Ortho-[2,3]-Wittig Rearrangement of Benzyl Propargyl Ethers: Striking Preference over the Competing [1,2]-Wittig Shift

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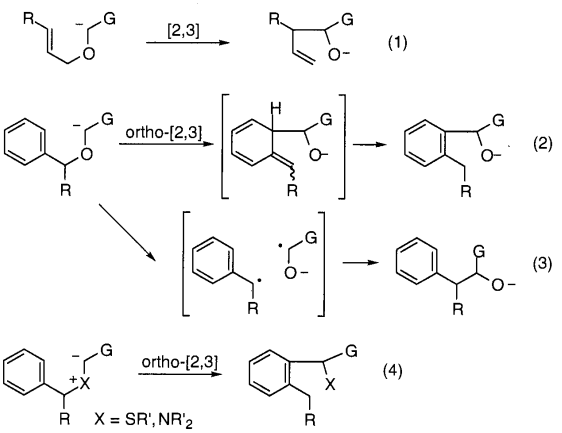
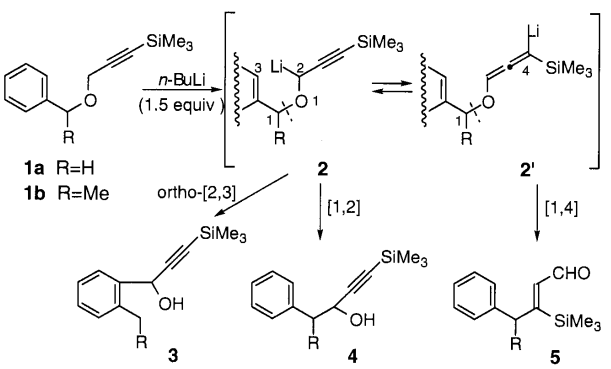
Treatment of benzyl γ-(trimethylsilyl)propargyl ether with *n*-BuLi is shown to afford the rarely precedent *ortho*-[2,3]-Wittig product in remarkable preference to the [1,2]-Wittig product. The factors governing the periselectivity in this type of carbanion rearrangement are discussed.

The [2,3]-Wittig rearrangement of α-allyloxy organolithiums (eq 1) currently enjoys wide application in many facets of organic synthesis.[1] In principle, on the other hand, a similar [2,3]-sigmatropic shift is conceivable for α-benzyloxy organolithiums to give, after the 1,3-hydrogen transfer, the *ortho*-alkylated benzylic alcohols (eq 2), though it is kinetically less favorable due to the involvement of the dearomatization step. However, most of α-benzyloxy organolithiums studied so far, such as G = Ph[2] and alkyls,[3] have not afforded any detectable amount of the *ortho*-[2,3]-Wittig product, instead producing the [1,2]-Wittig product via the radical cleavage–recombination pathway (eq 3), while a single exception has been reported where the rearrangement of the propargylic substrate (G = C≡CMe, R = H) affords the *ortho*-[2,3]-Wittig product together with the [1,2]-Wittig product.[4] In contrast, a similar *ortho*-[2,3]-shift has been amply precedent in the thia-[2,3]-Wittig rearrangement of α-benzylthio organolithiums[5] and the Sommelet–Hauser rearrangement of *N*- and *S*-benzyl ylides[6] (eq 4). These situations are rather peculiar from theoretical points of view, since an α-oxy carbanion, compared with the α-thio analog and the ylide counterpart, should have the HOMO at a higher level and hence should be more reactive as a migrating terminus for the [2,3]-sigmatropic shift. In order to define the factors directing the rearrangement to the *ortho*-[2,3]-Wittig shift, we systematically investigated the periselectivity in the carbanion rearrangement of various benzyl propargylic ethers.[7] Disclosed herein is that the carbanion rearrangement of benzyl γ-(trimethylsilyl)propargyl ether exhibits remarkably greater preference for the *ortho*-[2,3]-Wittig shift, compared with the non-silylated and γ-methylated counterparts.



