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Ligand Exchange Reactions of Aryl Pyridyl Sulfoxides with Grignard Reagents: Convenient Preparation of 3- and 4-Pyridyl Grignard Reagents and Examination of the Leaving Abilities of Pyridyl Anions

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ABSTRACT

Aryl 3- and 4-pyridyl sulfoxides undergo ligand exchange in reactions with aryl Grignard reagents to generate 3- and 4-pyridyl Grignard reagents, which, upon treatment with aldehydes or ketones, give the corresponding addition products in moderate-to-good yields. The mechanism for the exchange reaction was investigated by treating optically active 3- and 4-pyridyl p-*tolyl sulfoxides with a phenyl Grignard reagent. Inversion of the configuration of the sulfur atom was the stereochemical result of the reactions. In the reactions of phenyl 2-pyridyl sulfoxide with Grignard reagents, the leaving ability of the 2-pyridyl group competes with that of the phenyl group. Both the experimental and MO calculated enthalpy values for deprotonation of α-, β-, and γ-protons of pyridine in the gas phase [1] are in accordance with the following order of the leaving abilities of aryl and pyridyl Grignard reagents: 4-PyMgBr > 3-PyMgBr >> PhMgBr > p-TolMgBr > 2-PyMgBr.*

INTRODUCTION

Sulfoxides react with organolithium and/or Grignard reagents to undergo either ligand exchange, ligand coupling, or both. In the reactions of alkyl aryl sulfoxides with alkyllithiums, only the aryl groups are displaced *via* in initial attack of alkyllithium on the sulfinyl sulfur atom with inversion of configuration. This result indicates that the ligand which gives a more stable carbanion leaves preferentially from the sulfur atom [2].

In general, the preparation of Grignard reagents of azaheterocycles requires a special technique, and it formerly gave unreproducible results [3]. Recently, we have found that methyl 2-pyridyl sulfoxide reacts with appropriate Grignard reagents to give the 2-pyridyl Grignard reagent (2-PyMgBr) as an intermediate [4]. We have now developed this exchange process into a convenient preparation of azaheteroaromatic Grignard reagents and found that 3- and 4-pyridyl Grignard reagents are generated by simple Grignard exchange reactions of the corresponding pyridyl sulfoxides. However, the 2-pyridyl Grignard reagent has not been successfully generated by this process.

pK_a Values of heterocycles such as thiophene, furan, and some *o*-substituted phenyl derivatives have been measured by treatment with lithium diisopropylamide (LDA) and lithium tetramethylpiperidide (LTMP) in THF [5]. The protons at the 2-

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Dedicated to Leopold Horner on the occasion of his eightieth birthday.

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and 5-positions in five membered heterocycles such as thiophene and furan are more acidic than those at the 3- and/or 4-positions, and, hence, thiophene and furan would give preferentially the corresponding 2- and 5-carbanions. On the other hand, the deprotonation of pyridine is non-regioselective, and the mode of reaction is changeable with the reaction conditions employed [6]. Recently, the enthalpies for the formation of isomeric pyridyl carbanions have been reported by AM-1 calculations or by measurement of the pK_a values in the gas phase [1]. The enthalpy for formation of the 2-pyridyl carbanion is higher than those of its isomers and, hence, the 2-pyridyl carbanion is more reactive than the 3- and 4-pyridyl analogs and similar to the phenyl carbanion. The higher enthalpy of 2-pyridyl carbanion formation is ascribed to the repulsion between the lone pair of electrons of the nitrogen atom and the carbanionic center at the 2-position. This article summarizes the formation of 3- and 4-pyridyl Grignard reagents and differences in the reactivities of 2-, 3-, and 4-pyridyl sulfoxides in the Grignard exchange processes.

