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PREPARATION OF 1-ALKENYL PHENYL SULFIDES BY THE NICKEL(II)-COMPLEXES CATALYZED COUPLING REACTION OF 3-METHOXY-1-PHENYLTHIO-1-PROPENE WITH GRIGNARD REAGENTS

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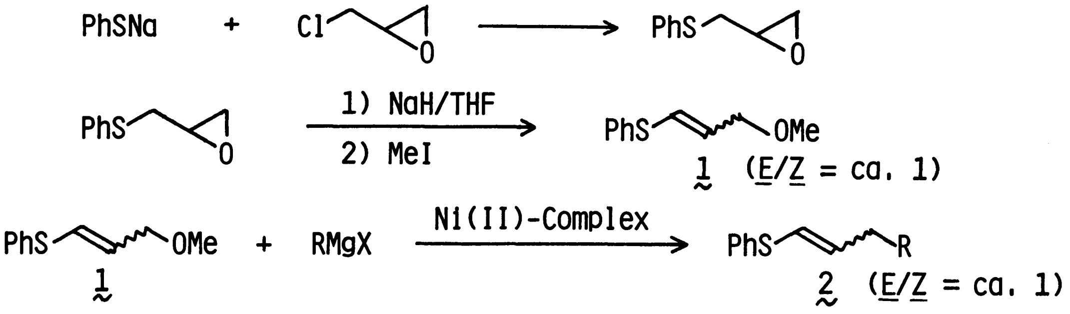
The reaction of 3-methoxy-1-phenylthio-1-propene with aryl and primary alkyl Grignard reagents in the presence of nickel(II)-phosphine complexes in benzene or toluene proceeded chemo- and regioselectively to give 1-alkenyl phenyl sulfides in high yields.

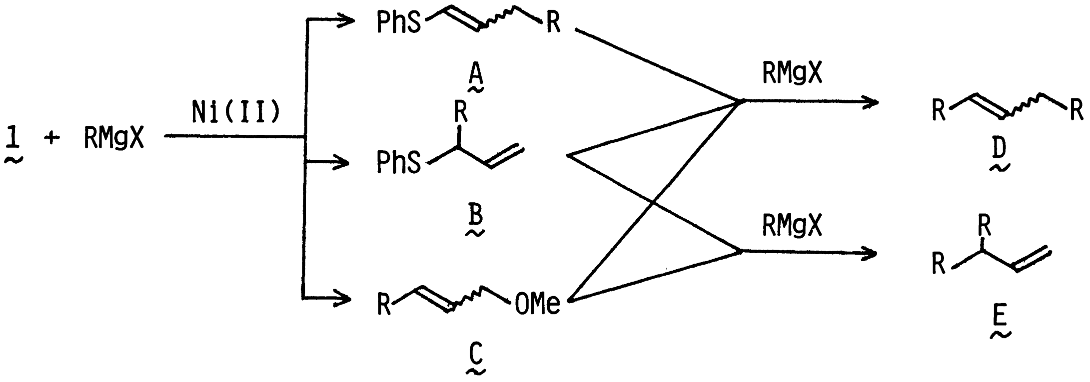
Recently, it was found in our laboratory that alkenyl, aryl,$^{1)}$ and allylic$^{2)}$ sulfides reacted with Grignard reagents in the presence of Ni(II)-phosphine complex to afford the corresponding coupling products in high yields. To study the coupling reactions further in detail, we needed a convenient preparative method of 1-alkenyl sulfides. On the other hand, it has been reported that allylic alcohols and ethers were capable of coupling with Grignard reagents in the presence of nickel catalysts.$^{3,4)}$ These reports suggested us that 3-methoxy-1-phenylthio-1-propene (1), which can be easily prepared from 1-chloro-2,3-epoxypropane and sodium benzenethiolate in high yield,$^{5)}$ might be used as an intermediate of 1-alkenyl sulfides.

In this communication, we describe a new synthetic method of 1-alkenyl sulfides by the coupling reaction of 1 with aryl or alkyl Grignard reagents in the presence of $NiCl_2(dppp)$ [dppp=$Ph_2PCH_2CH_2CH_2PPh_2$].



For the selective formation of 1-alkenyl sulfides, the coupling reaction must proceed chemo- and regioselectively, since it is possible to form 3 types of compounds, 1-alkenyl sulfide A, allylic sulfide B and allylic ether C, by the reaction with 1 molar equivalent of Grignard reagent. Moreover, these three compounds can also react with Grignard reagent to yield alkenes D and E.

Indeed, when the reaction of 1 with 3 equiv. of phenylmagnesium bromide in the presence of $NiCl_2(PPh_3)_2$ was carried out in refluxing ether for 8 h, 1,3-diphenylpropene, a type **D** compound, was obtained in 86% yield.