First, we carried out the rearrangement of benzyl γ-(trimethylsily)propargyl ether (**1a**) under various conditions (Scheme 1, Table 1). Under the standard condition (*n*-BuLi, THF, –78 °C), the *ortho*-[2,3]-product **3a** was obtained in large preference to the [1,2]-product **4a**, unexpectedly, together with the [1,4]-product **5a** (entry 1).[8] As expected, the *ortho*-[2,3] preference was remarkably enhanced when the reaction temperature was lowered (entry 2), while the [1,2]-product predominated when the temperature was raised to 0 °C (entry 3). Interestingly enough, the use of the lithium amide base led to the predominant formation of the [1,4]-product (entry 4). Of special interest is that the *ortho*-[2,3]/[1.2] ratio (62% : 4%) observed in entry 2 is significantly higher than that reported for the γ-methylpropargyl analog (45% : 18%).[4] Both the high *ortho*-[2,3] preference and the appreciable formation of the [1,4]-product can be explained in terms of the well-known conjugation of the propargylic lithium **2a** with the allenic form **2a** which makes the carbanion terminus more stable toward the radical cleavage leading to the [1,2]-shift and more favorable for the [1,4]-shift. In a similar rearrangement of the α-methylbenzyl analog (**1b**), the *ortho*-[2,3]-shift was considerably suppressed, instead the [1,2]-Wittig shift becoming predominant (entries 5–7),[9] presumably due to the radical-stabilizing effect of the α-methyl substituent.



Scheme 1.

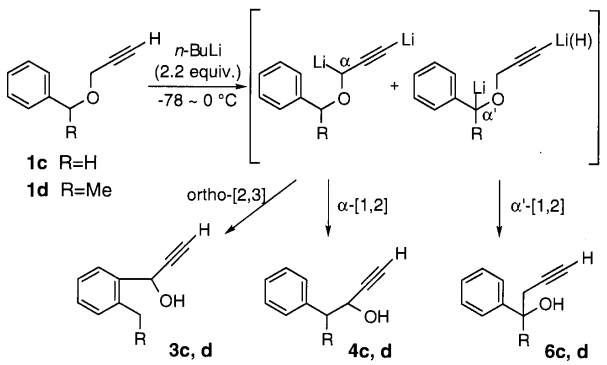
Table 1. Product distribution[a]

Entry	Substrate	Base	Conditions	Yield/% 3	4	5
1	**1a**	*n*-BuLi	THF, -78 °C	41	7	18
2	**1a**	*n*-BuLi	THF/Hex./Et_2O (4:1:1), -110 °C	62	4	8
3	**1a**	*n*-BuLi	Et_2O, 0 °C	~0	55	14
4	**1a**	LiTMP[b]	THF, -78 °C	10	8	40
5	**1b**	*n*-BuLi	THF, -78 °C	4	35	9
6	**1b**	*n*-BuLi	Et_2O, -78 °C → 0 °C	~0	62	9
7	**1b**	LDA[c]	THF, -78 °C	6	34	14

[a]The substrate was recovered in yields ranging from 0% (entry 3) to 20% (entry 7). [b]Lithium tetramethylpiperidide. [c]Lithium diisopropylamide.

In a similar way, we also examined the dianion rearrangement of benzyl propargyl ether where the conjugation with the allenic form would be inhibited (Scheme 2, Table 2). As expected, when the rearrangement of **1c** was performed in ether the *ortho*-[2,3]-shift competed considerably with the [1,2]-shift (entry 1).[10] Rather surprisingly, however, when the rearrangement was conducted in THF the α'-[1,2]-Wittig product **6c** arising from lithiation at the benzyl position (α') was formed as the major product (entry 2). That means that the second lithiation involved occurs predominantly at the propargylic position in ether and at the benzylic position in THF. At present, the exact reason for the regiochemical changeover is unclear. We also carried out the rearrangement of the α-methylbenzyl analog (**1d**) where the lithiation at the benzylic position might be considerably suppressed. Indeed, the rearrangement in ether gave the α-lithiation-derived *ortho*-[2,3]- (**3d**) and [1,2]-product (**4d**) in 22% and 51% yield, respectively (entry 3).[11] In THF, nearly the same ratio for [2,3]- vs [1,2]-product was observed, accompanied by the formation of the α'-[1,2]-product **6d** (entry 4). Furthermore, the rearrangement of the α-methylpropargyl analog (**1e**) in ether was found to result in the exclusive formation of the α-[1,2]- (**4e**) and α'-[1,2]-product (**6e**) without any detectable formation of the *ortho*-[2,3]-product.[12] This observation indicates that the dilithio species generated from the α-methylpropargyl moiety can no longer act as a migrating terminus for the *ortho*-[2,3]-Wittig shift.