RESULTS AND DISCUSSION

Preparation of Sulfoxides Bearing the Pyridine Ring

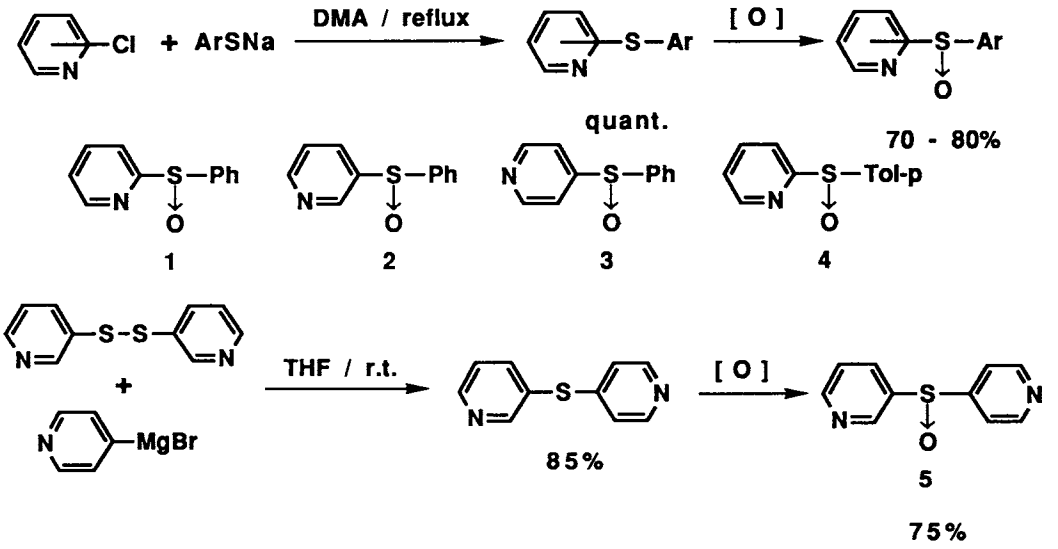
Pyridyl sulfoxides were prepared in good yields by the following procedures (Scheme 1): 1) halopyridines were treated with sodium thiolates in DMA, and the sulfides obtained were oxidized with H_2O_2 or *m*-chloroperbenzoic acid (*m*-CPBA); 2) pyridyl disulfides were treated with Grignard reagents in THF, and the sulfides obtained were oxidized by the same method.

Preparation and Reactions of 3- and 4-Pyridyl Grignard Reagents

Preparation of 3- and 4-pyridyl Grignard reagents was carried out by treating the appropriate aryl pyridyl sulfoxides with an equimolar amount of PhMgBr in THF. To each solution was added an equimolar amount of aldehyde or ketone in THF at room temperature. The products were separated and purified by column chromatography and preparative HPLC.

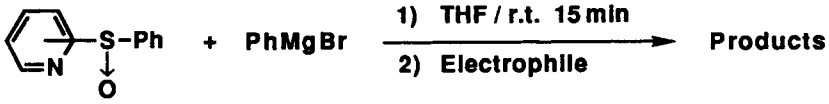
Alkyl or benzyl pyridyl sulfoxides cannot be recommended as starting materials since they gave the corresponding α-sulfinyl carbanions that then led to the formation of complex mixtures of products. Hence, 3- and 4-pyridyl phenyl sulfoxides were employed in the reactions in order to avoid such a disadvantage. On the other hand, phenyl 2-pyridyl sulfoxide (**1**) did not give the desired addition product but gave predominantly the coupling product 2,2′-bipyridyl in a substantial yield [4]. The results obtained from the reactions of 3- and 4-pyridyl Grignard reagents with carbonyl compounds are summarized in Table 1.

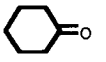
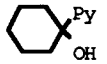
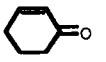
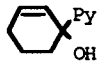
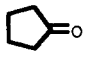
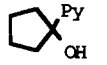
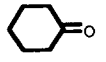
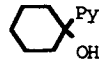
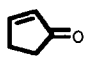
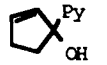
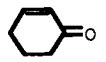
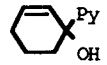
Inspection of these results demonstrates the following aspects of the reactions. Phenyl 3- and 4-pyridyl sulfoxides (**2**) and (**3**) react nicely with PhMgBr to generate the corresponding Grignard reagents that may then react in situ with aldehydes or ketones to afford the desired products in good-to-moderate yields together with diphenyl sulfoxide. However, the Grignard reagents did not react at all with esters, suggesting that 3- and 4-pyridyl Grignard reagents are weaker nucleophiles than a typical alkyl or phenyl Grignard reagent. On the other hand, the reaction of 3- or 4-pyridyl Grignard reagents with benzoic anhydride gave the corre-



