Wittig Rearrangements of (Heteroaryl)alkyl Propargyl Ethers − Synthesis of Allenic and Propargylic Alcohols

Saverio Florio,[b] Catia Granito,[a] Giovanni Ingrosso,[a] and Luigino Troisi*[a]

Keywords: Allenic and propargylic alcohols / (Heteroaryl)alkyl propargyl ethers / Heterocycles / Sigmatropic rearrangements

(Heteroaryl)alkyl propargyl ethers have been synthesized and treated with *n*BuLi in THF at −78 °C. The resulting α- or α′-lithio derivatives could be trapped with iodomethane, affording the corresponding α- or α′-methylated products. Treatment in the absence of an external electrophile resulted either in allenic alcohols or in propargylic alcohols, or in mixtures of both compounds, probably arising from competing [1,2]- and [2,3]-Wittig rearrangements, in varying ratios. A high *anti* diastereoselectivity was observed in the propargylic alcohols produced.

Introduction

Sigmatropic rearrangements are a powerful tool for new C−C bond formation, already widely exploited in the synthesis of several organic compounds of considerable biological and pharmacological interest.

While Claisen rearrangements of phenyl propargyl ethers,[1] thioethers[2] and amines[3] have been extensively studied, only a few examples of related [1,2]- and [2,3]-Wittig sigmatropic rearrangements have been reported. Enantioselective [1,2]-Wittig rearrangements of benzyl propargyl ethers in the presence of external chiral ligands[4] have been investigated by Nakai et al., as has the rearrangement of *O*-glycosides to afford potential precursors of interesting biological compounds.[5] Examples of [2,3]-Wittig rearrangements, proceeding with high diastereo- and enantioselectivities, have been reported for crotyl,[6] allyl[7] and cinnamyl[8] ethers. Competing [1,2]- and [2,3]-Wittig rearrangements have been described for allyl and propargyl furfuryl ethers[9] and for macrocyclic allyl propargyl ethers.[10] Such Wittig rearrangements provide allenic and propargylic alcohols, which can alternatively be prepared through the coupling reactions of carbanions with electrophiles.[11−13]

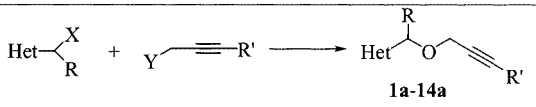
We have recently shown that deprotonated (*n*BuLi in THF at −78 °C) allyl (heteroaryl)alkyl ethers give rise to allylic and homoallylic alcohols as a result of competing [1,2]- and [2,3]-Wittig rearrangements, with interesting diastereoselectivity and good enantiomeric enrichment.[14] Encouraged by these findings, we next turned our attention to the behaviour of (heteroaryl)alkyl propargyl ethers with strong bases. In this paper we report a stereoselective preparation of propargylic and allenic alcohols, based on [1,2]- and [2,3]-Wittig rearrangements of (heteroaryl)alkyl propargyl ethers.

[a] Dipartimento di Scienze e Tecnologie Biologiche ed Ambientali, University of Lecce,
Via Prov.le Lecce-Monteroni, 73100 Lecce, Italy
Fax: (internat.) + 39-0832/320701
E-mail: luigino.troisi@unile.it
[b] CNR, Istituto di Chimica dei Composti Organometallici-ICCOM, Sezione di Bari, Dipartimento Farmaco-Chimico, University of Bari,
Via E. Orabona 4, 70125 Bari, Italy

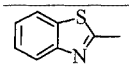
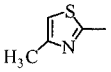
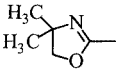
Results and Discussion

A number of (heteroaryl)alkyl propargyl ethers for subjection to sigmatropic rearrangements were prepared by three alternative synthetic routes (Scheme 1).

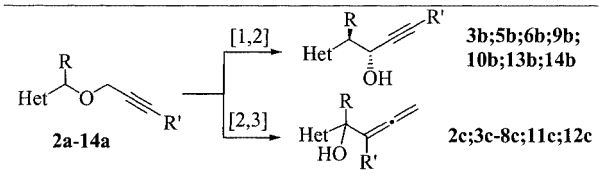
Compounds **1a**, **2a** and **5a**−**7a** were prepared by stirring a solution of the corresponding (heteroaryl)alkyl carbinol and the corresponding propargyl bromide in a two-phase system, with tetrabutylammonium bromide (TBAB) as phase-transfer catalyst. Compounds **3a** and **10a**−**14a** were prepared by treatment of the appropriate (heteroaryl)alkyl chloride with the propargyl alcohols in a two-phase system, again with TBAB as phase-transfer catalyst. Compounds **4a**, **8a** and **9a** were prepared from the corresponding (heteroaryl)alkyl carbinol and the propargyl chloride, with sodium hydroxide in acetone. A more detailed description is given in the Exp. Sect. During the above preparations, we found that compound **1a** is prone to desilylation, affording 2-(prop-2-ynyloxymethyl)benzothiazole in high yield (94%). The substrate **1a** could therefore not be used for our investigation. Compound **12a** could be isolated only by purification of the crude compound by flash column chromatography; attempted purification by column chromatography caused ring-cleavage to give (quantitative conversion) *N*-(2-hydroxy-1,1-dimethylethyl)-2-(3-phenylprop-2-ynyloxy)-



1a-14a

Het	R	X	Y	R'	Products	Yields (%)[a]
	H	OH	Br	$Si(CH_3)_3$	**1a**	94
„	H	OH	Br	CH_3	**2a**	60
„	H	Cl	OH	Ph	**3a**	85
„	CH_3	OH	Cl	Ph	**4a**	80
„	CH_3	OH	Br	CH_3	**5a**	80
	CH_3	OH	Br	CH_3	**6a**	80
„	Ph	OH	Br	CH_3	**7a**	84
„	Ph	OH	Cl	Ph	**8a**	50
„	CH_3	OH	Cl	Ph	**9a**	40
	H	Cl	OH	Ph	**10a**	95
„	H	Cl	OH	CH_3	**11a**	89
	H	Cl	OH	Ph	**12a**	60
„	CH_3	Cl	OH	CH_3	**13a**	70
„	CH_3	Cl	OH	Ph	**14a**	75

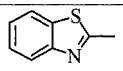
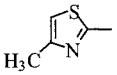
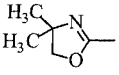
Scheme 1. Synthesis of (heteroaryl)alkyl propargyl ethers: [a]isolated yields



2a-14a

3b;5b;6b;9b; 10b;13b;14b

2c;3c-8c;11c;12c

2c:	Het =		R = H; R' = CH_3
3b, 3c:	Het =	„	R = H; R' = Ph
4c:	Het =	„	R = CH_3; R' = Ph
5b, 5c:	Het =	„	R = R' = CH_3
6b, 6c:	Het =		R = R' = CH_3
7c:	Het =	„	R = Ph; R' = CH_3
8c:	Het =	„	R = R' = Ph
9b:	Het =	„	R = CH_3; R' = Ph
10b:	Het =		R = H; R' = Ph
11c:	Het =	„	R = H; R' = CH_3
12c:	Het =		R = H; R' = Ph
13b:	Het =	„	R = R' = CH_3
14b:	Het =	„	R = CH_3; R' = Ph

Scheme 2. Synthesis of propargylic and allenic alcohols by competitive [1,2]- and [2,3]-Wittig rearrangements of (heteroaryl)alkyl propargyl ethers

Table 1. Summary of the [1,2]- and [2,3]-Wittig rearrangements of (heteroaryl)alkyl propargyl ethers

Substrate	Type of rearrangement	Products (% yield)[a]
2a	[2,3]	**2c** (66)
3a	[1,2]	**3b** (25)
3a	[2,3]	**3c** (45)
4a	[2,3]	**4c** (54)
5a	[1,2]	**5b** (9) (*anti*)
5a	[2,3]	**5c** (78)
6a	[1,2]	**6b** (75) (*anti*)
6a	[2,3]	**6c** (20)
7a	[2,3]	**7c** (79)
8a	[2,3]	**8c** (70)
9a	[1,2]	**9b** (90) (*anti*/*syn* = 75:25)
10a	[1,2]	**10b** (90)
11a	[2,3]	**11c** (80)
12a	[2,3]	**12c** (55)
13a	[1,2]	**13b** (50) (*anti*)
14a	[1,2]	**14b** (65) (*anti*/*syn* = 70:30)

[a] Isolated yields.

acetamide, the structure of which was established by IR, $^1H/^{13}C$ NMR and GC-MS analysis. Similar behaviour has been reported for analogous substrates.[15]

(Heteroaryl)alkyl propargyl ethers **2a**−**14a** were treated with *n*BuLi in THF at −78 °C. After the reaction mixture had been allowed to warm slowly to room temperature (1−2 h), we isolated propargylic alcohols, allenic alcohols or both compounds in varying ratios, probably arising from competing [1,2]- and [2,3]-Wittig rearrangements, in good yields (Scheme 2, Table 1).

