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[1,2]-WITTIG REARRANGEMENT OF A LITHIOALKYL BENZYL ETHER WITH INVERSION OF CONFIGURATION AT THE CARBANION C ATOM. DIASTEREOSELECTIVE REDUCTIONS OF CYCLOHEXYL RADICALS WITH LI^+ $ARENE^-$

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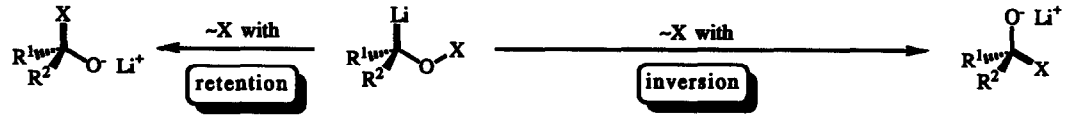
Abstract: Treatment of the diastereomeric O,Se-ketals *cis*- or *trans*-**4** with lithium naphthalenide provided, through stereoselective reduction of the radical intermediate **5**, the *axially* lithiated cyclohexyl ether *trans*-**6**. *trans*-**6** gave the *equatorially* benzylated cyclohexanol *cis*-**5** stereoselectively after [1,2]-Wittig rearrangement and aqueous work-up.

α-Lithioethers are pyramidal at the carbanion C atom [1] and at -78°C configurationally stable long enough to react stereoselectively with a variety of electrophiles [2]. This is also true when an electrophile X (X = alkyl or substituted silyl group) migrates *within* lithioethers **2** from the oxygen to the carbanion C atom in Wittig or retro-[1,2]-Brook rearrangements: As the case may be, complete retention (→**1**; retro-[1,2]-Brook rearrangements [3]) or complete inversion of configuration at the lithium bearing C atom (→*iso*-**1**; another retro-[1,2]-Brook rearrangement [4], [2,3]-Wittig rearrangements of crotyl [5] and allyl ethers [6,7], [1,2]-Wittig rearrangements of crotyl [5] and allyl ethers [8]) is observed. The latter course is also found in the [1,2]-Wittig rearrangement of a lithioalkyl *benzyl* ether (type **2**; X = CH_2Ph) described in the present study.



1

X	~[i,j]	Ref.
SiR_3	~[1,2]	3

2

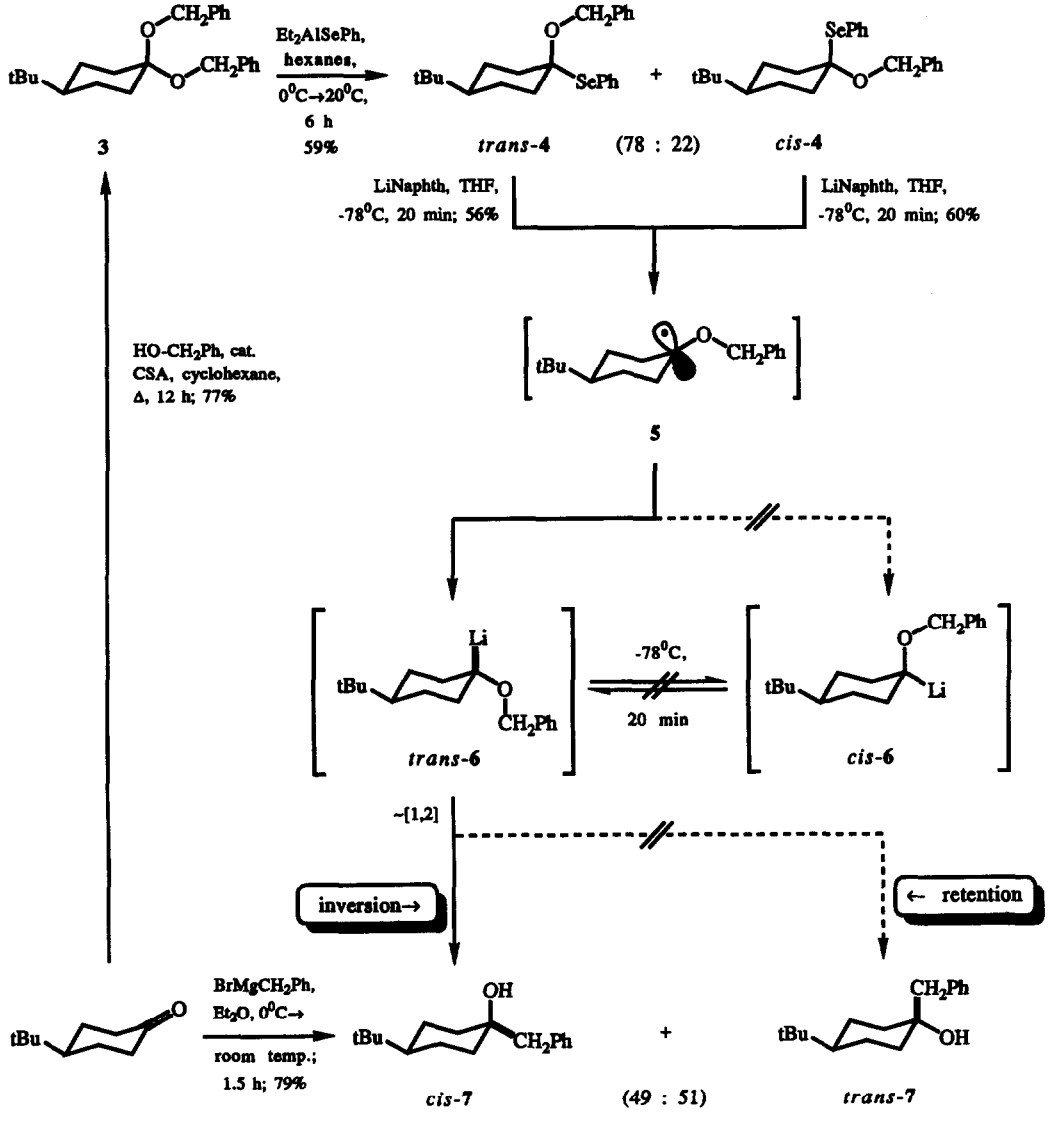
X	~[i,j]	Ref.
SiR_3	~[1,2]	4
crotyl	~[1,2]	5
allyl	~[1,2]	8