However, when the reaction using 1.5 equiv. of phenylmagnesium bromide was carried out at 0 °C for 1.5 h, 3-phenyl-1-phenylthio-1-propene, a type **A** compound, was obtained in 95% yield and none of type **B** and **C** compounds were detected in the reaction mixture (run 1 in Table 1).[4]

The results exhibited that the reaction is highly selective.[6] But reproducibility of the reaction was unsatisfactory, probably because a tarry material precipitated towards the end of the reaction. Then we examined the effect of solvent and catalyst and found that use of THF or benzene prevented the formation of the tarry material. But in THF the reaction was very slow (run 2), and benzene was found to be superior than the other solvent (run 3).

In the presence of $NiCl_2(dppp)$, the reaction also proceeded at 0 °C to afford the coupling product in 95% yield (run 4). Bis(2,4-pentanedionato)nickel or $PdCl_2(PPh_3)_2$ also gave the desired product, though the yields were poorer (runs 5 and 6).

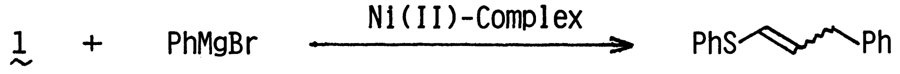


Table 1. Coupling reaction of **1** with phenylmagnesium bromide [a)]

Run	Catalyst	Solvent	Temp/°C	Time/h	Yield/%[b)]
1	$NiCl_2(PPh_3)_2$	Et_2O	0	1.5	95
2		THF	r.t.	24	41(50)
3		Benzene	0	2	95
4	$NiCl_2(dppp)$	Benzene	0	2.3	95
5	$Ni(acac)_2$	Benzene	r.t.	24	80
6	$PdCl_2(PPh_3)_2$	Benzene	0	6	37

a) The reaction was carried out as follows: To a mixture of **1** (1 mmol) and catalyst (3 mol%) in a solvent (5 cm^3) was added an ethereal solution of phenylmagnesium bromide (1.5 equiv. of ca. 1 mol dm^{-3}) and the resulted mixture was stirred.

b) The product (about 1:1 mixture of *E*,*Z* isomers) was isolated by silica gel TLC. The number of parentheses is the yield of recovered **1**.

Then, we applied the present coupling reaction for the preparation of various 1-alkenyl phenyl sulfides. The results were summarized in Table 2.

In the cases of primary alkyl Grignard reagents, other than methylmagnesium iodide, the better results were obtained when the reactions were carried out at -20 °C in toluene using $NiCl_2$(dppp) as a catalyst. The use of $NiCl_2(PPh_3)_2$ resulted in the formation of a reduction product, phenyl 1-propenyl sulfide.[7] In the case of secondary alkyl Grignard reagent, however, the coupling product was obtained in low yield even when $NiCl_2$(dppp) was employed as a catalyst.

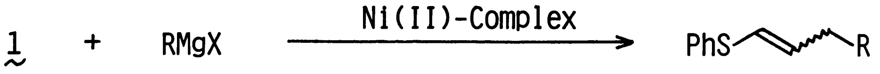
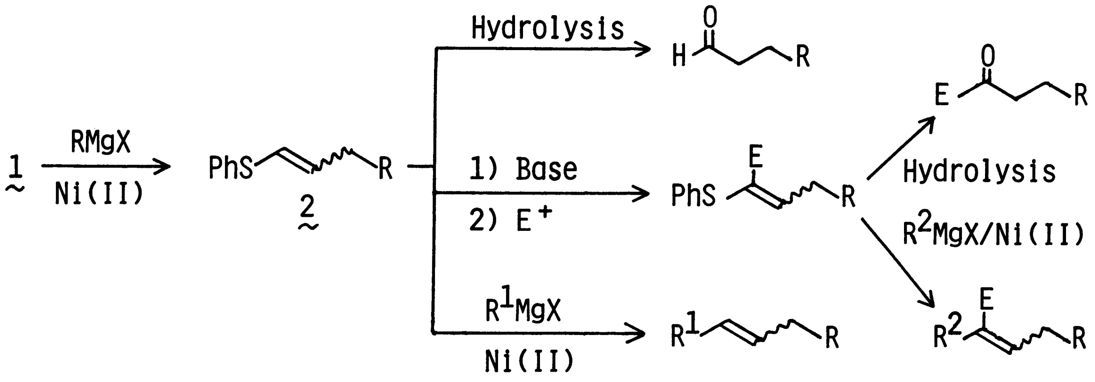


Table 2. Coupling reaction of **1** with alkyl grignard reagent [a]