In more detail, substrates **2a**, **4a**, **7a**, **8a**, **11a** and **12a** exclusively underwent the [2,3]-Wittig rearrangement to afford the allenic alcohols as the sole products. An analogous rearrangement for allyl (heteroaryl)alkyl ethers has recently been described[14] and extensively investigated for various substrates.[16] In contrast, substrates **9a**, **10a**, **13a** and **14a** underwent the [1,2]-Wittig rearrangement to give the propargylic alcohols as the sole products. Such a rearrangement is likely to proceed by a radical dissociation/recombination mechanism, according to the literature.[17] (Heteroaryl)alkyl propargyl ethers **3a**, **5a** and **6a**, underwent both the [1,2]- and [2,3]-Wittig rearrangements to generate the propargylic and the allenic alcohols in variable ratios (Table 1). The Het, R and R′ substituents seem to play a key role in stabilizing the α- and/or the α′-carbon atom deprotonated structure, which evolve to the allenic and/or the propargylic alcohol through the [2,3]- and/or the [1,2]-Wittig rearrangement. Contrary to what might have been expected from the influence of the R and R′ substituents, we noticed that the substrate **4a** produced only compound **4c**, by the [2,3]-Wittig rearrangement. Probably, the combined influence of Het, R and R′ substituents together with the aggregation and solvation of the intermediate lithium com-

pound give this unexpected result. An interestingly high *anti* diastereoselectivity was observed in the propargylic alcohols obtained; for the substrates **5a**, **6a** and **13a** the propargylic alcohol isolated was only of the *anti* type, as shown in Table 1. Deprotonation of substrates **9a** and **14a** resulted in reasonable *anti*/*syn* ratios (*anti*/*syn* = 75:25 and 70:30, respectively). The stereochemistry was assigned to the *syn* and *anti* isomers on the basis of coupling constant values (^3J) measured between the two vicinal protons H_A and H_B (Figure 1).

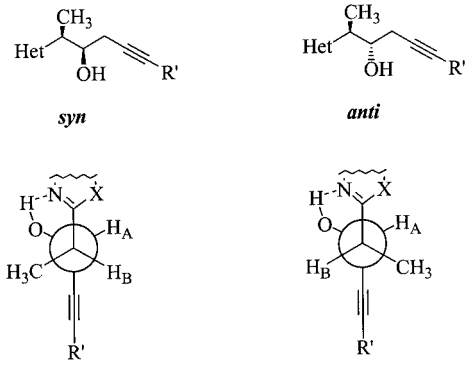


Figure 1. *syn* and *anti* isomers of a propargylic alcohol; the stereochemistry was assigned on the basis of coupling constant of the vicinal protons H_A and H_B

Since the substituents Het and the propargyl group linked to the stereogenic centre were bulkier than the others (CH_3 and OH), it is reasonable that the most stable conformations of both the *syn* and the *anti* isomer should be those in which there is an antiperiplanar orientation of Het and the propargyl group, with no *gauche* interaction between them.[18] This explains why H_A and H_B are coupled more strongly in the *anti* isomer ($^3J_{AB,anti}$ = 6.6 − 7.0 Hz) than in the *syn* isomer ($^3J_{AB,syn}$ = 3.9 − 4.0 Hz). The intramolecular hydrogen bonding occurring in each of the two rotamers (between OH and Het) supports the most probable conformation predicted for each diastereomer.

The observed *anti* diastereoselectivity might be explained in terms of transition state energy as illustrated in Figure 2. The lithiated starting propargylic ether, in a first step, radicalizes and then isomerizes, evolving into a six-membered chair-like transition state that places both the R and the R′ groups in equatorial situations. The final result is the propargylic alcohol of *anti* configuration.

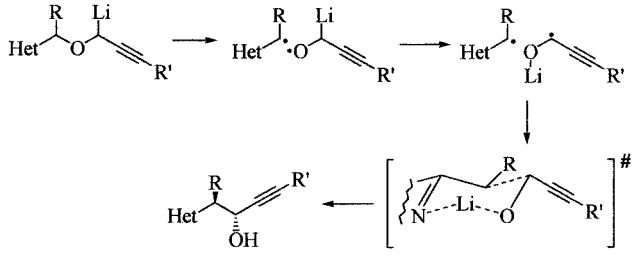
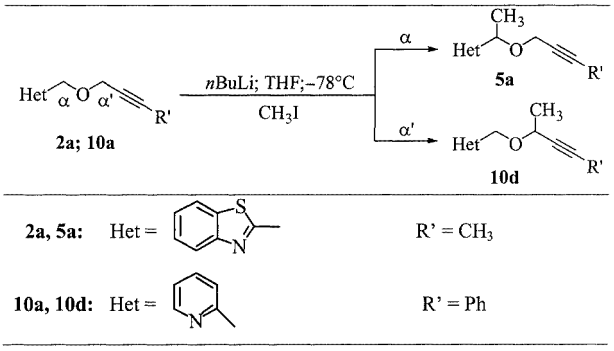


Figure 2. Supposed mechanism explaining the high *anti* diastereoselectivity of propargylic alcohols

In order to prove that the Wittig rearrangement occurs through the carbanionic intermediate, substrates **2a** and **10a** were deprotonated with *n*BuLi in the presence of iodomethane. Compound **2a** exclusively afforded the methylation product **5a** (95% yield), while **10a** gave the coupling product **10d** (30% yield) together with the [1,2]-rearranged product **10b**, thus confirming that the occurrence of the [2,3]- or the [1,2]-Wittig rearrangement is governed by the generation of the carbanion at the α- or at the α′-carbon atom, respectively[14] (Scheme 3).



Scheme 3. Deprotonation of (heteroaryl)alkyl propargyl ethers in the presence of iodomethane as the electrophile

No [1,2]-Wittig rearrangement product was isolated when the deprotonation took place at the α-carbon atom, and no [2,3]-Wittig rearrangement product was obtained when deprotonation occurred at the α′-carbon atom. Treatment of the above substrates with a stronger base such as *tert*-butyllithium (*t*BuLi) did not produce any change, contrarily to what has been reported by Tsubuki et al., for propargyl furfuryl ethers.[9]

In conclusion, we have shown that (benzothiazolyl-, thiazolyl-, pyridinyl- and oxazolinyl)alkyl propargyl ethers, when deprotonated with strong bases in THF and in the absence of an external electrophile, undergo competing [1,2]- and [2,3]-Wittig rearrangements. Either propargylic or allenic alcohols, or variable ratios of both, were isolated in good yields. The competition between the [2,3]- and [1,2]-rearrangements might be explained in terms of different proton acidities at the α- or the α′-carbon atom, due to the different electron-withdrawing ability of the heterocyclic group involved, while the high *anti* diastereoselectivity observed for the [1,2]-Wittig rearrangement might be explained in terms of transition state energy.

The various functionalities − such as the triple bond, the cumulated double bond, the alcohol and the heterocyclic function − confer remarkable synthetic interest on the above compounds. With benzothiazole, thiazole, and oxazoline as the heterocycle, the option of freeing the masked acyl groups makes them potential intermediates for more complicated organic syntheses.

