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FORMATION OF PHENYL SUBSTITUTED HETEROAROMATICS BY LIGAND COUPLING IN THE REACTION BETWEEN HETEROARYL SULFOXIDES WITH PHENYL GRIGNARD REAGENT

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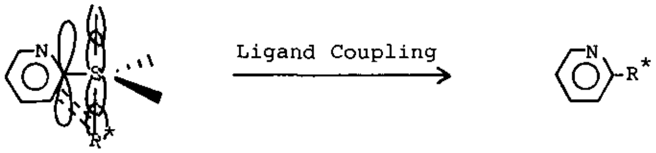
Abstract — In the reaction of heteroaryl alkyl sulfoxides with phenylmagnesium bromide, phenyl group was found to couple predominantly with 2-quinolyl group and 2-pyrimidinyl group.

In our previous papers[1~9], we have shown many examples of ligand coupling reaction which proceed via formation of the incipient σ-sulfurane intermediate. *Since the central sulfur atom in the σ-sulfurane intermediate is valence-shell* expanded, it tends to resume the normal octet by extruding a pair of electrons. There are three conceivable processes of expelling a pair of electrons, i.e. self-decomposition, ligand exchange and ligand coupling. The concerted nature of the *coupling of two ligands, one at an equatorial position and another at an* axial coordinate, has been shown by complete retention of the configuration of the coupling ligands.[1,8] The two ligands are considered to be eliminated concertedly from the central valence-shell expanded atom to afford a ligand *coupling product as illustrated by the following Scheme 1.*

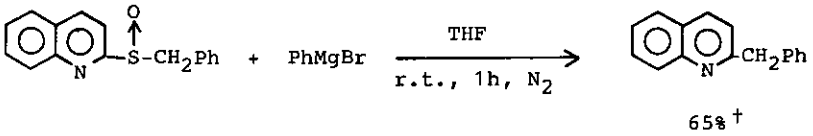


Scheme 1.

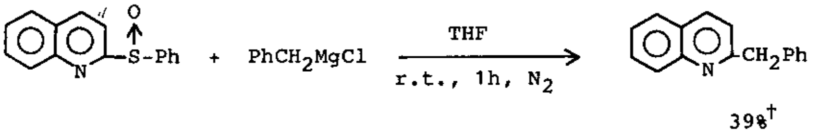
Earlier, it has been shown[4,5] that 2-benzylpyridine was afforded in the reaction of benzyl 2-pyridyl sulfoxide with phenylmagnesium bromide, while 2-phenylpyridine was the sole product in the reaction of t-butyl 2-pyridyl sulfoxide.

Similar experiments have now been carried out using the 2-quinolyl and the 2-pyrimidinyl sulfoxides instead of the 2-pyridyl derivative. Interestingly, phenyl group was found to couple predominantly with 2-pyrimidinyl group.

At first the reactions between benzyl 2-quinolyl sulfoxide with phenylmagnesium bromide and phenyl 2-quinolyl sulfoxide with benzylmagnesium chloride have been carried out as illustrated by the following Equations 1 and 2.



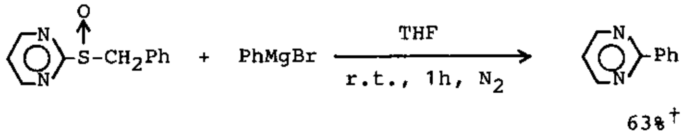
(1)



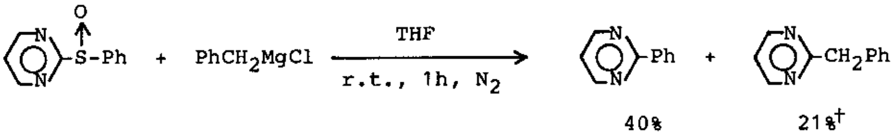
(2)

In these cases, like 2-pyridyl group, 2-quinolyl group has been found to couple predominantly with benzylic group in both reactions. No coupling with phenyl group was observed.

Then the same reaction with 2-pyrimidinyl group has been examined. Interestingly, 2-pyrimidinyl group tends to couple with phenyl group preferentially over benzyl group as shown in the following Equations 3 and 4.



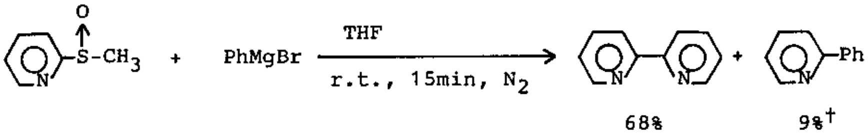
(3)



(4)

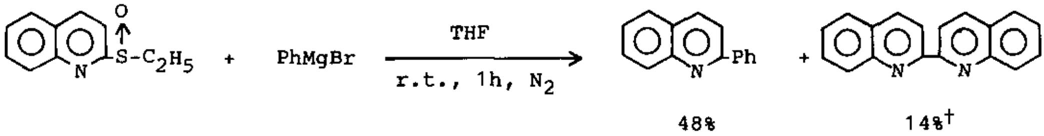
Only when phenyl 2-pyrimidinyl sulfoxide was treated with benzylmagnesium chloride, 2-benzylpyrimidine was obtained as the minor product.

We have reported[7)] that 2-pyridyl group was also coupled with phenyl group in the reaction of methyl 2-pyridyl sulfoxide with phenylmagnesium bromide, though the major product was 2,2'-bipyridyl.



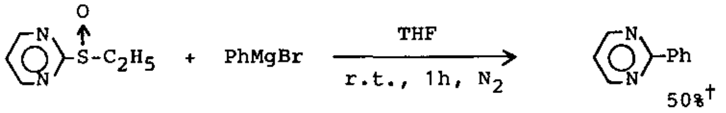
(5)

Then the reaction of 2-quinolyl methyl sulfoxide with phenylmagnesium bromide has been examined, in order to see how 2-quinolyl group would behave as compared to 2-pyrimidinyl group. In this reaction, phenyl group has been found to couple with 2-quinolyl group preferentially along with the formation of 2,2'-biquinolyl as the minor product, as shown by the Equation 6.



(6)

The reaction of ethyl 2-pyrimidinyl sulfoxide with phenylmagnesium bromide has now been examined.



(7)

As shown in the above Equation 7, the formation of 2,2'-bipyrimidinyl was not observed at all. Only 2-phenylpyrimidine can be obtained in this reaction.
Earlier, we have found that in the reaction between 2-pyridyl benzylic sulfoxides with other benzylic-magnesium halides, the incoming benzylic groups tend to couple preferentially over the benzylic groups of the starting sulfoxides. However, a slight change of electronic environment around the central sulfur atom in the incipient σ-sulfurane alters the trend. For example, in the reaction of p-benzenesulfonylphenyl p-chlorobenzyl sulfoxide with benzylmagnesium chloride, p-chlorobenzyl group was found to couple preferentially with benzenesulfonylphenyl group over benzyl group.9)
Pseudorotation seems to get more facile in the σ-sulfurane which is stabilized by substitution of an electron-withdrawing group. Probably, 2-pyrimidinyl group is electron-withdrawing enough to stabilize the incipient σ-sulfurane formed by the nucleophilic attack of benzylmagnesium chloride on 2-pyrimidinyl phenyl sulfoxide and the σ-sulfurane is just so long-lived enough that pseudorotation would place 2-pyrimidinyl group at an equatorial position and phenyl group at an axial coordinate ready for coupling.

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†) Yields are not optimized. The reaction was stopped within one hour, in order to avoid further reactions of the products with Grignard reagents. However, in most cases, unreacted sulfoxides were recoverd nearly quantitatively.

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