X	~[i,j]	Ref.
crotyl	~[2,3]	5
allyl	~[2,3]	6,7
benzyl	~[1,2]	here

iso-**1**

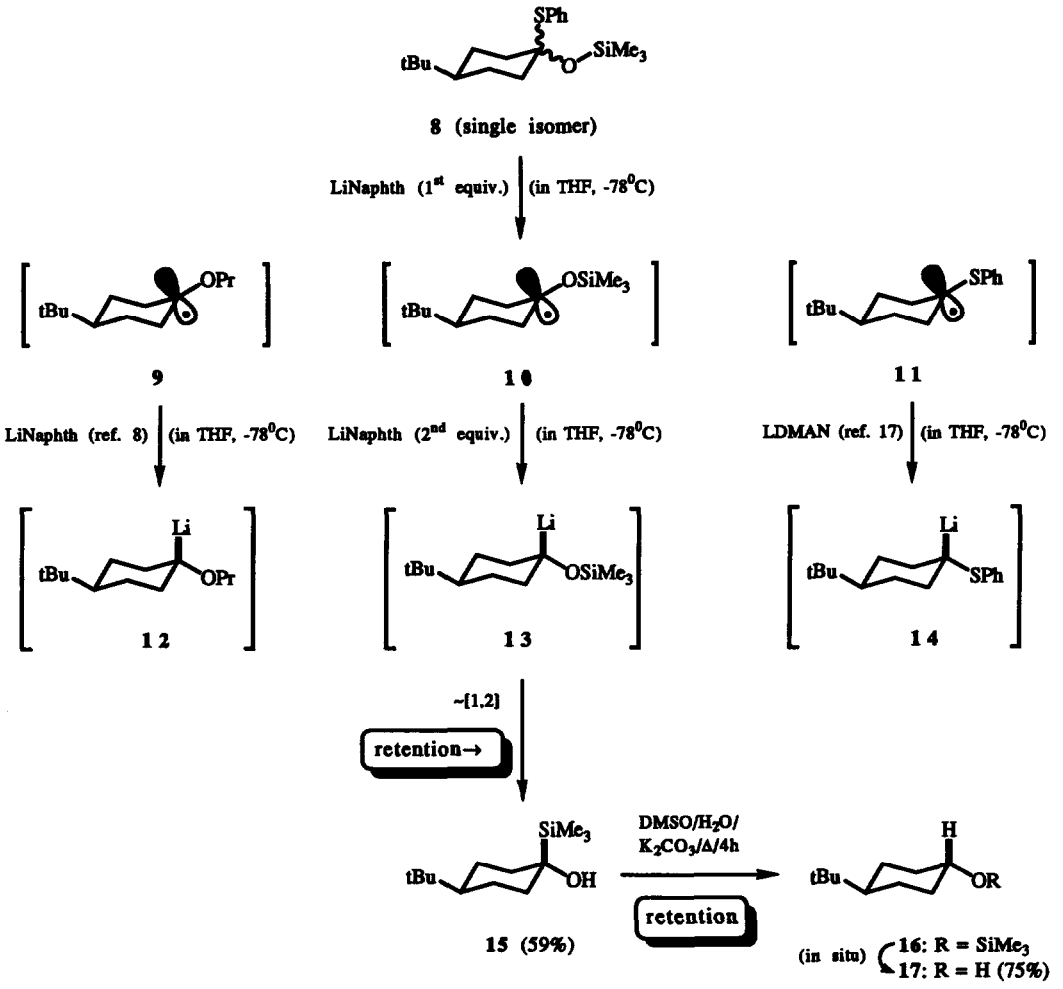
The substrates [9] of the novel Wittig rearrangement were the diastereomeric O,Se-ketals *cis*- and *trans*-**4** [10] which were separable by flash chromatography on silica [11]. They were obtained from dibenzyl ketal **3** and $Et_2AlSePh$ following the recently described procedure [8]. Each O,Se-ketal underwent - after reductive cleavage of its C_{sp^3}-Se bond [12] with lithium naphthalenide (LiNaphth) and via the radical **5** and a sterically homogenous lithioether obtained therefrom - a stereoselective [1,2]-Wittig rearrangement furnishing the cyclohexanol *cis*-**7** (60% from *cis*-**4**, 56% from *trans*-**4**) [13]. Therein, the newly formed C-C bond is *equato-*