Experimental Section

General Remarks: *n*BuLi was a commercial solution in hexanes (Aldrich) and was titrated with *N*-pivaloyl-*o*-toluidine prior to use.[19] THF, TBAB, benzothiazole, 4-methylthiazole, propargyl bromides [(3-bromoprop-1-ynyl)trimethylsilane, 1-bromobut-2-yne], but-2-

yn-1-ol, acetaldehyde and benzaldehyde were of commercial grade (Aldrich), as were 3-phenylprop-2-yn-1-ol, 2,4,4-trimethyl-2-oxazoline and 2-ethyl-4,4-dimethyl-2-oxazoline (Lancaster), and were used without further purification. 2-(Chloromethyl)pyridine is available (Aldrich) as the hydrochloride, from which it can be obtained by treatment with 5% NaOH solution. (3-Chloroprop-1-ynyl)benzene was prepared by chlorination of 3-phenylprop-2-yn-1-ol, as previously reported.[20] "Petroleum ether" refers to the 40−60 °C boiling fraction. The ^{1}H and the ^{13}C NMR spectra were recorded with a Bruker AC 200 apparatus (200 MHz and 50.3 MHz, for ^{1}H and ^{13}C, respectively), with $CDCl_3$ as solvent and TMS as internal standard (δ_H = 7.26 ppm for ^{1}H spectra; δ_H = 77.0 ppm for ^{13}C spectra). The IR spectra were recorded with a Perkin−Elmer Model 283 spectrometer. GC-MS analyses were performed with a Hewlett−Packard HP-5890 series II gas chromatograph (5% phenylmethylsiloxane capillary column, 30 m, 0.25 mm i.d.), equipped with an HP 5971 mass-selective detector operating at 70 eV (EI). Melting points are uncorrected. A Jasco P-1020 polarimeter was used for polarimetric measurements. TLC was performed on Merck silica gel plates with F-254 indicator; viewing was under UV light (254 nm). Column chromatography was performed on silica gel (63−200 μm), flash column chromatography was performed on silica gel (40−63 μm) with petroleum ether/diethyl ether (Et_2O) mixtures as eluents. All reactions involving air-sensitive reagents were performed under nitrogen in oven-dried glassware by syringe/septum cap techniques.

General Procedure for the Preparation of (Heteroaryl)alkyl Propargyl Ethers: Compounds **1a**, **2a** and **5a**−**7a** were prepared by stirring a solution of the appropriate (heteroaryl)alkyl carbinol (3 mmol) and the corresponding propargyl bromide (4 mmol) at room temperature in a two-phase system (50 mL of THF/50 mL of 10% aqueous NaOH solution) with TBAB (0.2 mmol) under phase-transfer conditions for 1 h. The resulting mixtures were quenched with 40−100 mL of a saturated aqueous NH_4Cl solution and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by column chromatography (silica gel 63−200 μm; petroleum ether/Et_2O, 1:1) to afford the pure (heteroaryl)alkyl propargyl ethers (oils); yields: 60−94%. The propargylic ether **5a** was alternatively prepared by means of the coupling reaction with iodomethane according to the procedure reported for compound **10d**.

2-(Prop-2-ynyloxymethyl)benzothiazole (1a): Yield: 572 mg (94%), oil. ^{1}H NMR (200 MHz): δ = 2.54 (t, *J* = 2.4 Hz, 1 H), 4.36 (d, *J* = 2.4 Hz, 2 H), 5.02 (s, 2 H), 7.35−7.52 (m, 2 H), 7.87 (d, *J* = 7.5 Hz, 1 H), 8.00 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 58.3, 68.7, 75.7, 78.4, 121.7, 123.2, 125.1, 126.0, 135.2, 152.9, 168.8 ppm. GC-MS (70 eV): *m*/*z* (%) = 203 (8) [M$^+$], 202 (13), 174 (27), 149 (100). IR (film): $\tilde{\nu}$ = 3300 cm^{-1}, 3060, 2920, 2850, 2120, 1520, 1440, 1350, 1310, 1100, 760.

2-(But-2-ynyloxymethyl)benzothiazole (2a): Yield: 391 mg (60%), oil. ^{1}H NMR (200 MHz): δ = 1.85 (t, *J* = 2.2 Hz, 3 H), 4.31 (q, *J* = 2.2 Hz, 2 H), 4.99 (s, 2 H), 7.32−7.50 (m, 2 H), 7.88 (d, *J* = 7.5 Hz, 1 H), 7.99 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 3.5, 59.2, 68.5, 74.3, 83.8, 121.7, 123.0, 125.1, 126.4, 131.1, 153.2, 169.5 ppm. GC-MS (70 eV): *m*/*z* (%) = 217 (10) [M$^+$], 216 (12), 202 (28), 187 (16), 149 (100). IR (film): $\tilde{\nu}$ = 3060 cm^{-1}, 2920, 2860, 2220, 1520, 1440, 1350, 1100, 760, 730.

2-(1-But-2-ynyloxyethyl)benzothiazole (5a): Yield: 554 mg (80%), oil. ^{1}H NMR (200 MHz): δ = 1.66 (d, *J* = 6.5 Hz, 3 H), 1.83 (t, *J* = 2.3 Hz, 3 H), 4.18 (dq, *J* = 2.3, 15.0 Hz, 1 H), 4.27 (dq, *J* = 2.3, 15.0 Hz, 1 H), 5.10 (q, *J* = 6.5 Hz, 1 H), 7.32−7.50 (m, 2 H), 7.88 (dd, *J* = 0.8, 7.7 Hz, 1 H), 7.99 (dd, *J* = 0.8, 8.0 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 3.6, 22.2, 57.5, 74.3, 74.7, 83.3, 122.1, 123.2, 125.1, 126.0, 135.0, 153.2, 175.3 ppm. GC-MS (70 eV): *m*/*z* (%) = 231 (8) [M$^+$], 216 (45), 201 (15), 186 (28), 163 (100), 162 (82), 136 (17). IR (film): $\tilde{\nu}$ = 3060 cm^{-1}, 2990, 2920, 2850, 2220, 1520, 1440, 1320, 1090, 760, 730.

2-(1-But-2-ynyloxyethyl)-4-methylthiazole (6a): Yield: 466 mg (80%), oil. ^{1}H NMR (200 MHz): δ = 1.56 (d, *J* = 6.5 Hz, 3 H), 1.82 (t, *J* = 2.4 Hz, 3 H), 2.41 (d, *J* = 0.8 Hz, 3 H), 4.10 (dq, *J* = 2.4, 12.0 Hz, 1 H), 4.19 (dq, *J* = 2.4, 12.0 Hz, 1 H), 4.95 (q, *J* = 6.5 Hz, 1 H), 6.85 (q, *J* = 0.8 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 2.8, 16.1, 21.7, 56.3, 73.0, 74.0, 82.0, 112.2, 151.1, 172.1 ppm. GC-MS (70 eV): *m*/*z* (%) = 194 (3) [M$^+$], 180 (71), 150 (14), 127 (100), 126 (65). IR (film): $\tilde{\nu}$ = 3100 cm^{-1}, 2990, 2915, 2860, 2230, 1530, 1450, 1370, 1315, 1200, 1090, 1040, 980, 740.

2-(But-2-ynyloxyphenylmethyl)-4-methylthiazole (7a): Yield: 648 mg (84%), oil. ^{1}H NMR (200 MHz): δ = 1.83 (t, *J* = 2.3 Hz, 3 H), 2.38 (d, *J* = 0.8 Hz, 3 H), 4.13 (dq, *J* = 2.3, 15.4 Hz, 1 H), 4.26 (dq, *J* = 2.3, 15.4 Hz, 1 H), 5.94 (s, 1 H), 6.81 (q, *J* = 0.8 Hz, 1 H), 7.27−7.55 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz): δ = 3.5, 16.9, 56.7, 74.1, 79.1, 83.3, 113.9, 127.2, 128.2, 128.5, 139.1, 152.0, 171.2 ppm. GC-MS (70 eV): *m*/*z* (%) = 257 (1) [M$^+$], 242 (24), 189 (100), 152 (16), 105 (38). IR (film): $\tilde{\nu}$ = 3100 cm^{-1}, 3060, 3030, 2920, 2850, 2220, 1530, 1500, 1450, 1300, 1140, 1080, 1060, 700.

Compounds 3a and 10a−14a: These compounds were prepared by stirring a solution of the corresponding (heteroaryl)alkyl chloride (3 mmol) and the propargylic alcohol (3 mmol) in a two-phase system (50 mL of THF/50 mL of 10% aqueous NaOH solution) with TBAB (0.2 mmol) under phase-transfer conditions for 1−3 h at 40 °C (monitoring the reaction by TLC). The resulting mixtures were quenched with 40−100 mL of a saturated aqueous NH_4Cl solution and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude products **3a**, **10a** and **11a** were purified by column chromatography (silica gel 63−200 μm; petroleum ether/Et_2O, 8:2 for **3a** and 1:1 for **10a** and **11a**) to afford the pure (heteroaryl)alkyl propargyl ethers (oils), yields: 85−95%. The crude products **12a**−**14a** were purified by flash column chromatography (silica gel 40−63 μm; petroleum ether/Et_2O, 1:1) to afford the pure (heteroaryl)alkyl propargyl ethers (oils), yields: 60−75%. On attempted purification by column chromatography (silica gel 63−200 μm), compound **12a** underwent ring-cleavage to afford (quantitative conversion) *N*-(2-hydroxy-1,1-dimethylethyl)-2-(3-phenylprop-2-ynyloxy)acetamide; yield 209 mg (80%), oil. ^{1}H NMR (200 MHz): δ = 1.26 (s, 3 H), 1.28 (s, 3 H), 3.55 (s, 2 H), 4.02 (s, 2 H), 4.41 (s, 2 H), 6.55 (br. s, 1 H, exchanges with D_2O), 6.65 (br. s, 1 H exchanges with D_2O), 7.26−7.42 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz): δ = 24.0, 24.5, 42.8, 56.0, 59.1, 68.9, 83.2, 87.1, 121.0, 128.2, 128.9, 130.8, 170.1 ppm. GC-MS (70 eV): *m*/*z* (%) = 261 (0) [M$^+$], 130 (17), 115 (55), 113 (100), 98 (48). IR (film): $\tilde{\nu}$ = 3480 (br.) cm^{-1}, 3070, 3030, 2990, 1710, 1580, 1500, 1430, 1310, 1150, 1100, 810, 740.

