STEREOCHEMISTRY IN THE OXIDATION OF ALIPHATIC SULPHIDES TO

DIASTEREOISOMERIC SULPHOXIDES

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Diastereoface differentiating reactions[1] occur in the oxidation of sulphides, 1a-f, where a chiral centre exists in the molecules. An extention of Cram's open-chain model predicts the predominant formation of the diastereoisomeric sulphoxide having erythro[2] configuration, 2 (Fig. 1). Thus the phenyl group is considered as ordinarily to be the bulkiest among the groups and one assumes that the reagent attacks from the less hindered side.

Fig. 1
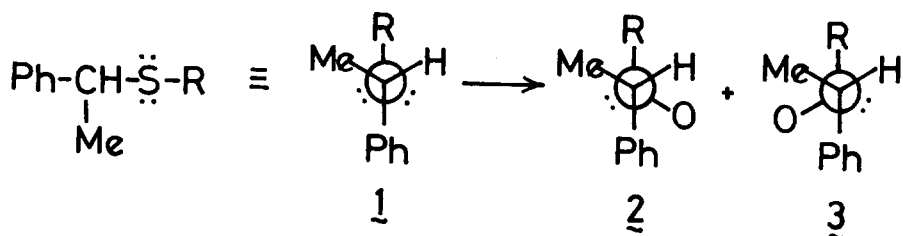
R = Me(a), Et(b), Pr^i(c), Bu^t(d), Ph(e), CH_2Ph(f)

This, however, has not been born out by the experiments. In every reactions examined, the predominantly produced products have been shown to have the threo configurations, 3. In Table 1 are listed the product ratios when oxidations were carried out at 25° with peroxyacetic acid. The proportion of the diastereoisomers has been shown to be not significantly affected by change in the oxidizing agent.[3]

We recently found that, by X-ray studies, in some sulphoxides having t-butyl group, 4 and 5, Bu^t orients itself anti to the methyl group and gauche to the phe-

Table 1

| Starting sulphide	Configuration of the major product	$\underline{3}/\underline{2}$-ratio	LIS(CH)[a]		ASIS(CH)[b]	
			$\underline{3}$	$\underline{2}$	$\underline{3}$	$\underline{2}$
1a	$(\alpha\underline{R},S\underline{R}/\alpha S,S\underline{S})$[c]	3.1	−0.94	−0.57	+0.31	+0.46
1b	(″)[d]	3.2	−1.10	−0.44	+0.25	+0.42
1c	(″)[d]	3.6	−1.12	−0.39	+0.18	+0.37
1d	$(\alpha\underline{R},S\underline{S}/\alpha\underline{S},S\underline{R})$[c]	49.0	−1.05	−0.40	+0.17	+0.30
1e	(″)[c]	2.5	−1.10[e]	−0.80[e]	+0.14	+0.25
1f	$(\alpha\underline{R},S\underline{R}/\alpha\underline{S},S\underline{S})$[d]	2.0	−0.71	−0.14	+0.14	+0.40

a   Shifts induced by the addition of 0.1 equiv. Eu(fod)_3 in CCl_4 solutions.

b $\delta(CCl_4) - \delta(\text{benzene})$ for the methine proton.

c   Configurations determined by chemical correlations.[3,4,5]

d   Configurations tentatively assigned by n.m.r. comparisons.   e   R = p-tolyl

nyl group(Fig. 2).[5] This led us to an X-ray study of a related sulphone, $\underline{6}$.

Although the refinement of the result is in progress, this compound also has

unambiguously been shown to exist with the conformation as depicted in Fig. 2.[6]

These are crystallographic results, however, N.m.r. O.r.d./C.d.[3,5] and dipole

moment evidences[7] strongly suggest that these conformations hold also in solution,

at least in the t-butyl sulphoxides, $\underline{2}$d, $\underline{3}$d, $\underline{4}$ and $\underline{5}$. Generallization should be

Fig. 2
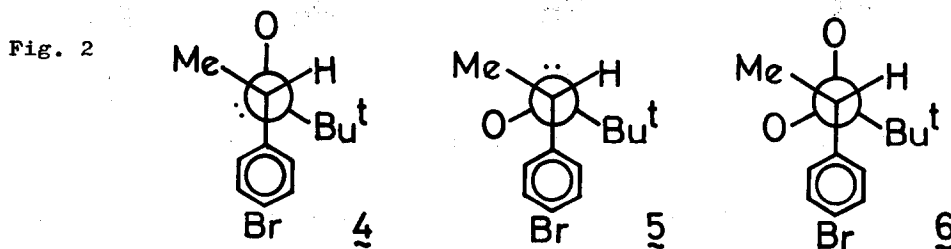
made with caution, however, it is likely that the alkyl (Bu^t in these cases) gro-

up prefers to be oriented anti to Me if this group is present in the molecule.