SCHEME 1

TABLE 1 Preparation and Reactions of 3- and 4-Pyridyl Grignard Reagents



Sulfoxide	*Electrophile*	*Product*	*Yield (%)*
3-PySOPh	PhCHO	PyPhCHOH (**8**)	88
3-PySOPh	PhCOMe	PyPhMeCOH (**9**)	47
3-PySOPh		 (**10**)	54
3-PySOPh		 (**11**)	61
3-PySOPh	PhCH=CHCOPh	PyPhCH—CH_2COPh (**12**)	64
3-PySOPh	$(PhCO)_2O$	PyCOPh (**13**)	75
4-PySOPh	PhCHO	PyPhCHOH (**14**)	64
4-PySOPh	*p*-MeO-C_6H_4CHO	Py(*p*-MeO-C_6H_4)CHOH (**15**)	73
4-PySOPh	PhCH=CHCHO	PhCH=CHCH(OH)—Py (**16**)	60
4-PySOPh	PhCOMe (60 °C)	PyPhMeCOH (**17**)	26
4-PySOPh		 (**18**)	55
4-PySOPh		 (**19**)	38
4-PySOPh		 (**20**)	64
4-PySOPh		 (**21**)	66
4-PySOPh	PhCH=CHCOPh	PyPhCH—CH_2COPh (**22**)	60
4-PySOPh	$(PhCO)_2O$	PyCOPh (**23**)	70
4-PySOPh	$PhCO_2Et$ (60 °C)	No reaction[a]	

[a] Ethyl benzoate was recovered quantitatively.

sponding pyridyl phenyl ketones in good yields. Thus, this procedure can be employed as a convenient method for preparation of azaheteroaromatic ketones. The reactions of 3- and 4-pyridyl Grignard reagents with 2-cyclopentenone or 2-cyclohexenone afforded the 1,2-adducts, while with chalcone the 1,4-adducts were obtained. These results demonstrate that the whole reaction proceeds via an initial nucleophilic attack by PhMgBr on the sulfinyl sulfur atom to displace the heteroaryl group.

Preparation and Reactions of Optically Active 3- and 4-Pyridyl p-*Tolyl Sulfoxides*

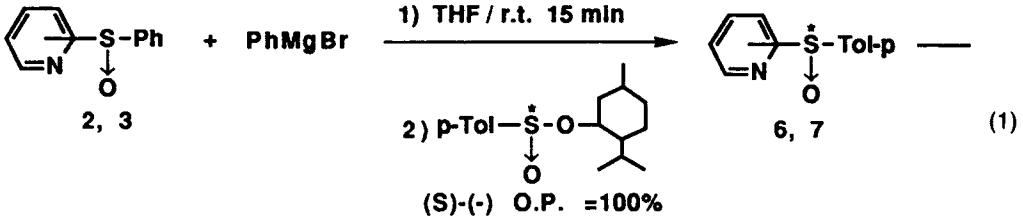
Stereochemical processes have been studied with both optically active 3- and 4-pyridyl *p*-tolyl sulfoxides (**6**) and (**7**) which were prepared by treating ℓ-menthyl *p*-tolylsulfinate with either 3- or 4-pyridyl Grignard reagent generated by the same procedure as described above. The absolute configurations of the sulfoxides (**6**) and (**7**) are determined to be S from their optical rotations and signs [7], provided the reactions of ℓ-menthyl *p*-tolylsulfinate with 3- and 4-pyridyl Grignard reagents proceed via an inversion process as in the Andersen's reaction of ℓ-menthyl *p*-tolylsulfinate with Grignard reagents [7]. The optical purities of **6** and **7** can be determined as ca. 100%. Then, the sulfoxides (**6**) and (**7**) were treated with PhMgBr, and subsequently with 1-naphthalenecarbaldehyde or chalcone to give phenyl *p*-tolyl sulfoxide and the addition products. The optical purities and the absolute configurations of the sulfoxides (**6**), (**7**), and phenyl *p*-tolyl sulfoxide are shown in Tables 2 and 3.