2-(3-Phenylprop-2-ynyloxymethyl)benzothiazole (3a): Yield: 711 mg (85%), oil. ^{1}H NMR (200 MHz): δ = 4.58 (s, 2 H), 5.08 (s, 2 H), 7.27−7.50 (m, 7 H), 7.86 (dd, *J* = 0.8, 7.5 Hz, 1 H), 8.0 (dd, *J* = 0.8, 7.5 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 59.3, 68.9, 84.1, 87.3, 121.8, 122.0, 123.2, 125.3, 126.1, 128.3, 128.7, 131.8, 135.0, 153.2, 169.3 ppm. GC-MS (70 eV): *m*/*z* (%) = 279 (7) [M$^+$], 249 (6), 149 (100), 115 (26). IR (film): $\tilde{\nu}$ = 3035 cm^{-1}, 2925, 2860, 2220, 1520, 1440, 1350, 1090.

2-(3-Phenylprop-2-ynyloxymethyl)pyridine (10a): Yield: 636 mg (95%), oil. ^{1}H NMR (200 MHz): δ = 4.4 (s, 2 H), 4.7 (s, 2 H),

7.03−7.38 (m, 7 H), 7.57 (td, J = 1.7, 6.0 Hz, 1 H), 8.46 (d, J = 3.0 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 59.1, 72.6, 84.8, 87.3, 121.6, 122.5, 128.2, 128.5, 131.7, 131.8, 136.6, 149.2, 158.0 ppm. GC-MS (70 eV): *m/z* (%) = 223 (3) [M$^+$], 115 (20), 93 (100). IR (film): ṽ = 3060 cm^{-1}, 3020, 2860, 2240, 1600, 1490, 1440, 1360, 1260, 1110, 1090, 760, 690.

2-(But-2-ynyloxymethyl)pyridine (11a): Yield: 430 mg (89%), oil. ^{1}H NMR (200 MHz): δ = 1.85 (t, J = 2.3 Hz, 3 H), 4.24 (q, J = 2.3 Hz, 2 H), 4.7 (s, 2 H), 7.24 (t, J = 4.5 Hz, 1 H), 7.46 (d, J = 8.0 Hz, 1 H), 7.69 (td, J = 1.7, 8.0 Hz, 1 H), 8.55 (d, J = 4.5 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 3.5, 58.5, 71.9, 74.6, 83.0, 121.5, 122.4, 136.8, 148.6, 157.7 ppm. GC-MS (70 eV): *m/z* (%) = 161 (1) [M$^+$], 160 (8), 146 (5), 130 (5), 118 (7), 93 (100), 78 (10). IR (film): ṽ = 3060 cm^{-1}, 3020, 2920, 2850, 2220, 1590, 1440, 1350, 1140, 1100, 1080, 740.

4,4-Dimethyl-2-(3-phenylprop-2-ynyloxymethyl)-4,5-dihydro-1,3-oxazole (12a): Yield: 440 mg (60%), oil. ^{1}H NMR (200 MHz): δ = 1.26 (s, 3 H), 1.27 (s, 3 H), 3.96 (s, 2 H), 4.27 (s, 2 H), 4.48 (s, 2 H), 7.25−7.30 (m, 3 H), 7.39−7.43 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz): δ = 28.1, 59.0, 63.6, 67.1, 79.1, 83.8, 87.0, 122.2, 128.1, 128.4, 131.6, 161.8 ppm. GC-MS (70 eV): *m/z* (%) = 243 (2) [M$^+$], 242 (9), 228 (23), 170 (27), 130 (58), 115 (81), 113 (100), 98 (83). IR (film): ṽ = 3040 cm^{-1}, 2950, 2870, 2220, 1660, 1590, 1430, 1100, 750, 680.

2-(1-But-2-ynyloxyethy)-4,4-dimethyl-4,5-dihydro-1,3-oxazole (13a): Yield: 405 mg (70%), oil. ^{1}H NMR (200 MHz): δ = 1.19 (s, 3 H), 1.21 (s, 3 H), 1.35 (dt, J = 0.7, 6.7 Hz, 3 H), 1.74−1.77 (m, 3 H), 3.88 (s, 2 H), 4.07−4.13 (m, 2 H), 4.25 (q, J = 6.7 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 3.4, 18.4, 28.06, 28.12, 56.9, 66.9, 69.4, 74.4, 79.0, 82.5, 164.7 ppm. GC-MS (70 eV): *m/z* (%) = 195 (0) [M$^+$], 194 (1), 180 (5), 140 (13), 127 (100), 126 (40), 112 (26), 108 (22), 53 (68). IR (film): ṽ = 3045 cm^{-1}, 2960, 2885, 2215, 1660, 1590, 1440, 1360, 1100.

4,4-Dimethyl-2-[1-(3-phenylprop-2-ynyloxy)ethyl]-4,5-dihydro-1,3-oxazole (14a): Yield: 580 mg (75%), oil. ^{1}H NMR (200 MHz): δ = 1.29 (s, 3 H), 1.30 (s, 3 H), 1.47 (d, J = 6.7 Hz, 3 H), 3.98 (s, 2 H), 4.43 (q, J = 6.7 Hz, 1 H), 4.47 (d, J = 4.8 Hz, 2 H), 7.28−7.33 (m, 3 H), 7.41−7.46 (m, 2 H) ppm. ^{13}C NMR (50.3 MHz): δ = 18.7, 28.2, 57.4, 67.1, 69.9, 79.2, 84.7, 86.3, 122.5, 128.2, 128.4, 131.8, 164.9 ppm. GC-MS (70 eV): *m/z* (%) = 257 (1) [M$^+$], 256 (1), 242 (2), 170 (5), 158 (7), 127 (100), 126 (38), 115 (57). IR (film): ṽ = 3040 cm^{-1}, 2950, 2880, 2220, 1660, 1590, 1440, 1360, 1100, 750, 685.

Compounds 4a, 8a and 9a: These compounds were prepared by stirring a solution of the corresponding (heteroaryl)alkyl carbinol (1 mmol) and (3-chloroprop-2-ynyl)benzene (2 mmol) in acetone (50 mL)/NaOH (2 g, 50 mmol) for 24 h at 60 °C. The resulting mixtures were quenched with 40−100 mL of a saturated aqueous NH_4Cl solution and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude products were purified by column chromatography (silica gel 63−200 μm; petroleum ether/Et_2O, 1:1) to afford the pure (heteroaryl)alkyl propargyl ethers (**4a** solid; **8a** and **9a** oils); yields: 40−80%.

2-[1-(3-Phenylprop-2-ynyloxy)ethyl]benzothiazole (4a): Yield: 234 mg (80%), m.p. 72−73 °C (*n*-hexane). ^{1}H NMR (200 MHz): δ = 1.71 (d, J = 6.5 Hz, 3 H), 4.45 (d, J = 16.0 Hz, 1 H), 4.56 (d, J = 16.0 Hz, 1 H), 5.20 (q, J = 6.5 Hz, 1 H), 7.24−7.52 (m, 7 H), 7.90 (dd, J = 1.4, 7.8 Hz, 1 H), 7.99 (dd, J = 1.4, 8.0 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 22.2, 58.3, 75.0, 84.1, 86.7, 121.8, 122.0, 123.3, 125.2, 126.0, 128.2, 128.5, 131.8, 135.1, 153.2, 175.0 ppm. GC-MS (70 eV): *m/z* (%) = 293 (12) [M$^+$], 263 (11), 163 (100), 115 (42). IR ($CHCl_3$): ṽ = 3060 cm^{-1}, 2980, 2805, 2240, 1600, 1520, 1490, 1440, 1310, 1190, 1090, 760, 730, 690.

