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THE [1,2] AND [1,4] WITTIG REARRANGEMENT OF OPTICALLY ACTIVE ALLYL α-PHENYLETHYL ETHER

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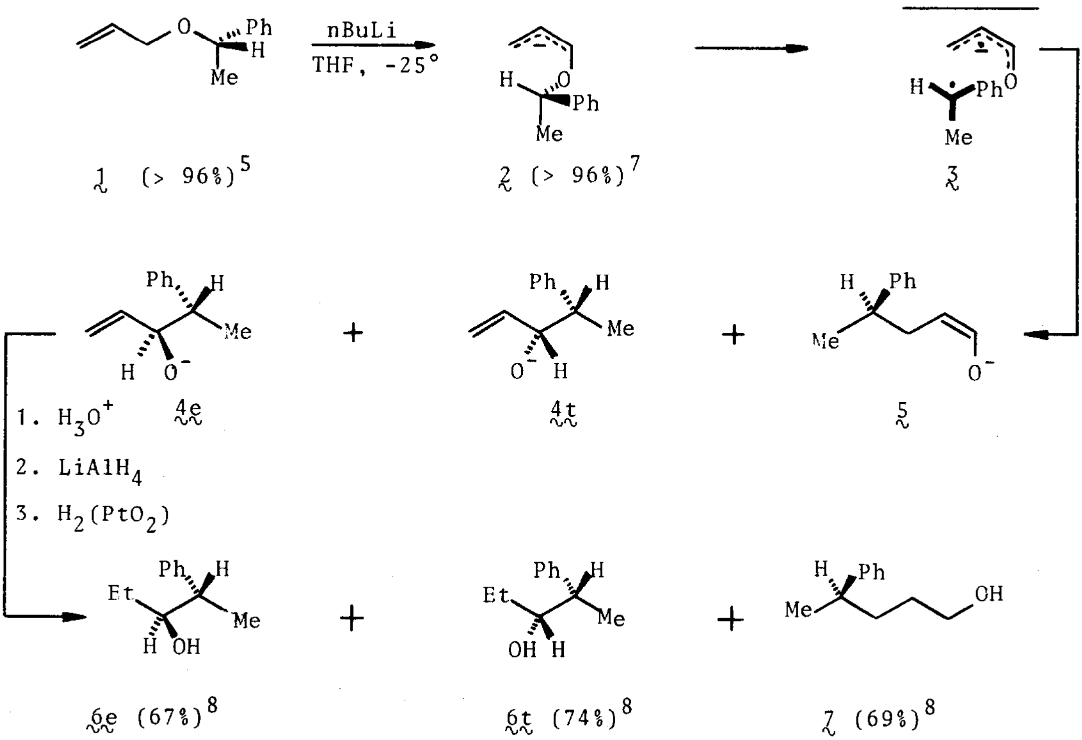
Recent interest in "electron-sufficient" [1,2] rearrangements of the Stevens[1,2] and Wittig[3] type has centred on the problem of their degree of concertedness. These rearrangements, which are formally symmetry-forbidden processes, are thought to occur (at least partly)[2] *via* a non-concerted radical (cf. **3** and **12**) cleavage-recombination mechanism,[4] and this view is consonant, among other things, with the fact that optically active precursors generally lead to partially racemised products.[4]

Here we report the stereochemical course of the [1,2] and [1,4] Wittig rearrangement of *S*-allyl α-phenylethyl ether **1**. Unlike the [1,2] rearrangement, the concerted (and therefore stereospecific) [1,4] rearrangement is formally symmetry-allowed,[4] and it was of interest to see if this difference would show up as a lesser degree of racemisation in the [1,4] rearrangement product **5** compared to the [1,2] rearrangement products **4**.

The ether **1**[5] was mixed with excess butyl lithium in THF at -25°C, and the mixture of anionic products **4** and **5** was treated as shown in Scheme 1. The alcohols **6e**, **6t** and **7**, which were formed in 60% overall yield and in a ratio of 16:20:64, were separated by chromatography. Their configurations and optical purities are shown in Scheme 1.[6,7,8]

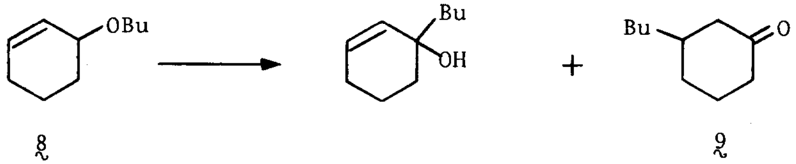
All three products are formed with predominant retention of configuration, as expected,[4] and the extent of racemisation is similar (30 ± 5%) for the [1,2] and [1,4] rearrangement products. This suggests very strongly that essentially all of the reaction, leading to both types of products, is occurring *via* the non-concerted radical mechanism **2** ⟶ **3**. Such a mechanism is indeed required in the case of the cyclic allylic ether **8**, which cannot adopt the cisoid conformation necessary for a concerted [1,4] alkyl shift and which nevertheless affords appreciable amounts of the [1,4] rearrangement product **9**.[9]