The results obtained from the four reactions shown in Equation 2 gave exclusively (S)-phenyl *p*-tolyl sulfoxide with 100% optical purity. Thus, these reactions of sulfoxides (**6**) and (**7**) with PhMgBr proceed with inversion of the configuration of the sulfinyl sulfur atom to give free 3- and 4-pyridyl Grignard reagents, as shown in Scheme II.

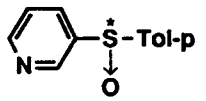
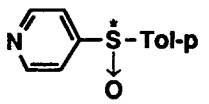
Reactions of 2-Pyridyl Sulfoxides with Grignard Reagents

Contrary to the reactions of aryl 3- and 4-pyridyl sulfoxides with Grignard reagents, the 2-pyridyl Grignard reagent was not obtained by treatment of the 2-pyridyl sulfoxide with Grignard reagents, but a mixture of many products was obtained [4] indicating that the reactivity of the 2-pyridyl group is quite different from that of 3- and 4-pyridyl groups.

TABLE 2 Preparation of Optically Active 3- and 4-Pyridyl Sulfoxides



(1)

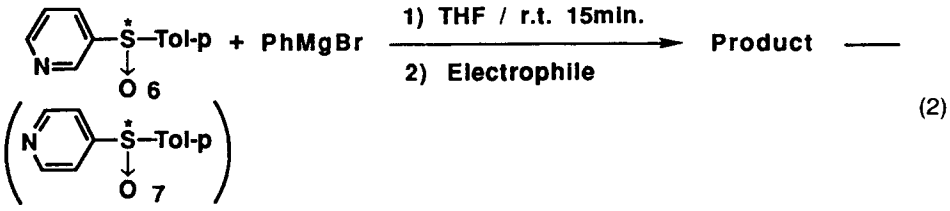
Sulfoxide		*Yield (%)*	$[\alpha]_D$ (c = 2, $CHCl_3$)	*e.e. (%)*
	(6)	80	+85°	100
	(7)	77	+134°	100

[a] The enantiometric excesses were determined by ^{1}H-NMR spectroscopy using Eu(tfc)$_3$ as chiral shift reagent.

The leaving ability of the 2-pyridyl group as compared to that of phenyl or *p*-tolyl was estimated by the reactions of phenyl 2-pyridyl sulfoxide with *p*-TolMgBr and of 2-pyridyl *p*-tolyl sulfoxide with PhMgBr. The products thus obtained are summarized in Table 4. When phenyl 2-pyridyl sulfoxide was treated with *p*-TolMgBr at −90 °C, the exchange reaction took place and PhMgBr was obtained roughly in 60% yield (sum of the yields of 2-pyridyl *p*-tolyl sulfoxide and di-*p*-tolyl sulfoxide), whereas the yield of 2-pyridyl Grignard reagent was only 8% (on the basis of the yield of phenyl *p*-tolyl sulfoxide). Thus, the ratio of the leaving ability of phenyl to 2-pyridyl is roughly calculated to be 7.5. These results suggest that the phenyl group is a better leaving group than 2-pyridyl (ca. 7.5 times) in this ligand exchange reaction. The reaction of 2-pyridyl *p*-tolyl sulfoxide with PhMgBr reveals that the leaving ability of the *p*-tolyl substituent is slightly better than that of 2-pyridyl (on the basis of comparison of the yield of phenyl 2-pyridyl sulfoxide (13%) and diphenyl sulfoxide (3%) to that of phenyl *p*-tolyl sulfoxide (11%)). The ratio of the leaving ability of the *p*-tolyl to the 2-pyridyl group should correspond to the product distribution, i.e., 16/11 = 1.5. The results are shown in Table 4.

