Stereochemistry and Mechanism of Vinyl-migrating [1,2]-Wittig Rearrangement of α-Lithioalkyl Vinyl Ethers

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Enantiomerically defined α-stannylalkyl or α-methylbenzyl vinyl ethers, when treated with butyllithium, are shown to undergo the 1,2-vinyl migration to afford the allylic alcohols in almost racemic form in low or high yield, respectively, thereby proposing the radical cleavage-recombination pathway.

Over decades the 1,2-alkyl migration on α-lithiated ethers, now called [1,2]-Wittig rearrangement, has attracted considerable interest from mechanistic and synthetic points of view.[1] This type of 1,2-alkyl migration is now well-recognized to proceed via the radical cleavage-recombination pathway with slight inversion of configuration at the Li-bearing terminus (eq 1). Meanwhile, another interesting variant has been reported which involves a 1,2-vinyl migration on α-vinyloxy benzylic or allylic organolithiums to yield the allylic alcohols (eq 2),[2] while its scope remains largely unexplored. This type of [1,2]-Wittig variant is of particular interest, since structurally related α-allyloxy and α-homoallyloxy organolithiums are known to undergo the concerted [2,3]-sigmatropy rearrangement[3] and the carbolithiative cyclization,[4] respectively. However, the mechanism of the 1,2-vinyl migration remains totally unsolved. The key question is whether the 1,2-vinyl migration proceeds via a radical mechanism similar to that proposed for the usual 1,2-alkyl migration or via an intramolecular carbolithiation mechanism similar to that recently proposed for the 1,2-carbamoyl migration (eq 3).[5] To answer this question, we investigated the steric course of the vinyl-migrating [1,2]-Wittig variant using enantiomerically-defined substrates, with the reasonable prediction that the carbolithiation pathway should result in almost complete retention of configuration at the Li-bearing stereocenter. Disclosed herein are the stereochemical outcomes of the 1,2-vinyl migrations of the enantio-defined α-stannylalkyl and α-methylbenzyl vinyl ethers, which provide solid evidence in support of the radical cleavage-recombination mechanism.

$$ \text{(1)} $$

$$ \text{(2)} \quad (\text{G} = \text{Ph}, \text{C(R')}=\text{CHR''}) $$

$$ \text{(3)} $$
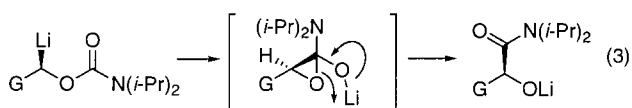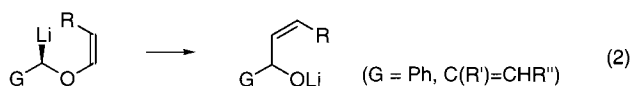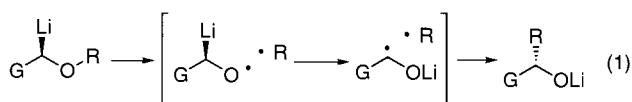
At the outset, our attention was focused on the rearrangement of the enantiomerically defined α-stannylalkyl vinyl ether (E)- or (Z)-**2** prepared from the allyl ether (R)-**1** via olefin

