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LIGAND COUPLING THROUGH σ-SULFURANE --- COMPLETE RETENTION OF CONFIGURATION OF 1-PHENYLETHYL GROUP IN THE REACTION OF 1-PHENYLETHYL 2-PYRIDYL SULFOXIDE WITH GRIGNARD REAGENT[1]

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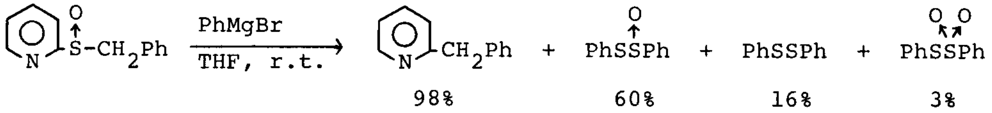
Abstract The reaction of benzyl or 1-phenylethyl 2-pyridyl sulfoxide with Grignard reagent proceeds via a σ-sulfurane as an intermediate to give the coupling product, 2-benzylpyridine or 2-(1-phenylethyl)pyridine in quantitative yield. Stereochemistry for this reaction is complete retention at the benzylic carbon atom.

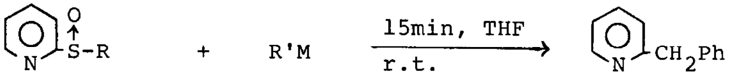
When a nucleophile attacks the tricoordinate sulfur compounds, an incipient formation of sulfurane has been suggested. If, in this sulfurane intermediate, the bonding orbitals of the polarizable basal bond and an electronegative apical bond overlaps sufficiently to form a bond overcoming the apical-apical[2] or apical-basal ligand exchange,[3] there could be a coupling reaction between basal and apical ligands.[1] In fact, coupling between polarizable heteroatom ligands at apical and basal axes around the central pentacoordinate sulfur atom has been proposed in some reactions of tricoordinate sulfur compounds with nucleophiles.[4] The coupling reactions between basal and apical carbon ligands are also suggested to have been observed.[5] Since the coupling reactions are believed to proceed intramolecularly in concerted manner, both ligands should retain their original configuration in the resulting coupling products. In fact, in the reaction of triphenyl sulfonium salt with trans- or cis-propenyl lithium, either trans- or cis-propenylbenzene, obtained in around 65%, was found to retain very highly the geometry of the propenyl group.[5d]

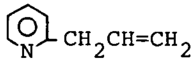
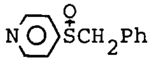
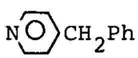
We have now found the first reaction which gives a coupling product in which the configuration of sp^3 aralkyl group is completely retained, thus, proving unequivocally the concerted nature of coupling reaction within a σ-sulfurane.[1] This letter gives a brief account of this reaction.

When benzyl 2-pyridyl sulfoxide was treated with an equimolar amount of phenylmagnesium bromide in THF at room temperature, 2-benzyl pyridine, the coupling product, was obtained in a quantitative yield along with a mixture of dimerized products of benzensulfenic acid[6] as shown below. Phenyl 2-pyridyl sulfoxide also reacts with benzylmagnesium chloride affording the same products. Other organometallic compounds such as n-butyllithium were found to react just like the Grignard reagents. The results of a few representative reactions are listed in the TABLE.