The final product distributions obtained in the Grignard exchange reactions demonstrate that the

TABLE 3 Reactions of Optically Active Pyridyl Sulfoxides with PhMgBr

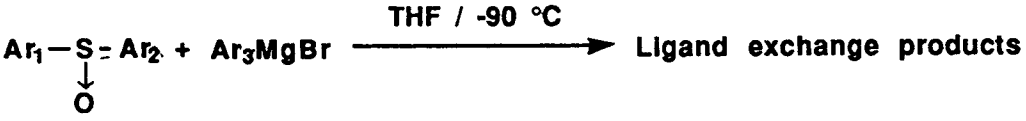


(2)

Sulfoxide	*Electrophile*	*Product Yield, $[\alpha]_D$ ($CHCl_3$)*	
		*(−)-PhS*OTol-p*[a]	*Adduct B*[b] *or C*[c]
6	1-NaphCHO	91%, −23°	B: 80%, 0°
7	1-NaphCHO	87%, −23°	B: 63%, 0°
6	PhCH=CHCOPh	90%, −23°	C: 64%, 0°
7	phCH=CHCOPh	88%, −24°	C: 57%, 0°

[a] (R)-(+)PhSOTol-*p*; $[\alpha]_D$ = + 22°.
[b] B, Py−CH(OH)−Naph-1.
[c] C, PyPhCH—CH_2COPh.

TABLE 4 Reactions of 2-Pyridyl Sulfoxides with Aryl Grignard Reagents

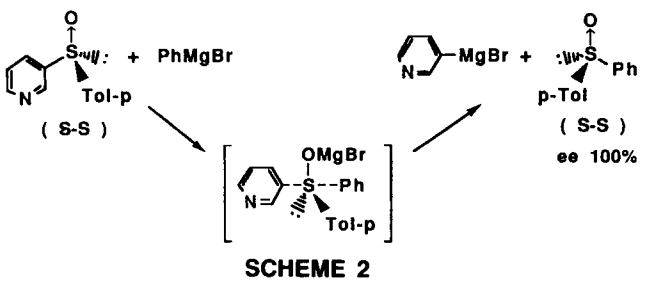


				Product Yield (%)				
Ar_1	AR_2	Ar_3	Time (h)	2-PySOPh	2-PySOLTol-p	$(Ph)_2SO$	PhSOLTol-p	$(p\text{-}Tol)_2SO$
2-Py	Ph	p-Tol	2	14	55	1	8	5
2-Py	p-Tol	Ph	10	13	42	3	11	3
Ph	p-Tol	2-Py [8]	10	No reaction*				

* No reaction even at −30 °C.

leaving ability among the three arylic ligands should be in the following order: Ph > *p*-Tol > 2-Py at −90 °C. At a low temperature, ligand exchange took place mainly as described above and ligand coupling products were obtained in low yields. However, the coupling between 2-pyridyl and phenyl or *p*-tolyl groups took place with the elevation of temperature to give 2-phenylpyridine or 2-(*p*-tolyl)pyridine. Furthermore, the 2-pyridyl Grignard reagent generated reacts with 2-pyridyl sulfoxides to give 2,2′-bipyridyl as the main product. The results of the coupling reactions are given in Table 5.

Furthermore, in order to study the stereochemistry of the ligand exchange process between 2-pyridyl aryl sulfoxide and aryl Grignard reagents, phenyl 2- (3-substituted) pyridyl sulfoxide (**1a**) was prepared as shown in Scheme 3 [9]. After the usual work-up, the two diastereoisomers of the alcohol (**1a**), $\mathbf{1a_1}$ (less polar isomer) and $\mathbf{1a_2}$ (more polar isomer) were separated into each isomer ((R_sR_c, S_sS_c) or (R_sS_c, S_sR_c)) by column chromatography. Their absolute configurations have not been determined. They were converted to the corresponding methyl ethers ($\mathbf{1a_{1'}}$) and ($\mathbf{1a_{2'}}$), respectively. One diastereoisomer ($\mathbf{1a_{1'}}$) was treated with *p*-TolMgBr as shown in Scheme 3, affording only one diastereoisomeric sulfoxide ($\mathbf{2a_{2'}}$) and recovered $\mathbf{1a_{1'}}$. On the basis of the ^{1}H-NMR spectrum the chemical shifts of the methyl groups of $\mathbf{2a_{2'}}$ (δ1.81 and 2.91 ppm) are nearly consistent with those of $\mathbf{1a_{2'}}$ (δ 1.82 and 2.89 ppm). This result indicates that the ligand exchange of the phenyl group by the *p*-tolyl group in the reaction