migration (Scheme 1). Thus, (R)-**1** (95% ee)[6] was first treated with RhCl(PPh$_3$)$_3$[7] to afford the vinyl ether **2**[8] in Z-riched form (Z/E=2/1) without appreciable loss of enantio-purity.[9] Interestingly, treatment of **1** with the hydride catalyst generated *in situ* from Ir(cod)(PMePh$_2$)$_2$[10] was found to result in the exclusive formation of (E)-**2**,[8] again, without loss of enantio-purity.[9] When (E)-**2** was transmetalated with *n*-BuLi (1.2 equiv) in THF at –78 °C to generate the lithio species (E)-**3** with complete retention of cofiguration[11] and then stirred at that temperature for 0.5 h followed by hydrolysis with D$_2$O, no vinyl-migrated product (**4**) was detected, but the deuterated ether (E)-**5a** was obtained in 72% yield. However, when the reaction temperature was raised up to –25 °C over a period of 14 h followed by hydrolysis with D$_2$O, the rearrangement product (E)-**4**[12] was obtained in 19% yield, together with 43% yield of the protonated ether (E)-**5b**; surprisingly, none of the deuterated one was formed.[13] Significantly enough, alcohol (E)-**4**[12] thus obtained was found to be almost racemic (9% ee),[14] while the E-geometry was completely retained as previously observed.[2,15] A similar reaction of (Z)-**2** (>95% Z) also afforded 16% yield of the racemic alcohol (Z)-**4**, again, with complete retention of Z-geometry, together with 18% recovery of (Z)-**5b**[13] and 16% yield of byproduct **6**.[16] Thus, these results reveal that the 1,2-vinyl migration onto an α-oxyalkyllithium occurs with much smaller facility, compared with the reported benzylic and allylic counterparts[2] and, more importantly, the present vinyl migration proceeds in almost non-stereospecific fashion at the Li-bearing terminus. Obviously, these findings are suggestive of the radical nature of the 1,2-vinyl migration.
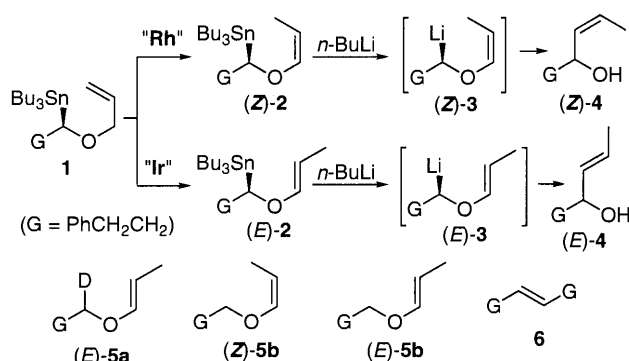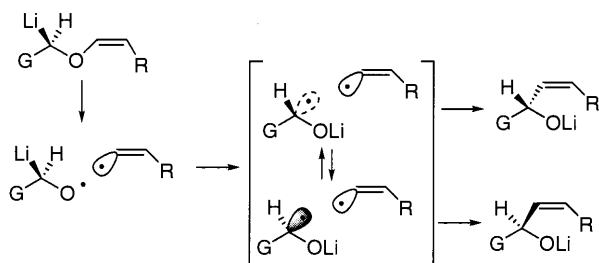

Scheme 1.

In order to gain more evidence supporting the radical mechanism, we next carried out the rearrangement of enantio-defined benzylic vinyl ethers. Thus, the (R)-α-deuterobenzyl vinyl ether **8**, prepared as an E-riched mixture (E/Z=12/1)[8] in 89% yield from the enatio-enriched allyl ether **7** (96% ee) by using the aforementioned iridium catalyst, was treated with *n*-BuLi (1.2 equiv.) in THF-TMEDA (20% vol) at –78 °C to

afford, after hydrolysis, the vinyl-migration product **9** in 59% yield (eq 4). Alcohol **9** thus obtained was essentially racemic as revealed by chiral HPLC assay. However, this outcome, while consistent with the radical mechanism, does not necessarily serve as solid evidence for the radical mechanism, since α-oxybenzyllithiums in general are known to be configurationally labile.[17] Thus, we next examined the rearrangement of (*R*)-α-methylbenzyl vinyl ether (**11**) of which the lithium species should be configurationally more stable.[17] Thus, treatment of (*R*)-**11** (100% ee), prepared from (*R*)-**10** by the literature method,[18] with *n*-BuLi in THF at –78 °C was found to afford the vinyl-migration product (*R*)-**12**[19] in 87% yield in slightly inverted form (22% ee)[20] (eq 5).
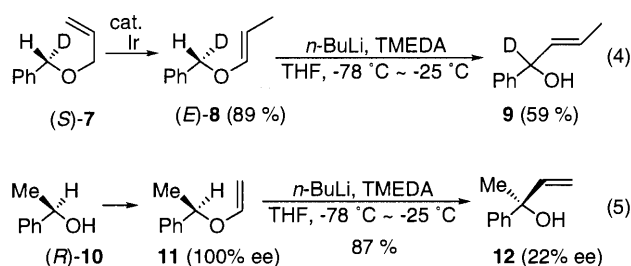
This result provides solid evidence for the radical mechanism and against the carbolithiation mechanism as well. Overall, it is safe to conclude that the present 1,2-vinyl migration proceeds via the radical pathway, wherein the configurational integrity at the Li-bearing terminus is mostly lost, while the geometry of the migrating vinyl group is completely retained (Scheme 2).

Scheme 2.

In summary, we have proved that the vinyl-migrating [1,2]-Wittig rearrangement on α-lithiated alkyl and benzyl vinyl ethers, like the well-known alkyl-migrating variant, proceeds via the radical cleavage-recombination pathway based on the elucidation of the steric course of the asymmetric versions using enantio-defined substrates. Furthermore, we have pointed out the importance of a radical stabilizing element in the carbanion part as a key factor to facilitate the 1,2-vinyl migration. Further works on synthetic applications of the present [1,2]-Wittig variant as well as the development of the enantioselective version are in progress.

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