (s, C-1), 80.1 (d, C-1′), 85.5, 87.8 (2 s, C-2′, C-3′), 122.6, 128.4, 128.6, 131.9 (s, 3 d, Ph).

HRMS (pos. ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{20}O_2Na$: 267.1356; found: 267.1368.

Anal. Calcd for $C_{16}H_{20}O_2$ (244.3): C, 78.65; H, 8.25. Found: C, 78.54; H, 8.33.

5-Methoxy-3-(4-methoxyphenyl)-2,2-dimethyl-2,5-dihydrofuran (24)

According to **GP1**, propargyl ether **23** (200 mg, 1.14 mmol) in Et_2O (7 mL) was treated with *n*BuLi (0.55 mL, 1.36 mmol) for 15 min at –78 °C. Acetone (329 mg, 5.67 mmol) was added and the mixture was quenched after 2 h with water to give after work-up the crude product (384 mg).

According to **GP2**, the crude product mixture was stirred with $AgNO_3$ (39 mg, 0.23 mmol), K_2CO_3 (788 mg, 5.70 mmol) in acetonitrile (10 mL) for 19 h at room temperature. Purification by chromatography (alumina, hexanes/EtOAc 20:1 to 4:1) furnished **24** (132 mg, 50%) and **25** (55 mg, 21%) as yellow oils.

IR (ATR): 3075–2835 (=C-H, C-H), 1610 (C=C) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.47, 1.55 (2 s, 3 H each, Me), 3.42 (s, 3 H, OMe), 3.79 (s, 3 H, OMe), 5.66 (d, *J* = 1.3 Hz, 1 H, 5-H), 5.79 (d, *J* = 1.3 Hz, 1 H, 4-H), 6.84–6.88, 7.32–7.36 (2 m, 2 H each, Ar).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.1, 29.1 (2 q, Me), 54.3 (q, OMe), 55.3 (q, OMe), 88.3 (s, C-2), 106.6 (d, C-5), 113.9 (d, Ar), 120.2 (d, C-4), 125.6 (s, Ar), 128.6 (d, Ar), 152.28 (s, C-3), 159.6 (s, Ar).

HRMS (pos. ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{18}O_3Na$: 257.1148; found: 257.1163.

3-Methoxy-5-(4-methoxyphenyl)-2-methylpent-4-yn-2-ol (25)

IR (ATR): 3470 (O-H), 2975–2825 (=C-H, C-H), 2220 (C≡C), 1605 (C=C) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32, 1.33 (2 s, 3 H each, Me), 3.51 (s, 3 H, OMe), 3.79 (s, 3 H, OMe), 3.93 (s, 1 H, 3-H), 6.79–6.86, 7.34–7.41 (2 m, 2 H each, Ar); the signal of OH could not be detected.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 24.5, 25.6 (2 q, Me), 55.4 (q, OMe), 57.6 (q, OMe), 73.0 (s, C-2), 80.0 (d, C-3), 84.1, 87.3 (2 s, C-4, C-5), 114.0 (d, Ar), 114.6 (s, Ar), 133.3 (d, Ar), 159.9 (s, Ar).

HRMS (pos. ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{18}O_3Na$: 257.1148; found: 257.1149.

Anal. Calcd for $C_{14}H_{18}O_3$ (234.3): C, 71.77; H, 7.74; found: C, 71.53; H, 7.59.

1-Fluoro-4-(3-methoxy-1-propynyl)benzene (26)

Analogously to a literature procedure,[24] to a flame-dried flask under an atmosphere of argon were added methyl propargyl ether (1.40 g, 20.0 mmol), 1-fluoro-4-iodobenzene (5.62 g, 24.0 mmol), $Pd(PPh_3)_2Cl_2$ (421 mg, 0.60 mmol) and NEt_3 (30 mL). After stirring for 5 min at room temperature, CuI (114 mg, 0.60 mmol) was added and the mixture was stirred until the starting materials were fully converted (TLC control). The mixture was filtered through a pad of Celite which was washed with EtOAc and the filtrate was concentrated in vacuo. The crude product was purified by chromatography (silica gel, hexanes/EtOAc 20:1 to 10:1) to afford compound **26** (2.53 g, 94%) as colorless oil.

IR (ATR): 3075–2825 (=C-H, C-H), 2240, 2210 (C≡C), 1605 (C=C) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.44 (s, 3 H, OMe), 4.30 (s, 2 H, 3′-H), 6.97–7.03, 7.40–7.45 (2 m, 2 H each, Ar).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 57.8 (q, OMe), 60.4 (t, C-3′), 84.7 (d, J_{CF} = 1.6 Hz, C-1′), 85.4 (s, C-2′), 115.7 (dd, J_{CF} = 22.1 Hz, Ar), 118.8 (d, J_{CF} = 3.5 Hz, Ar), 133.8 (dd, J_{CF} = 8.4 Hz, Ar), 162.7 (d, J_{CF} = 249.6 Hz, Ar).

HRMS (EI, 80 eV, 70 °C): *m*/*z* [M]$^+$ calcd for $C_{10}H_9FO$: 164.06375; found: 164.06386.

3-(4-Fluorophenyl)-5-methoxy-2,2-dimethyl-2,5-dihydrofuran (27)

According to **GP1**, propargyl ether **26** (200 mg, 1.22 mmol) in diethyl ether (10 mL) was treated with *n*BuLi (0.45 mL, 1.46 mmol) for 15 min at –78 °C. Acetone (353 mg, 6.09 mmol) was added and the mixture was quenched after 2 h with water to give after work-up the crude product (364 mg).