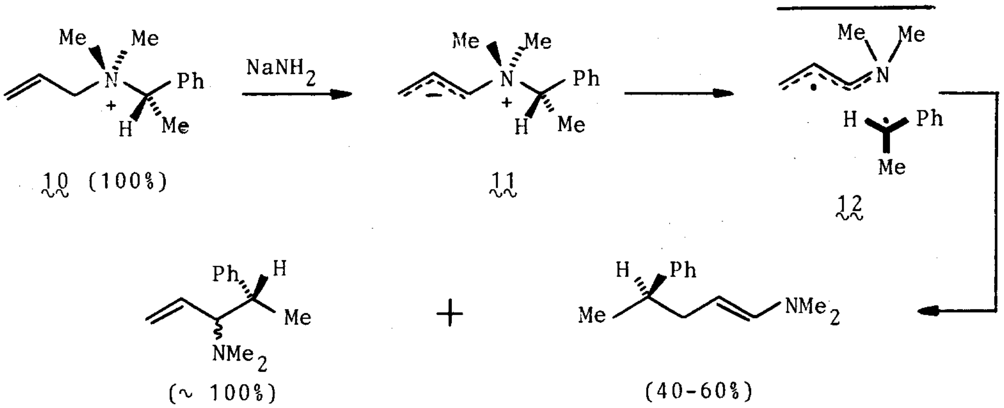
The Stevens rearrangement of the analogous optically active allylic ammonium salt **10** was studied some years ago by Jenny and Druey,[10] who found that the [1,4] migration of the phenylethyl group is accompanied by considerable racemisation,



Scheme 1 (Optical purities are shown in parentheses)

whereas the [1,2] rearrangement (the major process) is essentially stereospecific (see Scheme 2). This difference in the stereochemical course of the two reactions may be due to a difference in the configurations of the ions **2** and **11**, and hence of the radical pairs **3** and **12**, as suggested in the Schemes. Allylic anions such as **2** are well known[11] to prefer the <u>cis</u> configuration shown; this configuration leads to a radical pair **3** in which the migrating α-phenylethyl radical is situated somewhere near the middle of the allylic moiety. The result is approximately equal amounts of [1,2] and [1,4] rearrangement products, and a similar degree of racemisation. The ammonium zwitterion in the Stevens rearrangement, on the other hand, is constrained, for steric reasons,[12] to adopt the <u>trans</u> configuration **11**; this leads to a radical pair **12** in which the migrating radical is placed close to the carbon atom bearing the nitrogen, and remote from the terminal carbon. The result is a predominance of [1,2] over [1,4] rearrangement,[10]

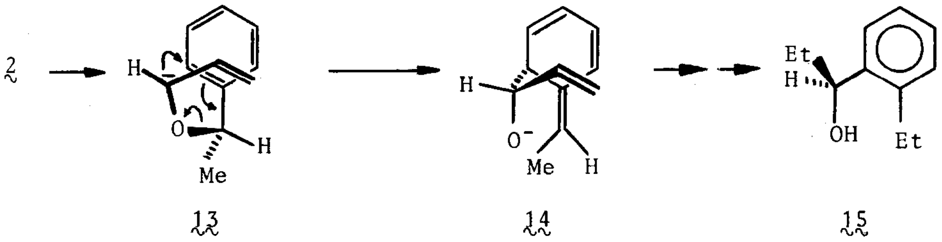




Scheme 2 (Optical purities are shown in parentheses)[10]

and a far greater extent of racemisation in the [1,4] rearrangement product, where the migrating radical has farther to go.

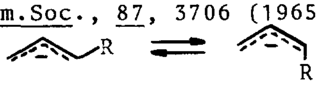
One last point deserves mention. The reaction between the ether **1** and butyl lithium leads (after treatment as shown in Scheme 1) not only to the expected



products **6** and **7**, but also, in about 9% yield, to the *S*-alcohol **15**, α_D^{25} -29.7° (neat, l = 1 dm). This alcohol must arise from the intermediate **14**, which in turn must be formed from the allylic anion **2** *via* a cyclic transition state such as **13**. A route *via* the radical pair **3** (recombination of the allylic moiety with the *ortho* position of the phenyl ring) is excluded since (a) none (< 0.5%) of the corresponding *para* isomer is formed and (b) the optical purity of the alcohol **15** is at least 90%,[13] whereas the diastereoisomer ratio **4t**/**4e** is very low (about 1.2). Such an unexpectedly high degree of transfer of chirality (> 90%) must imply an extremely "tight" transition state **13**.

