Absolute Configuration of Acyclic Sulphoxides

By M. NISHIO* and K. NISHIHATA

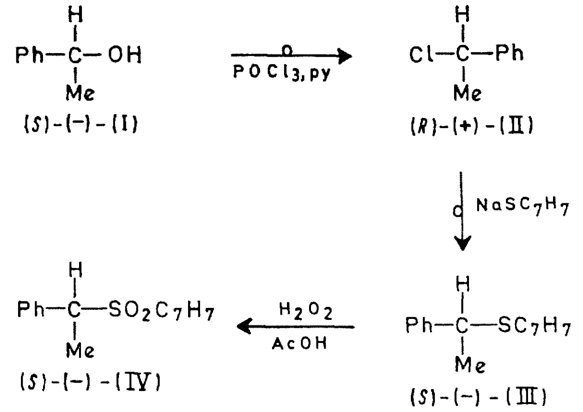
(*Central Research Laboratories, Meiji Seika Kaisha Ltd., Morooka, Kohoku, Yokohama,* 222 *Japan*)

Summary. Absolute configuration of diastereomeric α-phenethyl *p*-tolyl sulphoxides has been determined by chemical correlations, giving a result that is rather unusual in view of the steric factors involved.

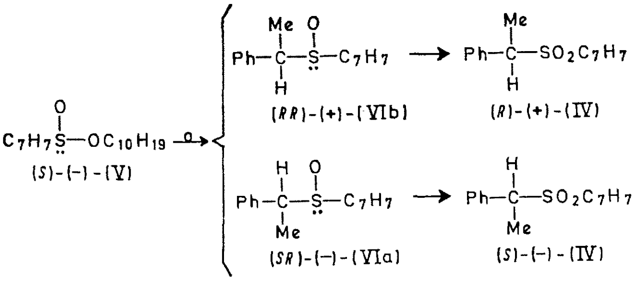
IN a previous paper,[1] we reported a method of assignment of configuration of diastereomeric sulphoxides by analysis of n.m.r. solvent effects. However, the assignment based on analogy with cyclic models[2] may not be reliable.[3] Also open to question is our *a priori* assumption that the conformer having *trans*-phenyl groups predominates under normal conditions.

To establish the absolute assignment of these sulphoxides, we prepared optically active α-phenethyl *p*-tolyl sulphoxides and sulphones *via* two different routes and examined their optical properties.

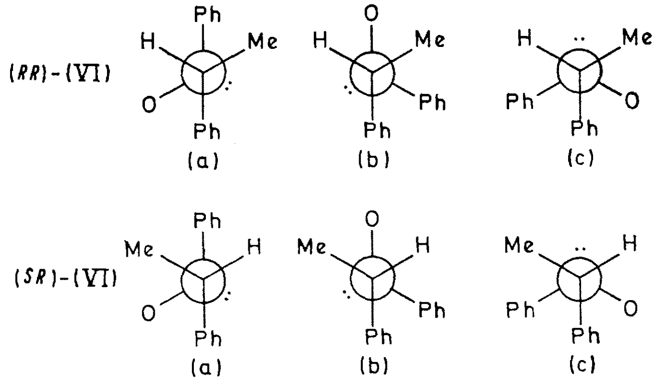
Optically pure (*S*)-(−)-α-phenethyl alcohol (I) $[\alpha]_D$ −44·5° (neat) (lit.[4] −44·2°), was transformed, *via* phenethyl chloride (II), $[\alpha]_D$ +80·5° (neat) (lit.[5] +109°), to phenethyl *p*-tolyl sulphide (III), $[\alpha]_D$ −143·5° (neat). Chlorination of phenethyl alcohol by Burwell's method[5] ($POCl_3$ in pyridine) proceeds with inversion and the latter reaction has been known to proceed with S_N2 mechanism, so this sulphide (III) is assigned the (*S*)-configuration. Oxidation of the sulphide with hydrogen peroxide in hot acetic acid gave α-phenethyl *p*-tolyl sulphone (IV), $[\alpha]_D$ −93° (acetone), m.p. 126·5°. In the oxidation of sulphide to sulphone the configuration of the carbon was unaltered and therefore the sulphone obtained is assigned the (*S*)-configuration.



Reaction of (*S*)-(−)-menthyl *p*-tolylsulphinate,[6] $[\alpha]_D$ −200° (acetone) (lit.[7] −198°), with an excess of α-phenethylmagnesium chloride yielded a diastereomeric mixture of α-phenethyl *p*-tolyl sulphoxides (VI). Fractional crystallization from ethanol and chromatography on silica gel, using 1 : 2 ether–petroleum as eluant afforded materials having m.p. 122°, $[\alpha]_D$ −11° (acetone), and m.p. 91°, $[\alpha]_D$ +183° (acetone). The high- (VIa) and low-melting (VIb) diastereomers were identified with the major (assigned earlier the *RR*/*SS* configuration; see ref. 1) and the minor (similarly assigned as *RS*/*SR*) components of the oxidation products of the racemic sulphide,[1] respectively, by their n.m.r. spectra.



(−)-Menthyl *p*-tolylsulphinate is known to have the (*S*)-configuration[7] and the Grignard reaction proceeds with inversion.[7-9] Therefore, diastereomeric sulphoxides (VIa and VIb) must have the (*R*)-configuration at sulphur and differ only in their configurations at carbon. Oxidation of (VIa) with hydrogen peroxide in hot acetic acid gave a sulphone, m.p. 126°, $[\alpha]_D$ −100° (acetone), identified with (*S*)-(−)-(IV).† This indicates that the configuration of (VIa) is (*SR*), in contrast to the earlier conclusion[1] which requires the configuration of (VIa) to be (*RR*).



The disagreement of the present result with the earlier conclusion calls into question the basis on which the earlier assignment was made or the basis of the chemical correlations used in the present work. To reconcile these results, either our assumption on the conformational equilibria is incorrect [to explain the present result on the basis of evidence‡ previously reported, the conformer (a) in which phenyl groups are *trans*-oriented is in fact not important and the conformer (c) in (*RR*)-(VI), and (b) and (c) in (*SR*)-(VI) are expected to be most populated, a result rather surprising in view of steric factors], or the Grignard

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† Oxidation of (VIb) gave sulphone (IVb), m.p. 125°, $[\alpha]_D$ + 99° (acetone).

‡ Larger ΔTFA [τ(TFA) −τ(CCl_4) for methine proton] and smaller ΔC_6H_6 [τ(C_6H_6) −τ(CCl_4)] for (*SR*)-(VI). See ref. 1.

reaction proceeds with retention of configuration in this particular case. To remove the last ambiguity, o.r.d. and c.d. studies[7] are currently being undertaken.[7] Dipole moment and X-ray studies are also being made and will be reported elsewhere.

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