Here we suggest that the apparently abnormal phenomena cited so far can be

interpreted on the basis of a simple premise that "Me is effectively bulkier than

Ph in these molecular circumstances". With respect to the van der Waals inter-

action with the alkyl group, a methyl group can be regarded to be effectively more

crowded than Ph due to the three hydrogens symmetrically arranged on the carbon

atom.   On the other hand a phenyl group can relieve the interaction with R by a

rotation about the C-C(Ph) bond.[5b]   This argument is in line with the recent pro-

posal of Wertz and Allinger[8] that vicinal H/H interactions are most important in

determining the conformations of some molecules.   Unexpected results encountered

in the oxidation of sulphides can be rationalized if one assumes that the sulphide

adopts a conformation as sulphoxides (R is anti to Me: Fig. 3) and that the attack

of the oxidizing agents occurs preferentially from the less hindered side.

Fig. 3
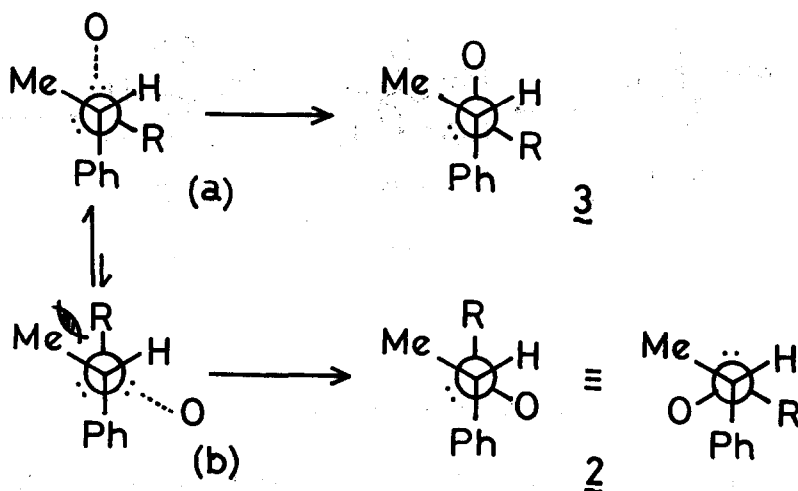
On the basis of the above premise it is expected that the free energy difference

between the transition state (a) and another one (b; this leads to the epimeric

sulphoxide) becomes larger as the steric bulk of R increases.   The product ratio

($3/2$) in fact varies from 3.1 (R = Me) to 3.2 (Et), 3.6 (Pr^i) and to 49.0 (Bu^t).

We feel that some phenomena which have hitherto been poorly understood can

better be explained on a similar basis.   These include an apparent failure of

Cram's model to explain Felkin's results.   Felkin and his co-workers[9] studied the

effect of systematic variations in the bulk of the achiral alkyl group attached

to the carbonyl centre in the hydride reductions of a series of 1-phenylethyl al-

kyl ketones, 7.   The configurations of the predominantly produced alcohols 8 (ery-

thro) are correctly predicted by Cram's (Fig. 4a) or Karabatsos' model (Fig. 4b).[9]

These models, however, fail to explain the trend observed in the product ratio;

Felkin found that the ratio ($8/9$) varies from 2.9 (R = Me) to 3.2 (Et), 5.7 (Pr^i)

and to 49.0 (Bu^t). The inversed trend should indeed be observed with the above

models if one assumes the steric repulsion between R and the phenyl group to be

the dominant factor in determining the selectivity of the reaction. The apparent

paradox, however, will be solved with our present theme that "a methyl group is

effectively bulkier than a phenyl group with regard to the interaction with the

vicinal alkyl group". This explains a gradual increase of 8/9 ratio accompanied

with the increase in the bulk of R and the almost exclusive formation of the

erythro t-butyl alcohol, 8.

Fig. 4
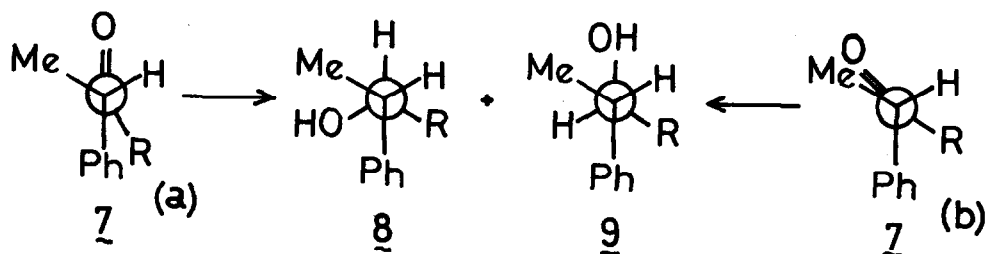
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