The overall spectrum of the periselectivity observed herein reveals that a key structural factor for effecting the *ortho*-[2,3]-Wittig rearrangement is not the HOMO level of the carbanion terminus involved, but its kinetic stability toward the radical cleavage leading to the competing [1,2]-Wittig shift. In other words, the more the [1,2]-Wittig shift is suppressed, the more the *ortho*-[2,3]-Wittig produst is formed. The same argument could be extended to explain why α-benzylthio carbanions and *S*- and *N*-benzyl ylides can easily undergo the *ortho*-[2,3]-shift.



Scheme 2.

Table 2. Product distribution

Entry	Substrate	Solvent	Yield/%		
			3	**4**	**6**
1	**1c**	Et_2O	39	25	6
2	**1c**	THF	2	5	67
3	**1d**	Et_2O	22	51	0
4	**1d**	THF	17	34	12

In summary, we have shown that benzyl γ-(trimethylsilyl)-propargyl ether (**1a**), when treated with *n*-BuLi, undergoes the rarely precedent *ortho*-[2,3]-Wittig rearrangement in remarkably large preference to the competing [1,2]- and [1,4]-shifts. Furthermore, we have pointed out the importance of the kinetic stability of the carbanion terminus toward the radical cleavage as a key factor directing the rearrangement to the *ortho*-[2,3]-Wittig shift.

References and Notes

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4 U. Schölkopf, K. Fellenberger, and M. Rizk, *Liebigs Ann. Chem.*, **734**, 106 (1970). In this paper, any mechanistic reason for the exceptional periselectivity has not been given. Note that a similar [2,3]-Wittig shift has been reported in the carbanion rearrangement of several 3-furylmethyl ethers: B. Cazes and S. Julia, *Synth. Commun.*, **1977**, 113; M. Tsubuki, H. Okita, and T. Honda, *J. Chem. Soc., Chem. Commun.*, **1995**, 2135 .

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7 Note that the *ortho*-[2,3]-Wittig shift requires benzylic ethers as substrates which could be lithiated on the benzyloxy-bearing carbon preferentially over the benzylic carbon. In this regard, allyl benzyl ether, e.g., is not qualified as an substrate, since its lithiation occurs exclusively on the benzylic carbon.

8 The three products are distinguishable by ^{1}H NMR spectra ($CDCl_3$): **3a**, δ 2.44 (s, *o*-Me) and δ 5.60 (d, C*H*–OH); **4a**, δ 2.95–3.06 (m, CH_2Ph) and δ 4.53–4.59 (m, C*H*–OH); **5a**, δ 10.01 (d, CHO), and δ 6.32 (dt, =C*H*CHO).

9 The ^{1}H NMR spectra of products **3b**, **4b**, and **5b** are in accord with the assigned structures.

10 The three products are distinguishable by ^{1}H NMR spectra: **3c**, δ 2.45 (s, *o*-Me), δ 5.63 (d, C*H*–OH), and δ 2.65 (d, HC≡); **4c**, δ 2.97–3.09 (m, CH_2Ph), δ 4.59 (ddd, C*H*–OH), and δ 2.50 (d, HC≡); **6c**, δ 4.88 (t, C*H*–OH), δ 2.65 (ddd, CH_2C≡), and δ 2.08 (t, HC≡).

11 The ^{1}H NMR spectra of products **3d**, **4d**, and **6d** are in accord with the assigned structures.

12 ^{1}H NMR ($CDCl_3$): **4e**, δ 2.94, 3.00 (dd, CH_2Ph) and δ 1.56 (s, *Me*–C–OH); **6e**, δ 4.52 (d, C*H*–OH) and δ 1.11 (d, *Me*–CH).