4-Methyl-2-[(3-phenylprop-2-ynyloxy)methylphenyl]thiazole (8a): Yield: 159 mg (50%), oil. ^{1}H NMR (200 MHz): δ = 2.4 (d, J = 0.8 Hz, 3 H), 4.4 (d, J = 16.0 Hz, 1 H), 4.55 (d, J = 16.0 Hz, 1 H), 6.03 (s, 1 H), 6.84 (q, J = 0.8 Hz, 1 H), 7.24−7.52 (m, 10 H) ppm. ^{13}C NMR (50.3 MHz): δ = 17.1, 57.3, 76.3, 79.6, 84.2, 113.9, 122.0, 127.2, 128.1, 128.4, 128.5, 128.6, 131.8, 139.0, 152.7, 171.2 ppm. GC-MS (70 eV): *m/z* (%) = 319 (13) [M$^+$], 290 (7), 242 (15), 189 (100), 115 (87). IR (film): ṽ = 3060 cm^{-1}, 3020, 2215, 1910, 1840, 1600, 1480, 1440, 1170, 1080, 1060, 750, 680.

4-Methyl-2-[1-(3-phenylprop-2-ynyloxy)ethyl]thiazole (9a): Yield: 103 mg (40%), oil. ^{1}H NMR (200 MHz): δ = 1.63 (d, J = 6.7 Hz, 3 H), 2.44 (d, J = 0.8 Hz, 3 H), 4.39 (d, J = 16.0 Hz, 1 H), 4.48 (d, J = 16.0 Hz, 1 H), 5.05 (q, J = 6.7 Hz, 1 H), 6.85 (q, J = 0.8 Hz, 1 H), 7.26−7.45 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz): δ = 17.0, 22.6, 57.4, 74.5, 77.1, 86.5, 113.6, 128.2, 128.5, 131.5, 131.8, 152.4, 171.1 ppm. GC-MS (70 eV): *m/z* (%) = 257 (11) [M$^+$], 242 (33), 180 (20), 127 (100), 115 (85). IR (film): ṽ = 3060 cm^{-1}, 2910, 2840, 1650, 1490, 1440, 1360, 1300, 1200, 1080, 750, 680.

General Procedure for the Preparation of (Heteroaryl)alkyl Carbinols and Chlorides: (Benzothiazol-2-yl)methanol[21] used for the preparation of ethers **1a** and **2a**, (1-benzothiazol-2-yl)ethanol[21] used for ethers **4a** and **5a**, 1-(4-methylthiazol-2-yl)ethanol[14] used for **6a** and **9a**, and (2-chloromethyl)benzothiazole[21] used for ether **3a** were prepared as reported. (4-Methylthiazol-2-yl)phenylmethanol, needed for the preparation of the substrates **7a** and **8a**, was prepared by direct deprotonation of 4-methylthiazole (5 mmol) in 50 mL of THF at −78 °C, by dropwise addition, under N_2, first of a solution of *n*BuLi in hexanes (2.5 M, 2.4 mL, 6.0 mmol) and then of a solution of benzaldehyde (6 mmol) in THF (3 mL). The mixture was allowed to warm slowly to room temperature (over ca. 1 h), then quenched with 50 mL of a saturated aqueous NH_4Cl solution and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by column chromatography (silica gel 63−200 μm; petroleum ether/Et_2O, 1:1) to afford pure (4-methylthiazol-2-yl)phenylmethanol (solid); yield 95%. 2-(Chloromethyl)pyridine, needed for the preparation of the ethers **10a** and **11a**, was obtained by treatment of the commercially available hydrochloride (Aldrich) with 5% NaOH solution. The (chloroalkyl)oxazolines needed for the ethers **12a**−**14a** were prepared by chlorination of the corresponding commercially available 2-methyl and 2-ethyl derivatives as reported.[22]

(4-Methylthiazol-2-yl)phenylmethanol: Yield: 974 mg (95%), m.p. 90−92 °C (petroleum ether). ^{1}H NMR (200 MHz): δ = 2.33 (d, J = 0.7 Hz, 3 H), 4.2 (br. s, 1 H, exchanges with D_2O), 6.0 (s, 1 H), 6.77 (q, J = 0.7 Hz, 1 H), 7.26−7.56 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz): δ = 16.8, 73.4, 113.9, 126.5, 128.2, 128.5, 141.5, 152.2, 174.1 ppm. GC-MS (70 eV): *m/z* (%) = 205 (88) [M$^+$], 176 (20), 128 (18), 105 (15), 100 (100), 79 (25), 77 (33). IR ($CHCl_3$): ṽ = 3600 cm^{-1}, 3350 br., 3060, 2990, 1530, 1450, 1380, 1300, 1160, 1130, 1030.

General Procedure for the [1,2]- and [2,3]-Wittig Rearrangements of (Heteroaryl)alkyl Propargyl Ethers: The [1,2]- and [2,3]-Wittig rearrangements were performed by stirring a solution of the propargylic ether (1 mmol) in 10 mL of THF under N_2 at − 78 °C with dropwise addition of a solution of *n*BuLi in hexanes (2.5 M, 0.44 mL, 1.1 mmol). The mixture was allowed to warm slowly to room

temperature (over ca. 1 h), and was then quenched with 30 mL of a saturated aqueous NH_4Cl solution and extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude products **2c**, **3c**−**8c**, **11c**, **3b**, **5b**, **6b**, **9b** and **10b** were purified by column chromatography (silica gel 63−200 μm; petroleum ether/Et_2O, 1:1) to afford the pure propargylic and allenic alcohols; yields: 54−95%. The crude products **12c**, **13b** and **14b** were purified by flash column chromatography (silica gel 40−63 μm; petroleum ether/Et_2O, 1:1) to afford the pure propargylic and allenic alcohols (oils), yields: 50−65%.

1-(Benzothiazol-2-yl)-2-methylbuta-2,3-dien-1-ol (2c): Yield: 143 mg (66%), oil. ^{1}H NMR (200 MHz): δ = 1.68 (t, *J* = 3.0 Hz, 3 H), 3.55 (br. s, 1 H, exchanges with D_2O), 4.82−4.86 (m, 2 H), 5.48 (t, *J* = 1.7 Hz, 1 H), 7.30−7.44 (m, 2 H), 7.80 (dd, *J* = 0.9, 7.1 Hz, 1 H), 7.93 (dd, *J* = 7.9 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 13.8, 73.3, 78.2, 100.1, 121.8, 123.2, 125.0, 126.2, 136.2, 153.1, 169.5, 206.3 ppm. GC-MS (70 eV): *m*/*z* (%) = 217 (3) [M$^+$], 216 (6), 200 (100), 164 (26), 136 (27). IR (film): $\tilde{\nu}$ = 3300 (br.) cm^{-1}, 3065, 3000, 2940, 2860, 1940, 1520, 1440, 1330, 1150, 1050, 860, 760, 730.

1-(Benzothiazol-2-yl)-4-phenylbut-3-yn-2-ol (3b): Yield: 70 mg (25%), oil. ^{1}H NMR (200 MHz): δ = 3.56−3.63 (m, 2 H), 4.6 (br. s, 1 H, exchanges with D_2O), 5.17 (dd, *J* = 6.2, 5.1 Hz, 1 H), 7.24−7.50 (m, 7 H), 7.83 (dd, *J* = 1.4, 7.7 Hz, 1 H), 8.0 (dd, *J* = 0.8, 7.6 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 41.4, 61.5, 84.5, 90.1, 121.5, 122.7, 125.2, 126.0, 128.2, 128.5, 128.7, 131.7, 136.2, 152.1, 171.3 ppm. GC-MS (70 eV): *m*/*z* (%) = 279 (14) [M$^+$], 260 (100), 149 (46). IR (film): $\tilde{\nu}$ = 3400 (br.) cm^{-1}, 3060, 3040, 2935, 2860, 2250, 1600, 1495, 1440, 1320.

1-(Benzothiazol-2-yl)-2-phenylbuta-2,3-dien-1-ol (3c): Yield: 125 mg (45%), oil. ^{1}H NMR (200 MHz): δ = 3.2 (br. s, 1 H, exchanges with D_2O), 5.25 (s, 2 H), 6.09 (t, *J* = 1.7 Hz, 1 H), 7.15−7.51 (m, 7 H), 7.84 (dd, *J* = 1.2, 7.9 Hz, 1 H), 7.99 (dd, *J* = 1.1, 7.5 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 71.5, 81.5, 110.2, 121.8, 123.0, 125.3, 126.2, 126.9, 127.4, 128.6, 133.0, 136.1, 153.1, 173.2, 208.1 ppm. GC-MS (70 eV): *m*/*z* (%) = 279 (28) [M$^+$], 278 (11), 264 (38), 149 (100), 115 (31). IR (film): $\tilde{\nu}$ = 3400 (br.) cm^{-1}, 3065, 2960, 2920, 2865, 1945, 1600, 1500, 1440, 1320, 1090.