SCHEME 2

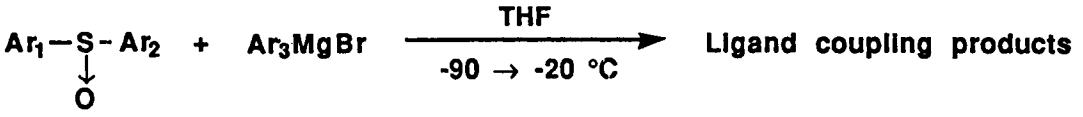
of 2-pyridyl aryl sulfoxide with the appropriate Grignard reagent takes place via a complete inversion of the configuration of the sulfinyl sulfur atom as well as the Grignard exchange reactions of 3- and 4-pyridyl phenyl sulfoxides. In a separate experiment, between optically active 2-quinolylphenylethyl sulfoxide and a suitable methyl Grignard reagent, ligand exchange was shown to proceed via inversion of configuration of the sulfinyl sulfur atom with retention of the configuration of the 2-phenyl-ethyl group [10], as will be reported later.

Comparison of the Stabilities of Pyridyl Carbanions

Recently, the enthalpies of deprotonation (DPE) at the different positions in pyridine in the gas phase as well as by calculation (AM-1 method) [1] (Table 6) have been reported by Mautner et al. [1b]. The 2-pyridyl carbanion should be as stable as the phenyl carbanion if the repulsion energy value between the lone pair electrons on the nitrogen atom of the pyridine ring and the carbanionic center at the 2-position is estimated to be about 10 kcal/mol [1]. The enthalpies of deprotonation to give the 3- and 4-pyridyl carbanions are about 5–7 kcal/mol smaller than those to give phenyl and 2-pyridyl carbanions demonstrating that 3- and 4-pyridyl carbanions are more stable and, hence, have a better leaving ability than phenyl and 2-pyridyl carbanions.

The difference in the leaving ability between 3- and 4-pyridyl carbanions in the intramolecular Grignard exchange reaction was determined by treatment of 3-pyridyl 4-pyridyl sulfoxide with less than one equivalent of *p*-TolMgBr. Both 3-pyridyl *p*-tolyl and 4-pyridyl *p*-tolyl sulfoxides were obtained in 61% yield in the ratio of 1.24:1 along with the recovered starting sulfoxide. This clearly demonstrates that the 4-pyridyl group has a better leaving ability than the 3-pyridyl group as shown in Scheme 4.

TABLE 5 Ligand Coupling Reaction of Aryl 2-Pyridyl Sulfoxides with Grignard Reagents



			Yield (%)		
Ar_1	Ar_2	Ar_3	2-Py-Ph	2-Py-Tol-p	2-Py-Py-2
2-Py	Ph	*p*-Tol	7	6	30
2-Py	*p*-Tol	Ph	12	3	16

Furthermore, the ratio of the remaining unreacted starting materials obtained in the intermolecular competitive ligand exchange reaction using an equimolar mixture of 3- and 4-pyridyl phenyl sulfoxides with 0.3 mol of *p*-TolMgBr indicates that the 4-pyridyl derivative reacts faster than the 3-pyridyl derivative as shown in Scheme 5.