References and footnotes

1. W.D.Ollis, M.Rey, I.O.Sutherland, and G.L.Closs, *J.C.S.Chem.Comm.*, 543 (1975).
2. U.H.Dolling, G.L.Closs, A.H.Cohen, and W.D.Ollis, *J.C.S.Chem.Comm.*,545 (1975).
3. J.F.Garst and C.D.Smith, *J.Amer.Chem.Soc.*, 98,. 1526 (1976).

4. U.Schöllkopf, *Angew.Chem.Int.Ed.*, 9, 763 (1970).
5. The ether **1**, $[\alpha]_D^{25}$ -82.4° (c = 1, toluene), was prepared from optically pure S(-)-Ph-CHOH-Me, $[\alpha]_D^{25}$ -51.1° (c = 1.7, toluene), NaH and allyl bromide in DME. It was > 96% optically pure, since it was converted back to Ph-CHOH-Me, $[\alpha]_D^{25}$-49.1° (c = 1.7, toluene), when treated with $RhCl(PPh_3)_3$ [E.J.Corey and J.W.Suggs, *J.Org.Chem.*, 38, 3224 (1973)], followed by $HgCl_2$ and HgO [R. Gigg and C.D. Warren, *J.Chem.Soc.(C)*, 1903 (1968)].
6. A reaction done with nBuLi and TMEDA in pentane (see ref. 9) gave very similar results as regards both optical purities and yields.
7. The ether **1** could be recovered with unchanged rotation after 40% reaction with nBuLi in THF.
8. The optical purities shown in Scheme 1 are based upon the following maximum rotations: **6e**, α_D^{25} + 7.34° (neat, 1 = 1 dm), and **6t**, α_D^{25} -11.4° (neat, 1 = 1 dm) [D.J.Cram, *J.Amer.Chem.Soc.*, 74, 2159 (1952)]; **7**, α_D^{25} -19.4° (neat, 1 = 1 dm), $[\alpha]_D^{25}$ -20.2° (c = 4.8, ethanol). The values for **7** are slightly higher than those found previously: α_D^{25} -18.2° (neat, 1 = 1 dm) [P.A.Levene and R.E.Marker, *J.Biol.Chem.*, 110, 329 (1935)] and $[\alpha]_D^{20}$ -14.2° (c = 4.6, ethanol) [Y.Senda and S.Mitsui, *Nippon Kagaku Zasshi*, 86, 229 (1965); *Chem. Abstr.*, 63, 4134 (1965)]. They are based upon the rotations of an 83% optically pure sample of **7** prepared (*via* Arndt-Eistert chain lengthening and subsequent $LiAlH_4$ reduction) from 3-phenyl butyric acid, α_D^{25} -47.2° (neat, 1 = 1 dm) and $[\alpha]_D^{25}$ -48.1° (c = 3, benzene): optically pure 3-phenyl butyric acid has α_D^{25} -56.5° (neat, 1 = 1 dm) and $[\alpha]_D^{25}$ -58.5° (c = 3, benzene) [D.J.Cram, *J.Amer.Chem.Soc.*, 74, 2137 (1952)].
9. H. Felkin and A.Tambuté, *Tetrahedron Letters*, 821 (1969).
10. E.F.Jenny and J.Druey, *Angew.Chem.*, 74, 152 (1962).
11. See, *inter al.*, C.D.Broaddus, *J.Amer.Chem.Soc.*, 87, 3706 (1965).
12. Compare the positions of the equilibria:  ; *cis*/*trans* ∿ 50 when R = Me, and *trans*/*cis* ∿ 4 when R = tBu [A.Schriesheim and C.A. Rowe, *Tetrahedron Letters*, 405 (1962)].
13. The optical purity of **15** was found to be 94 ± 4% using the chiral shift reagent $Eu(dcm)_3$ [M.D.McCreary, D.W.Lewis, D.L.Wernick and G.M.Whitesides, *J. Amer.Chem.Soc.*, 96, 1038 (1974)]. The absolute configuration (S), and also the optical purity (85.3 ± 4.3%), were very kindly determined for us by A. Schoofs and A.Horeau on a 20 mg sample using their ingenious new (but as yet unpublished) enantioselective esterification method.