rial. Since, as shown below, the lithioether precursor of *cis*-**7** must be *trans*-**6** with an *axial* C-Li bond, this Wittig rearrangement proceeds with inversion of configuration at the carbanion C atom. This means that the steric course of the [1,2]-Wittig rearangements of lithioalkyl benzyl, allyl [5,6], and crotyl ethers [5,8] with respect to a stereogenic carbanion C atom is identical as one would expect if a common mechanism holds.



That the axial (*trans*-**6**) rather than the equatorial lithioether (*cis*-**6**) is formed from the radical intermediate **5** of the Wittig rearrangement and LiNaphth is concluded from *related* reductions: Cyclohexyl radical **9** with an *isopropoxy* group picks up an electron from LiNaphth to give the *axial* lithioether **12** exclusively [8]. Axial selectivity intervenes also in the LiNaphth mediated cleavage of the C_{sp^3}-S bond of the O-silyl O,S-ketal **8** (obtained by Chan's procedure [14] as a single diastereomer of un-known configuration): The *silyloxy* substituted cyclohexyl radical **10** obtained there must react with LiNaphth to an *axial* lithioether (**13**) again,

as revealed by the subsequent conversion into the axially silylated alcohol **15** [15] by a retro-[1,2]-Brook rearrangement which is known to occur with retention of configuration [3].



The stereoselectivity of the reductions of cyclohexyl radicals **5**, **9**, and **10** furnishing the *axially* lithiated ethers *trans*-**6**, **12**, and **13**, respectively, is probably due to a steric effect. The latter was in part already addressed by Cohen in discussing the axial-selective reduction of the (phenylthio) substituted radical **11** [17]. The trivalent carbon of a cyclohexyl radical is probably pyramidalized. As a consequence, its exocyclic substituent should be - for steric reasons - pseudo-equatorial. This notion is supported calculationally [18] by the slight preference of the pseudo-equatorially hydroxylated radical $\mathbf{18}_{\psi\text{-eq}}$ over its conformer $\mathbf{18}_{\psi\text{-ax}}$ [19]. If the pseudo-equatorial substituent adhered to the principle of least motion in the reduction step, it should become *fully* equatorial rather than axial. *This is tantamount to obtaining the axially lithiated cyclohexane.* The same kind - but maybe not degree - of selectivity would arise if the reduction were a non-Curtin/Hammett reaction and "froze" a mixture of radicals consisting almost only of pseudo-equatorially substituted ones.

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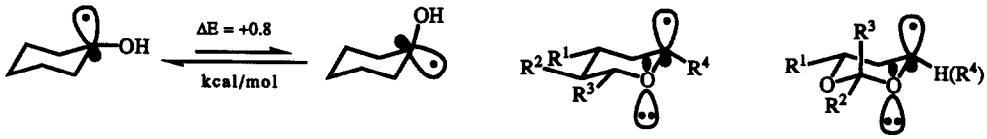

$18_{\psi\text{-eq}}$ $18_{\psi\text{-ax}}$ **19** **20**

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