According to **GP2**, the crude product mixture was stirred with $AgNO_3$ (41 mg, 0.24 mmol), K_2CO_3 (842 mg, 6.09 mmol) in acetonitrile (10 mL) for 19 h at room temperature. Purification by chromatography (alumina, hexanes/EtOAc 20/1 to 10/1) furnished **27** (140 mg, 52%) and **28** (42 mg, 16%) as yellow oils.

IR (ATR): 3080–2825 (=C-H, C-H), 1605 (C=C) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44, 1.53 (2 s, 3 H each, Me), 3.43 (s, 3 H, OMe), 5.65 (s, 1 H, 5-H), 5.81 (s, 1 H, 4-H), 7.02 (t, J_{HH} = J_{HF} = 8.6 Hz, 2 H, Ar), 7.35 (dd, J_{HH} = 8.6 Hz, J_{HF} = 5.5 Hz, 2 H, Ar).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 27.9, 28.9 (2 q, Me), 54.5 (q, OMe), 88.3 (s, C-2), 106.5 (d, C-5), 115.5 (dd, J_{CF} = 21.5 Hz, Ar), 121.9 (dd, J_{CF} = 1.3 Hz, C-4), 129.1 (dd, J_{CF} = 8.1 Hz, Ar), 129.5 (d, J_{CF} = 3.5 Hz, Ar), 151.9 (s, C-3), 162.7 (d, J_{CF} = 248.1 Hz, Ar).

HRMS (pos. ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{18}O_3Na$: 245.0948; found: 245.0930.

5-(4-Fluorophenyl)-3-methoxy-2-methylpent-4-yn-2-ol (28)

IR (ATR): 3450 (O-H), 3070–2825 (=C-H, C-H), 2225 (C≡C), 1660 (C=C) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.325, 1.333 (2 s, 3 H each, Me), 3.51 (s, 3 H, OMe), 3.93 (s, 1 H, 3-H), 6.97–7.03, 7.40–7.44 (2 m, 2 H each, Ar); the signal of OH could not be detected.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 24.1, 25.1 (2 q, Me), 57.2 (q, OMe), 72.5 (s, C-2), 79.4 (d, C-3), 84.9 (d, J_{CF} = 1.5 Hz, C-5), 85.8 (s, C-4), 115.2 (dd, J_{CF} = 22.1 Hz, Ar), 118.1 (d, J_{CF} = 3.7 Hz, Ar), 133.3 (dd, J_{CF} = 8.4 Hz, Ar), 162.3 (d, J_{CF} = 250.1 Hz, Ar).

HRMS (pos. ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{15}FO_2Na$: 245.0948; found: 245.0942.

2-(Methoxymethoxy)-1,4-diphenylbut-3-yn-1-ol (31)

According to **GP1** but using THF, propargyl ether **29** (205 mg, 1.16 mmol) in THF (10 mL) was treated with *n*BuLi (0.46 mL, 1.05 mmol) for 15 min at –78 °C. Benzaldehyde (136 mg, 1.28 mmol) was added and the mixture was quenched after 1 h with water. Work-up provided the crude product (350 mg) as a mixture of compounds **30** and **31**.

According to **GP2**, the crude product mixture was stirred with $AgNO_3$ (36 mg, 0.21 mmol), K_2CO_3 (723 mg, 5.24 mmol) in acetonitrile (10 mL) for 19 h at room temperature. Purification by chromatography (silica gel, hexanes/EtOAc 50:1 to 20:1) furnished **6** (32 mg, 14%) and **31** (236 mg, 80%, ratio of diastereomers *syn*/*anti* ≈ 4:1).

Data of *syn*-31

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.00 (br s, 1 H, OH), 3.23 (s, 3 H, OMe), 4.68 (d, *J* = 6.7 Hz, 1 H, OCH_2O), 4.73, 4.95 (2 d, *J* = 4.9 Hz, 1 H each, 2-H, 1-H), 4.98 (d, *J* = 6.7 Hz, 1 H, OCH_2O), 7.27–7.41, 7.48–7.52 (2 m, 8 H, 2 H, Ph).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 55.8 (q, OMe), 72.0, 75.6 (2 d, C-1, C-2), 84.1, 88.4 (2 s, C-3, C-4), 94.4 (t, OCH_2O), 122.5, 127.0, 128.1, 128.2, 128.4, 128.8, 131.9, 139.5 (s, 6 d, s, Ph).

Data of *anti*-31

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.00 (br s, 1 H, OH), 3.28 (s, 3 H, OMe), 4.59 (d, *J* = 7.4 Hz, 1 H, 2-H), 4.74 (d, *J* = 6.7 Hz, 1 H, OCH_2O), 4.88 (d, *J* = 7.4 Hz, 1 H, 1-H), 5.05 (d, *J* = 6.7 Hz, 1 H, OCH_2O), 7.27–7.41, 7.48–7.52 (2 m, 8 H, 2 H, Ph).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 56.1 (q, OMe), 72.1, 76.5 (2 d, C-1, C-2), 84.7, 88.0 (2 s, C-3, C-4), 94.7 (t, OCH_2O), 122.5, 127.4, 128.7, 131.7, 139.2 (s, 3 d, s, Ph); several Ph signals of the minor isomer are covered by those of the major isomer.

The data agree with those of the literature.[19]

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Supporting Information

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