2-(Benzothiazol-2-yl)-3-phenylpenta-3,4-dien-2-ol (4c): Yield: 158 mg (54%), oil. ^{1}H NMR (200 MHz): δ = 1.54 (s, 3 H), 3.6 (br. s, 1 H, exchanges with D_2O), 4.46 (d, *J* = 2.5 Hz, 2 H), 7.10−8.2 (m, 9 H) ppm. ^{13}C NMR (50.3 MHz): δ = 27.2, 74.0, 74.2, 100.2, 121.2, 123.2, 125.1, 125.5, 126.2, 128.0, 128.2, 129.6, 138.1, 152.3, 168.2, 205.1 ppm. GC-MS (70 eV): *m*/*z* (%) = 293 (0) [M$^+$], 177 (81), 162 (12), 149 (40), 135 (100). IR (film): $\tilde{\nu}$ = 3200 (br.) cm^{-1}, 2960, 2830, 1900, 1640, 1450, 1400, 1200, 1080, 710, 680, 650.

2-(Benzothiazol-2-yl)hex-4-yn-3-ol (5b): *anti*, yield: 21 mg (9%) oil. ^{1}H NMR (200 MHz): δ = 1.62 (d, *J* = 7.0 Hz, 3 H), 1.81 (d, *J* = 2.2 Hz, 3 H), 3.35 (quint, *J* = 7.0 Hz, 1 H), 3.8 (br. s, 1 H, exchanges with D_2O), 4.60 (dq, *J* = 7.0, 2.2 Hz, 1 H), 7.32−7.50 (m, 2 H), 7.83 (dd, *J* = 1.4, 7.7 Hz, 1 H), 8.0 (dd, *J* = 0.8, 7.6 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 3.6, 17.4, 45.2, 66.1, 79.2, 82.1, 121.2, 123.2, 125.1, 126.0, 138.1, 151.5, 178.0 ppm. GC-MS (70 eV): *m*/*z* (%) = 231 (10) [M$^+$], 214 (10), 178 (100), 136 (95), 109 (12). IR (film): $\tilde{\nu}$ = 3300 (br.) cm^{-1}, 2995, 2920, 2855, 2240, 1510, 1440, 1370, 1315, 1220, 1140, 1020, 850, 760, 730.

2-(Benzothiazol-2-yl)-3-methylpenta-3,4-dien-2-ol (5c): Yield: 180 mg (78%) oil. ^{1}H NMR (200 MHz): δ = 1.75 (t, *J* = 3.0 Hz, 3 H), 1.85 (s, 3 H), 4.15 (br. s, 1 H, exchanges with D_2O), 4.88−4.98 (m, 2 H), 7.30−7.5 (m, 2 H), 7.83 (dd, *J* = 1.4, 7.8 Hz, 1 H), 8.01 (dd, *J* = 1.2, 7.5 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 14.3, 28.6, 75.2, 78.4, 105.0, 121.7, 123.0, 125.0, 126.0, 135.7, 152.6, 178.0, 208.0 ppm. GC-MS (70 eV): *m*/*z* (%) = 231 (1) [M$^+$], 214 (100), 178 (27), 136 (66), 109 (13). IR (film): $\tilde{\nu}$ = 3400 (br.) cm^{-1}, 3060, 2995, 2930, 2850, 1960, 1510, 1440, 1370, 1315, 1120, 855, 760, 730.

2-(4-Methylthiazol-2-yl)-hex-4-yn-3-ol (6b): *anti*, yield: 146 mg (75%), oil. ^{1}H NMR (200 MHz): δ = 1.47 (d, *J* = 7.0 Hz, 3 H), 1.81 (d, *J* = 2.0 Hz, 3 H), 2.40 (d, *J* = 0.9 Hz, 3 H), 3.30 (quintet, *J* = 7.0 Hz, 1 H), 3.80 (br. s, 1 H, exchanges with D_2O), 4.53 (dq, *J* = 2.0, 7.0 Hz, 1 H), 6.75 (q, *J* = 0.9 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 3.5, 16.8, 17.5, 44.2, 66.1, 78.0, 82.3, 112.2, 152.2, 172.3 ppm. GC-MS (70 eV): *m*/*z* (%) = 195 (6) [M$^+$], 180 (10), 127 (96), 126 (100). IR (film): $\tilde{\nu}$ = 3300 (br.) cm^{-1}, 2990, 2920, 2850, 2240, 1530, 1450, 1310, 1220, 1140, 1020.

3-Methyl-2-(4-methylthiazol-2-yl)penta-3,4-dien-2-ol (6c): Yield: 39 mg (20%), oil. ^{1}H NMR (200 MHz): δ = 1.69 (t, *J* = 3.0, Hz, 3 H), 1.75 (s, 3 H), 2.42 (d, *J* = 0.9 Hz, 3 H), 3.50 (br. s, 1H exchanges with D_2O), 4.87 (q, *J* = 3.0 Hz, 2 H), 6.81 (q, *J* = 0.9 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 14.1, 17.3, 28.7, 74.6, 78.0, 105.1, 114.2, 151.3, 172.1, 205.2 ppm. GC-MS (70 eV): *m*/*z* (%) = 195 (1) [M$^+$], 194 (3), 180 (16), 178 (100), 142 (64), 100 (85). IR (film): $\tilde{\nu}$ = 3300 (br.) cm^{-1}, 2990, 2920, 2850, 1920, 1530, 1440, 1370, 1300, 1100.

2-Methyl-1-(4-methylthiazol-2-yl)-1-phenylbuta-2,3-dien-1-ol (7c): Yield: 203 mg (79%), oil. ^{1}H NMR (200 MHz): δ = 1.77 (t, *J* = 3.0 Hz, 3 H), 2.41 (d, *J* = 0.9 Hz, 3 H), 4.49 (br. s, 1 H, exchanges with D_2O), 4.63 (q, *J* = 3.0 Hz, 2 H), 6.78 (q, *J* = 0.9 Hz, 1 H), 7.30−7.40 (m, 3 H), 7.62 (dd, *J* = 2.0, 8.3 Hz, 2 H) ppm. ^{13}C NMR (50.3 MHz): δ = 14.8, 16.6, 77.2, 79.5, 105.0, 114.2, 126.1, 127.6, 127.8, 142.1, 151.3, 174.0, 205.1 ppm. GC-MS (70 eV): *m*/*z* (%) = 257 (4) [M$^+$], 240 (100), 204 (50), 126 (30), 105 (40), 77 (25). IR (film): $\tilde{\nu}$ = 3420 (br.) cm^{-1}, 3100, 3060, 3020, 2920, 2850, 1960, 1530, 1450, 1170, 1040, 850, 760, 700.

1-(4-Methylthiazol-2-yl)-1,2-diphenylbuta-2,3-dien-1-ol (8c): Yield: 223 mg (70%), oil. ^{1}H NMR (200 MHz): δ = 2.41 (d, *J* = 0.9 Hz, 3 H), 4.8 (br. s, 1 H, exchanges with D_2O), 4.89 (s, 2 H), 6.78 (q, *J* = 0.9 Hz, 1 H), 7.20−7.40 (m, 8 H), 7.68 (dd, *J* = 1.5, 8.0 Hz, 2 H) ppm. ^{13}C NMR (50.3 MHz): δ = 16.9, 79.5, 80.0, 112.1, 115.3, 126.6, 126.7, 127.9, 128.0, 128.2, 128.5, 143.1, 151.3, 175.2, 209.1 ppm. GC-MS (70 eV): *m*/*z* (%) = 319 (10) [M$^+$], 204 (100), 126 (30), 105 (40), 77 (15). IR (film): $\tilde{\nu}$ = 3350 (br.) cm^{-1}, 3060, 2905, 2840, 1935, 1600, 1490, 1430, 1160, 1040, 1025, 850, 750, 690.