Run	R in RMgX	Catalyst	Solvent	Temp/°C	Time/h	Yield/%[b]
1	Ph	$NiCl_2$(dppp)	Benzene	0	2	95
2	CH_3-	$NiCl_2$(dppp)	Benzene	r.t.	2.5	97
3		$NiCl_2(PPh_3)_2$	Benzene	r.t.	18	39(49)
4	C_4H_9-	$NiCl_2$(dppp)	Benzene	0	0.5	76
5		$NiCl_2$(dppp)	Toluene	-20	1.5	90
6		$NiCl_2(PPh_3)_2$	Toluene	-20	2	trace[c]
7	C_6H_{13}-	$NiCl_2$(dppp)	Toluene	-20	2	85
8	C_8H_{17}-	$NiCl_2$(dppp)	Toluene	-20	2	89
9	$Ph(CH_2)_3$-	$NiCl_2$(dppp)	Toluene	-20	3	95
10	c-C_6H_{11}-	$NiCl_2$(dppp)	Toluene	0	3	17[c]

a) In all cases, the **1**/RMgX/catalyst ratio 1/1.5/0.03 (mmol) was used.
b) The products (about 1:1 mixtures of E,Z isomers) were isolated by silica gel TLC and gave satisfactory NMR and IR spectra. The number of parentheses is the yield of recovered **1**.
c) All of **1** was consumed and phenyl 1-propenyl sulfide was a main product.[6]

Alkenyl sulfides are known to be useful intermediate in organic synthesis and can be converted into a variety of compounds.[10] Some representative transformation are shown in the following scheme. Therefore, it can be concluded that **1** can be regarded as a versatile three carbon building block in organic synthesis.



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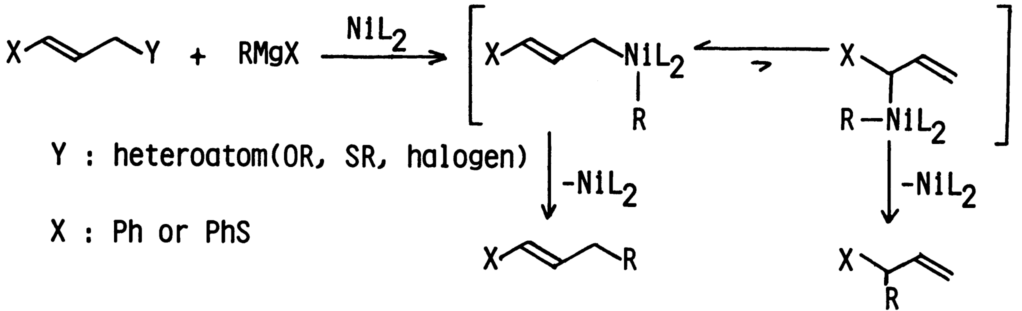
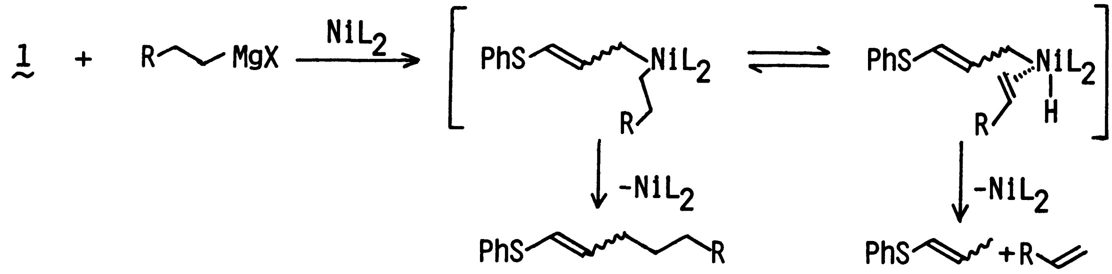
6) Felkin and coworkers[3)] reported the coupling reaction of allylic alcohols with Grignard reagents in the presence of $NiCl_2(PPh_3)_2$. In most cases, the reaction was not regioselective and both S_N and S_N'type reaction products were formed. But the reaction of cinnamyl alcohol with methyl magnesium bromide gave (E)-1-phenyl-1-butene selectively. We also observed the similar phenomena in the coupling reaction of allylic sulfides.[2)] On the basis of above results coupled with the present investigation, we assume that the conjugation between X (phenyl or phenylsulfenyl group) and double bond in allyl group may play an important role in exhibiting the regioselectivity.



7) In the $NiCl_2(PPh_3)_2$ catalyzed coupling reactions of unsaturated halides[8)] or sulfides[1,9)] with primary alkyl Grignard reagents having β-hydrogen, reduction products were often produced. By changing PPh_3 into dppp as a ligand of nickel, the reduction was considerably prevented. But, generally, sec- or tert-alkyl Grignard reagents gave the coupling products in poor yields even in the presence of $NiCl_2$(dppp).



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