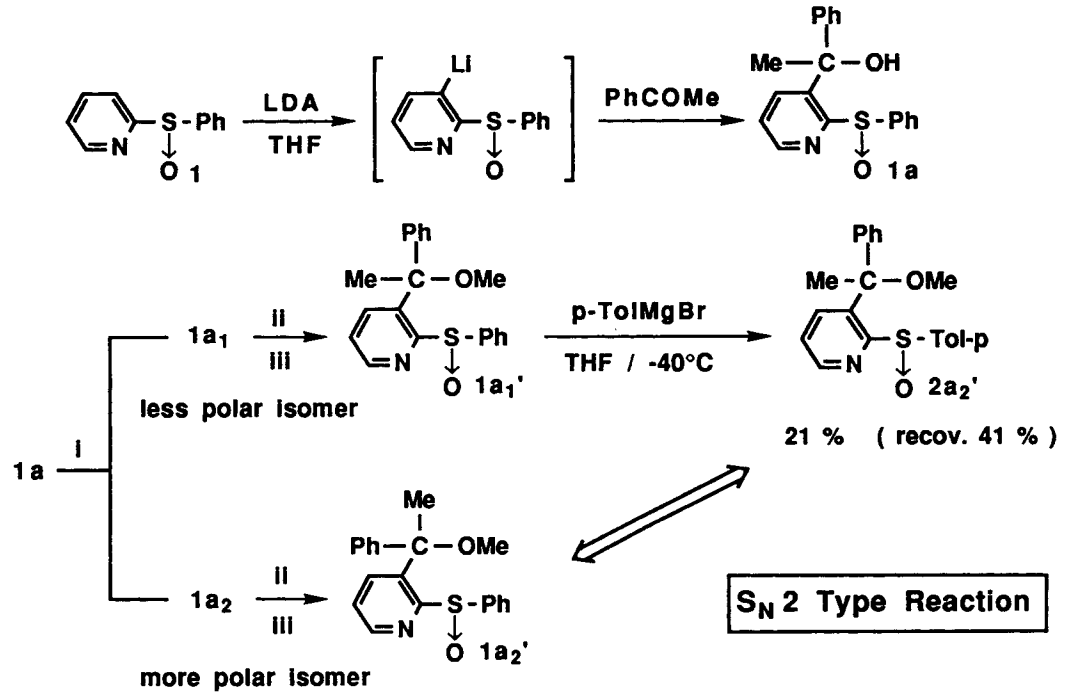
On the basis of these results, it is concluded that the order of the leaving ability of pyridyl and aryl groups in the substitution reactions carried out at temperatures below −78 °C on the sulfinyl sulfur atom is as shown below.

4-PyMgBr > 3-PyMgBr >> PhMgBr
> *p*-TolMgBr > 2-PyMgBr

This leaving ability should have the same trend as the sequence of the apicophilicities of the corresponding ligands.

EXPERIMENTAL

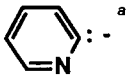
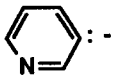
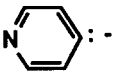
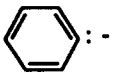
All melting points were uncorrected and were taken on a Yanaco micro-melting point apparatus. NMR spectra were obtained on a HITACHI R-600, a JEOL LMN-MH-100, a JEOL EX-270, or a BRUKER A-500 FT-NMR spectrometer in $CDCl_3$ solution using tetramethylsilane as internal standard. IR spectra were obtained on a JASCO A-3 spectrometer. Mass spectra were provided with use of the gas chromatographic method and were taken with a HI-



I) Separation by column chromatography; II) NaH/THF, 0 °C; III) MeI.

SCHEME 3

TABLE 6 Deprotonation Enthalpies (DPE) of Pyridine

Molecule	Anion	DPE (kcal/mol) Expetl	AM1	corrected AM1
	 [a]		389.9	400.6
			395.7	
		391.0	394.8	
		400.7	402.6	

[a] Lone–pair–lone–pair repulsion is estimated to be ca. 10 kcal/mol.