4-(4-Methylthiazol-2-yl)-1-phenylpent-1-yn-3-ol (9b): Total yield: 231 mg (90%), oil. *anti*, yield: 173 mg (75%), oil. ^{1}H NMR (200 MHz): δ = 1.57 (d, *J* = 6.6 Hz, 3 H), 2.44 (s, 3 H), 3.48 (quintet, *J* = 6.6 Hz, 1 H), 3.65 (br. s, 1 H, exchanges with D_2O), 4.78 (d, *J* = 6.6 Hz, 1 H), 6.8 (s, 1 H) 7.27−7.7 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz): δ = 16.9, 17.5, 44.2, 66.5, 66.9, 88.0, 112.6, 128.1, 128.3, 131.7, 135.7, 152.2, 172.3 ppm. GC-MS (70 eV): *m*/*z* (%) = 257 (20) [M$^+$], 242 (5), 228 (7), 131 (28), 127 (100), 126 (70). IR (film): $\tilde{\nu}$ = 3300 (br.) cm^{-1}, 3060, 3020, 2990, 2920, 2850, 2240, 1600, 1530, 1450, 1310, 1220, 1140, 1020. *syn*, yield: 58 mg (25%), oil. ^{1}H NMR (200 MHz): δ = 1.55 (d, *J* = 6.6 Hz, 3 H), 2.44 (s, 3 H), 3.60 (m, 1 H), 3.60 (br. s, 1 H, exchanges with D_2O), 4.88 (d, *J* = 4.0 Hz, 1 H), 6.8 (s, 1 H) 7.27−7.7 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz): δ = 16.9, 17.4, 45.0, 67.1, 67.5, 88.3, 113.2, 128.1, 128.5, 132.2, 135.7, 152.2, 172.1 ppm. GC-MS (70 eV): *m*/*z* (%) = 257 (20) [M$^+$], 242 (4), 228 (6), 131 (30), 127 (100), 126 (75). IR (film): $\tilde{\nu}$ = 3300 (br.) cm^{-1}, 3060, 3020, 2990, 2920, 2850, 2240, 1600, 1530, 1450, 1310, 1220, 1140, 1020.

4-Phenyl-1-(pyridin-2-yl)but-3-yn-2-ol (10b): Yield: 201 mg (90%), oil. ^{1}H NMR (200 MHz): δ = 3.23−3.32 (m, 2 H), 4.65 (br. s, 1 H, exchanges with D_2O), 5.07 (dd, *J* = 4.7, 6.5 Hz, 1 H), 7.13−7.35 (m, 7 H), 7.63 (td, *J* = 1.8, 8.4 Hz, 1 H), 8.50 (dd, *J* = 0.8, 5.0 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 44.2, 62.1, 84.6, 89.7, 121.9, 122.8, 124.1, 128.0, 128.2, 131.1, 136.8, 148.6, 158.7 ppm. GC-MS (70 eV): *m*/*z* (%) = 223 (15) [M$^+$], 207 (25), 204 (41), 130 (35), 93 (100). IR (film): $\tilde{\nu}$ = 3350 (br.) cm^{-1}, 3060, 2960, 2920, 2840, 2230, 1600, 1570, 1470, 1440, 1050, 755, 690.

2-Methyl-1-(pyridin-2-yl)buta-2,3-dien-1-ol (11c): Yield: 129 mg (80%), oil. ^{1}H NMR (200 MHz): δ = 1.52 (t, *J* = 3.3 Hz, 3 H), 4.7−4.8 (m, 3 H, one of which is attributable to OH, after exchange with D_2O), 5.25 (s, 1 H), 7.25−7.40 (m, 2 H), 7.69 (td, *J* = 1.7, 7.6 Hz, 1 H), 8.53 (d, *J* = 4.0 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 13.0, 74.1, 75.6, 100.9, 121.2, 122.5, 136.7, 147.3, 159.0, 208.2 ppm. GC-MS (70 eV): *m*/*z* (%) = 161 (3) [M$^+$], 160 (10), 144 (20), 93 (100), 78 (20). IR (film): $\tilde{\nu}$ = 3400 (br.) cm^{-1}, 3060, 3020, 2920, 2850, 1960, 1450, 1050, 900, 760, 700.

1-(4,4-Dimethyl-4,5-dihydro-1,3-oxazol-2-yl)-2-phenylbuta-2,3-dien-1-ol (12c): Yield: 135 mg (55%), oil. ^{1}H NMR (200 MHz): δ = 1.28 (s, 6 H), 3.83 (br. s, 3 H, one of which is attributable to OH, after exchange with D_2O) 5.05 (s, 2 H), 5.87 (s, 1 H), 7.30−7.50 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz δ = 28.1, 68.2, 71.5, 80.5, 110.2, 122.2, 123.0, 126.1, 126.9, 127.0, 164.9, 206.2 ppm. GC-MS (70 eV): *m*/*z* (%) = 243 (9) [M$^+$], 226 (40), 128 (100), 116 (52), 115 (67). IR (film): $\tilde{\nu}$ = 3400 (br.) cm^{-1}, 3060, 2960, 2865, 1600, 1500, 1440, 1320, 1095, 750, 695.

2-(4,4-Dimethyl-4,5-dihydro-1,3-oxazol-2-yl)hex-4-yn-3-ol (13b): *anti*, yield: 100 mg (50%), oil. ^{1}H NMR (200 MHz): δ = 1.23 (s, 3 H), 1.25 (s, 3 H), 1.32 (d, *J* = 7.0 Hz, 3 H), 1.42 (d, *J* = 0.7 Hz, 3 H), 2.6 (m, 1 H), 2.8 (br. s, 1 H, exchanges with D_2O), 3.95 (s, 2 H), 4.80 (d, *J* = 7.0 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 3.5, 13.8, 18.5, 18.8, 28.2, 57.0, 62.4, 66.9, 69.5, 79.1, 165.0 ppm. GC-MS (70 eV): *m*/*z* (%) = 195 (1) [M$^+$], 194 (3), 178 (85), 142 (42), 124 (30), 43 (100). IR (film): $\tilde{\nu}$ = 3400 (br.) cm^{-1}, 3050, 2990, 2850, 2230, 1660, 1510, 1440, 1375, 1305, 1100.

4-(4,4-Dimethyl-4,5-dihydro-1,3-oxazol-2-yl)-1-phenylpent-1-yn-3-ol (14b): Total yield: 167 mg (65%), oil. *anti*, yield: 120 mg (70%), oil. ^{1}H NMR (200 MHz): δ = 1.28 (s, 6 H), 1.35 (d, *J* = 7.0 Hz, 3 H), 2.80 (quint, *J* = 7.0 Hz, 1 H), 3.00 (br. s, 1 H, exchanges with D_2O), 3.93 (s, 2 H), 4.62 (d, *J* = 7.0 Hz, 1 H), 7.2−7.9 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz): δ = 14.6, 28.2, 28.3, 29.6, 40.1, 65.0, 66.9, 78.7, 126.1, 128.1, 128.3, 131.7, 170.0 ppm. GC-MS (70 eV): *m*/*z* (%) = 257 (1) [M$^+$], 241 (5), 142 (100), 116 (40). IR (film): $\tilde{\nu}$ = 3400 (br.) cm^{-1}, 3060, 2995, 2940, 2850, 2230, 1660, 1510, 1450, 1370, 1315, 1120, 855, 760, 730. *syn*, yield: 45 mg (30%), oil. ^{1}H NMR (200 MHz): δ = 1.28 (s, 6 H), 1.35 (d, *J* = 7.0 Hz, 3 H), 2.80 (m, 1 H), 3.0 (br. s, 1 H, exchanges with D_2O), 3.93 (s, 2 H), 4.77 (d, *J* = 3.9 Hz, 1 H), 7.20−7.90 (m, 5 H) ppm. ^{13}C NMR (50.3 MHz): δ = 14.6, 28.2, 28.3, 29.6, 40.1, 65.0, 66.9, 78.7, 126.1, 128.1, 128.3, 131.7, 170.0 ppm. GC-MS (70 eV): *m*/*z* (%) = 257 (1) [M$^+$], 241 (5), 142 (100), 116 (40). IR (film): $\tilde{\nu}$ = 3400 (br.) cm^{-1}, 3060, 2995, 2940, 2850, 2230, 1660, 1510, 1450, 1370, 1315, 1120, 855, 760, 730.

