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Asymmetric Organic Reactions, IV.

ASYMMETRIC SELECTION DURING A MEERWEIN-PONNDORF-VERLEY TYPE REACTION IN THE PRESENCE OF AN OPTICALLY ACTIVE SOLVENT

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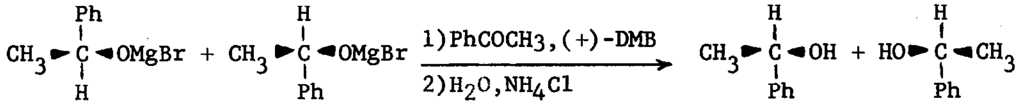
Reaction of the bromomagnesium salt of racemic methylphenylcarbinol with acetophenone leads to an equilibration *via* MPV reduction. This equilibration is an invisible process in achiral solvent systems. In the presence of an optically active ether, however, we have found that an intriguing partial resolution occurs. For example, to a suspension of 1-phenylethoxymagnesium bromide (I) in benzene was added a solution of acetophenone in (2*R*,3*R*)-(+)-dimethoxybutane, (+)-DMB (1). After distillation of some benzene this mixture which contained a suspended white precipitate, was stirred for five days. Following hydrolysis with aqueous ammonium chloride the organic products were isolated by distillation and purified by preparative gas chromatography. The 1-phenylethanol (II) isolated had $[\alpha]^{29}_{589}$ - 16.8 (neat) which corresponds to a 39 per cent excess of the *S*-enantiomer.



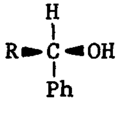
$$\mathrm{CH_3}{\blacktriangleright}\overset{\mathrm{Ph}}{\underset{\mathrm{H}}{\mathrm{C}}}{\blacktriangleleft}\mathrm{OMgBr} + \mathrm{CH_3}{\blacktriangleright}\overset{\mathrm{H}}{\underset{\mathrm{Ph}}{\mathrm{C}}}{\blacktriangleleft}\mathrm{OMgBr} \xrightarrow[\text{2) } \mathrm{H_2O, NH_4Cl}]{\text{1) } \mathrm{PhCOCH_3}\text{, (+)-DMB}} \mathrm{CH_3}{\blacktriangleright}\overset{\mathrm{H}}{\underset{\mathrm{Ph}}{\mathrm{C}}}{\blacktriangleleft}\mathrm{OH} + \mathrm{HO}{\blacktriangleright}\overset{\mathrm{H}}{\underset{\mathrm{Ph}}{\mathrm{C}}}{\blacktriangleleft}\mathrm{CH_3}$$

50% 50% 30.5% 69.5%

Racemic I *R*-(+)-II *S*-(-)-II

The same kind of equilibrating conditions were applied to a series of four other racemic phenyl alkyl carbinol salts with the result that in each case there was a low order of partial resolution. Curiously, the alcohols obtained in these cases were all members of the opposite configurational series (III) as compared to the predominant enantiomer (*S*-II) obtained from methylphenylcarbinol.

The fact that optically active alcohols result could be a consequence of MPV equilibration involving diastereomeric complexes of the bromomagnesium salts and (+)-DMB. The equilibrium constant would not be expected to be unity. In certain cases one diastereomeric complex might even selectively precipitate. A more intensive study of this phenomenon is in progress.



III

R	[α]D	% Excess of III
Et	+0.13	0.5
iPr	+0.51	2.1
tBu	+0.28	1.1
CF_3	+1.31	3.1

This preliminary report, aside from its intrinsic interest, is intended to convey a note of caution regarding the interpretation of stereochemical data in any system involving salts of secondary alcohols and chiral additives. For example, French and Wright (2) obtained optically active methylphenylcarbinol (levorotatory) from the reaction of dimethylmagnesium or the Grignard reagent from methyl chloride with benzaldehyde in benzene containing (+)-DMB. This was attributed to an asymmetric addition to the enantiotopic faces of the carbonyl group involving chiral complexes of (+)-DMB with the organomagnesium reagents. Our results indicate that optically active II could have resulted from some post-addition process (3). The higher enantiomeric excess observed (2) with Me_2Mg as opposed to methyl Grignard* can also be accommodated without reliance on a kinetically controlled asymmetric addition hypothesis. Since Me_2Mg is known to be less reactive than methyl Grignard reagent, the higher enantiomeric excess of *S*-II obtained could be due to slower consumption of benzaldehyde and consequently more extensive asymmetric MPV equilibration *via* reaction of a magnesium salt of II with either benzaldehyde or acetophenone (3). There are numerous other examples of apparent asymmetric syntheses in which asymmetric equilibration might cause complications (5-7).

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*Based on the accepted value (4) for the maximum specific rotation of methylphenylcarbinol (43.5°, neat), French and Wright (2) actually obtained a 5.5-6.0% excess of *S*-(-)-II with Me_2Mg and a 1.4-1.7% excess with "MeMgCl", rather than the approximately four times greater values they reported.

References

(1) We are grateful to Dr. J. A. Morrison for a sample of (-)-2,3-butanediol from which (+)-DMB was prepared (82% enantiomeric purity).
(2) W. French and G. F. Wright, *Can. J. Chem.*, **42**, 2474 (1964).
(3) A considerable amount of benzyl alcohol and acetophenone were present among the reaction products obtained by French and Wright (2), indicating appreciable MPV reaction.
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(8) We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work.