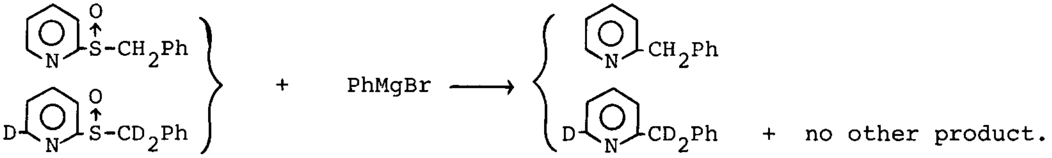


TABLE

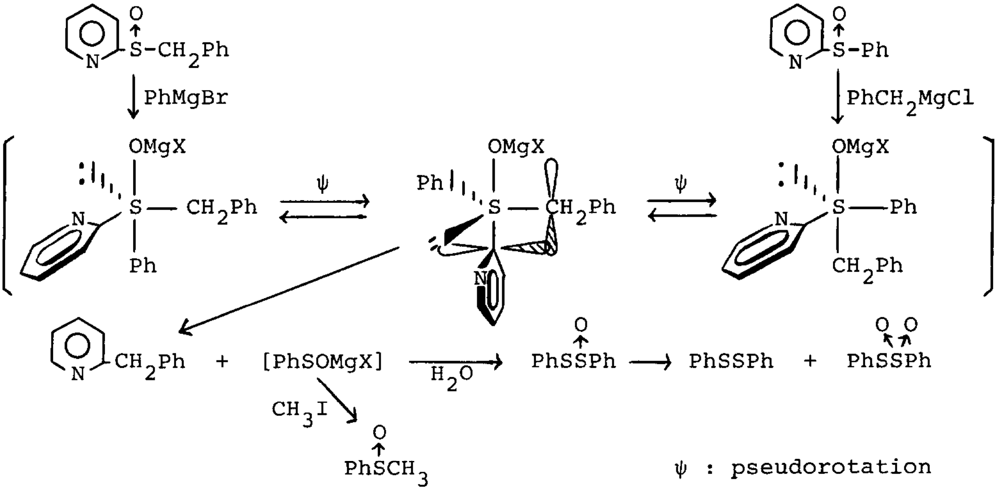


R	R'M	Yield (%)	R	R'M		Yield (%)
$-CH_2Ph$	PhMgBr	98	$-Ph$	$PhCH_2MgCl$		71
$-CH_2Ph$	CH_3MgBr	83				
$-CH_2Ph$	n-BuLi	46	$-CH_2CH=CH_2$	PhMgBr	 $CH_2CH=CH_2$	61
$-CH_3$	$PhCH_2MgCl$	79	 SCH_2Ph	PhMgBr	 CH_2Ph	60

The cross-over experiment shown below reveals the intramolecular nature of the coupling reaction.



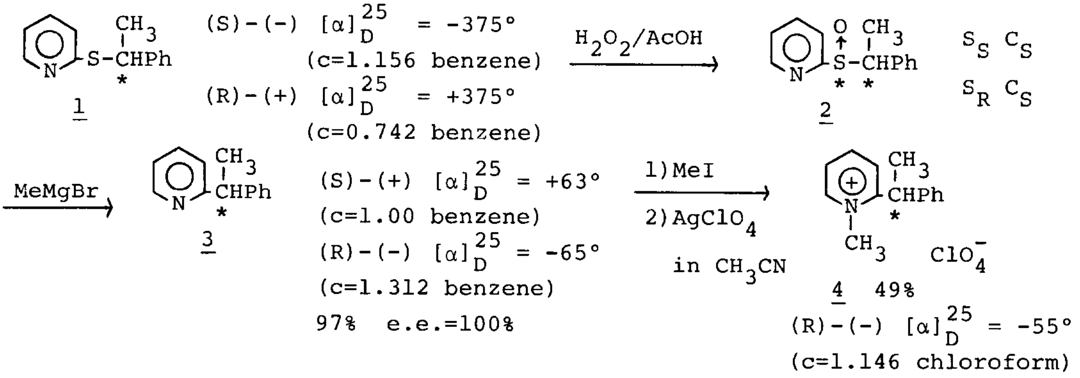
The most plausible mechanistic path is shown in the following scheme.



ψ : pseudorotation

If the coupling of 2-pyridyl and benzyl groups takes place while keeping the angle of ca. 90° around the sulfur atom of the incipient σ-sulfurane, the configuration around the benzylic carbon of the resulted 2-benzylpyridine should be maintained. Indeed, it has been found to be the case, when we have carried out a similar reaction with optically active 1-phenylethyl 2-pyridyl sulfoxide 2.

The optically pure (S)-(-) 1-phenylethyl 2-pyridyl sulfide 1 (e.e.=100%) was oxidized with H_2O_2/AcOH to a diastereomeric mixture of the corresponding sulfoxide 2. The sulfoxide 2, thus obtained, was either separated into pure diastereomeric forms or allowed to react directly without separation, with an equimolar amount of methylmagnesium bromide. Thus the coupling product, 2-(1-phenylethyl)pyridine 3 was obtained in 97% yield. The optical activity of the product 3, was $[\alpha]_D^{25} = +63°$ in benzene, while the e.e. was 100% as determined by nmr shift reagent, regardless of diastereomeric purity of the sulfoxide 2, as we have anticipated. The other enantiomer, (R)-(+)-1 has been found to afford the same stereochemical result with opposite optical activity. All these results are illustrated in the following scheme.



In order to confirm the absolute configuration of the liquid product 3 of (R)-(-) enantiomer, it was converted to (R)-(-)-2-(1-phenylethyl)-1-methylpyridinium perchlorate 4 by treatment with methyl iodide and silver perchlorate. Then the crystalline perchlorate 4 was subjected to X-ray crystallographic analysis, which indeed has confirmed the perchlorate 4 to be of pure (R)-configuration[7] clearly indicating that the chirality of 1-phenylethyl group in the product 3 is maintained 100% through the reaction.

Thus, the coupling of apical 2-pyridyl group and basal 1-phenylethyl group has now been found to proceed concertedly.[8] The result of this experiment would lead to new mechanistic schemes for many hitherto unexplainable reactions which take place between tricoordinate or even tetracoordinate organic sulfur compounds with nucleophiles,[9] and may open up a new chemistry of organic sulfur compounds.

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6. magnesium benzenesulfenate formed can be converted to methyl phenyl sulfoxide upon treatment with methyl iodide.
7. on courtesy of Prof.F.Iwasaki; to be published separately soon.
8. a preliminary ab initio calculation of a similar model system by K.Nishimoto et al. also suggests a substantial orbital interaction between α-pyridyl and benzylic carbon.
9. to be summarized in a review shortly.

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