General Procedure for the Preparation of (Heteroaryl)alkyl Propargyl Ethers by Coupling Reactions: Compound **10d** was prepared by dropwise addition, at −78 °C under N_2, first of a solution of *n*BuLi in hexanes (2.5 M, 0.5 mL, 1.25 mmol) and then of the iodomethane (4 mmol) to a stirring solution of compound **10a** (1 mmol) in 15 mL of THF. The mixture was allowed to warm slowly to room temperature (over ca. 1 h), and was then quenched with 40 mL of a saturated aqueous NH_4Cl solution and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by column chromatography (silica gel 63−200 μm; petroleum ether/Et_2O, 6:4) to afford the pure (heteroaryl)alkyl propargyl ether **10d** (oil, 30% yield) and the [1,2]-rearranged product **10b** (oil, 40% yield).

2-[(1-Methyl-3-phenylprop-2-ynyloxy)methyl]pyridine (10d): Yield: 71 mg (30%), oil. ^{1}H NMR (200 MHz): δ = 1.61 (d, *J* = 5.5 Hz, 3 H), 4.57 (q, *J* = 5.5 Hz, 1 H), 4.73 (d, *J* = 16.0 Hz, 1 H), 4.98 (d, *J* = 16.0 Hz, 1 H), 7.16−7.52 (m, 7 H), 7.69 (t, *J* = 7.6 Hz, 1 H), 8.56 (d, *J* = 4.4 Hz, 1 H) ppm. ^{13}C NMR (50.3 MHz): δ = 22.2, 66.2, 71.3, 85.2, 88.6, 121.6, 122.3, 128.1, 128.3, 128.4, 131.7, 136.7, 148.9, 158.0 ppm. GC-MS (70 eV): *m*/*z* (%) = 237 (4) [M$^+$], 208 (10), 194 (7), 128 (17), 107 (48), 93 (100). IR (film): $\tilde{\nu}$ = 3060 cm^{-1}, 3010, 2920, 2860, 2240, 1600, 1490, 1440, 1370, 1260, 1110, 1090, 760, 690.

Acknowledgments

This work was carried out in the framework of the National Project "Stereoselezione in sintesi Organica: Metodologie ed Applicazioni" supported by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, Rome. We also thank the Italian Consiglio Nazionale delle Ricerche (CNR), Rome and the University of Lecce for financial support.

[1] [1a] I. Iwai, J. Ide, *Chem. Pharm. Bull. Jpn.* **1962**, *10*, 926. [1b] I. Iwai, J. Ide, *Chem. Pharm. Bull. Jpn.* **1963**, *11*, 1042. [1c] I. Iwai, J. Ide, *Quart. Rev.* **1968**, *22*, 411. [1d] J. Zsindely, H. Schmid, *Helv. Chim. Acta* **1968**, *51*, 1510.[1e] H.J. Hansen, H. Schmid, *Chimia* **1970**, *24*, 89. [1f] N. Sarcevic, J. Zsindely, H. Schmid, *Helv. Chim. Acta* **1973**, *56*, 1457. [1g] W. S. Trahanovsky, P. W. Mullen, *J. Am. Chem. Soc.* **1972**, *94*, 5911−5913. [1h] W. S. Trahanovsky, S. L. Emeis, A. S. Lee, *J. Org. Chem.* **1976**, *41*, 4043.

[2] [2a] L. Brandsma, P. J. W. Schuijl, *Recl. Trav. Chim. Pays-Bas* **1969**, *88*, 30. [2b] P. J. W. Schuijl, H. J. T. Bos, L. Brandsma, *Recl. Trav. Chim. Pays-Bas* **1969**, *88*, 597. [2c] Y. Makisumi, A. Murabayashi, *Tetrahedron Lett.* **1969**, 1971. [2d] H. Kwart, T. J. George, *J. Chem. Soc., Chem. Commun.* **1970**, 433. [2e] B. W. Bycroft, W. Landon, *J. Chem. Soc., Chem. Commun.* **1970**, 168. [2f] J. Meijer, L. Brandsma, *Recl. Trav. Chim. Pays-Bas* **1972**, *91*, 578.

[3] [3a] K. Berg-Nielson, L. Skattebøl, *Acta Chem. Scand., Ser. B* **1978**, *32*, 553. [3b] P. Cresson, J. Corbier, *C. R. Acad. Sci. Paris, Ser. C* **1969**, 1614.

[4] K. Tomooka, K. Yamamoto, T. Nakai, *Angew. Chem. Int. Ed.* **1999**, *38*, 3741−3743.

[5] K. Tomooka, M. Kikuchi, K. Igawa, P. H. Keong, T. Nakai, *Tetrahedron Lett.* **1999**, *40*, 1917−1920.

[6] [6a] K. Tomooka, N. Komine, T. Nakai, *Tetrahedron Lett.* **1998**, *39*, 5513−5516. [6b] M. Tsubuki, T. Kamata, M. Nakatani, K. Yamazaki, T. Matsui, T. Honda, *Tetrahedron: Asymmetry* **2000**, *11*, 4725−4736.

[7] J. A. Marshall, J. Lebreton, *J. Am. Chem. Soc.* **1988**, *110*, 2925−2931.

[8] J. Kang, W. O. Cho, H. G. Cho, H. J. Oh, *Bull. Korean Chem. Soc.* **1994**, *15*, 732−739.

[9] M. Tsubuki, T. Kamata, H. Okita, M. Arai, A. Shigihara, T. Honda, *Chem. Commun.* **1999**, 2263−2264.

[10] J. Liang, D. W. Hoard, V. V. Khau, M. J. Martinelli, E. D. Moher, R. E. Moore, M. A. Tius, *J. Org. Chem.* **1999**, *64*, 1459−1463.

[11] K. Tomooka, L. F. Wang, N. Komine, T. Nakai, *Tetrahedron Lett.* **1999**, *40*, 6813−6816.

[12] J. A. Marshall, N. D. Adams, *J. Org. Chem.* **1999**, *64*, 5201−5204.

[13] N. Kurono, K. Sugita, M. Tokuda, *Tetrahedron* **2000**, *56*, 847−854.
[14] V. Capriati, S. Florio, G. Ingrosso, C. Granito, L. Troisi, *Eur. J. Org. Chem.* **2002**, *3*, 478−484.
[15] S. Florio, V. Capriati, R. Luisi, A. Abbotto, D. J. Pippel, *Tetrahedron* **2001**, *57*, 6775−6786.
[16] [16a] T. Nakai, K. Mikami, *Org. React.* **1994**, *46*, 105−209. [16b] T. Nakai, K. Tomooka, *Pure Appl. Chem.* **1997**, *69*, 595−600. [16c] S. Manabe, *Chem. Commun.* **1997**, 737−738. [16d] S. E. Gibson, P. Ham, G. R. Jefferson, *Chem. Commun.* **1998**, 123−124. [16e] T. Kawasaky, T. Kimachi, *Synlett* **1998**, 1429 1431.[16f] M. Hiersemann, C. Lauterbach, A. Pollex, *Eur. J. Org. Chem.* **1999**, 2713−2724.
[17] [17a] G. Wittig, L. Löhmann, *Justus Liebigs Ann. Chem.* **1942**, *550*, 260. [17b] U. Schöllkopf, *Angew. Chem. Int. Ed. Engl.* **1970**, *9*, 763. [17c] J. A. Marshall, in *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), Pergamon Press, London, **1991**, vol. 3, p. 975. [17d]K. Tomooka, T. Nakai, *J. Synth. Org. Chem. Jpn.* **1996**, *54*, 1000. [17e] H. Yamamoto, K. Tomooka, T. Nakai, *Liebigs Ann./Recueil* **1997**, 1275.
[18] A. Gaudemar, in *Stereochemistry: Fundamentals and Methods* (Eds.: H. B. Kagan), Georg Thieme Publishers, Stuttgart, **1977**, vol. 1, p. 62−73.
[19] J. Suffert, *J. Org. Chem.* **1989**, *54*, 509−512.
[20] [20a] V. M. Zubarovskii, *Zh. Obsch. Khim.* **1954**, *24*, 1664. [20b] *Chem. Abstr.* **1955**, *49*, 13223. [20c]M. Altamura, E. Perrotta, *J. Org. Chem.* **1993**, *58*, 272−274.
[21] H. Chikashita, S. Ikegami, T. Okumura, K. Itoh, *Synthesis* **1986**, *5*, 375−377.
[22] [22a] P. Breton, C. André-Barrès, Y. Langlois, *Synth Commun.* **1992**, *22*, 2543−2554. [22b] S. Florio, V. Capriati, R. Luisi, *Tetrahedron Lett.* **1996**, *37*, 4781−4784. [22c] *t*BuOCl could conveniently be prepared as described in: M. J. Mintz, C. Walling, *Org. Synth., Collect. Vol.* **1973**, *5*, 184−187.

Received March 11, 2002
[O02133]