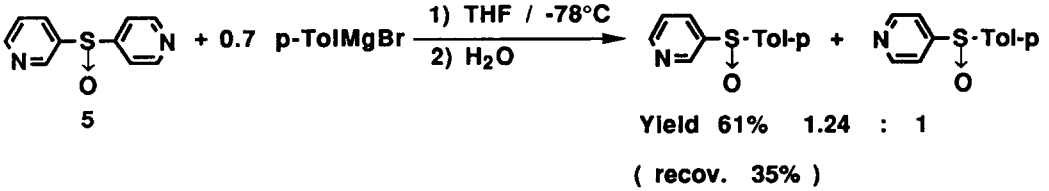
TACHI RMU-6MG spectrometer. Elemental analyses were carried out by the Analytical Center at Tsukuba University. GLC and HPLC analyses were performed on a HITACHI 163 or a 263 gas chromatograph using 10% OV-1 on chromosorb W (80–100 mesh) and a HITACHI R-655 model liquid chromatograph equipped with an ODS or a DAISEL OB column. NIHON BUNSEKI KOGYO LC-9 was used for preparative LC. All the reactions were monitored by chromatography, namely, TLC (Merck Kieselgel 60-GF_{254} or aluminum oxide 60-GF_{254}), GLC, and HPLC. Silica gel used for column chromatography was Wako-gel C-200. Alumina used for column chromatography was Wako activated aluminum oxide, about 200 mesh.

All reagents were obtained from Wako Pure Chemical Industries Ltd., Tokyo Kasei Co., or Aldrich Chemical Co. The reagents used and solvents were further purified by general methods.

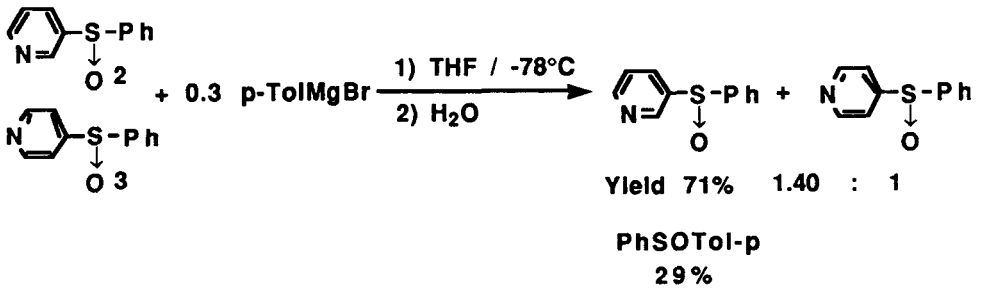
All sulfoxides were prepared from the corresponding sulfides that were obtained by the reactions of pyridyl halides (PyCl) with sodium thiolates (ArSNa) in DMA or pyridyl disulfides (PySSPy) with Grignard reagents (ArMgBr) in THF. The sulfides obtained were oxidized with H_2O_2 or *m*-CPBA. A typical experimental procedure is as follows.

Preparation of Phenyl 2-Pyridyl Sulfoxide (1)

To a stirred solution of NaOEt (0.14 mol) in 50 ml of EtOH was added dropwise thiophenol (15.4 g, 0.15 mol) dissolved in 30 mL dimethylacetamide (DMA). To this solution 20.0 g of 2-bromopyridine (0.127 mol) in 30 mL DMA was added with stirring at room temperature. The solution was refluxed overnight and DMA was removed by distillation. Phenyl 2-pyridyl sulfide was purified by distillation under vacuum, bp. 121 °C/3 mmHg. Yield was 19.2g (84%). The sulfide (5.2 g, 29 mmol) was dissolved in 40 mL of acetic acid and was oxidized with 3 mL of 30% H_2O_2 overnight at 40 °C with stirring. After the work-up, the crude sulfoxide was purified by column chromatography by using Alumina and CH_2Cl_2 as an eluent. Yield 4.0 g (70%), mp 69–70 °C; IR(KBr) 1048 cm^{-1}; ^{1}H-NMR($CDCl_3$, 270 MHz) δ 7.28(ddd, 1H, 5-Py—H, J = 1.0, 4.6, 7.6 Hz), 7.41–7.52(m, 3H, Ph—H), 7.77–7.83(m, 2H, Ph—H), 7.86(ddd, 1H, 4-Py—H, J = 1.0, 7.6, 7.8 Hz), 8.04(dd, 1H, 3-py—H, J = 1.0, 7.8 Hz), 8.54(dd, 1H, 6-Py—H, J = 1.0, 4.6 Hz); ^{13}C-NMR($CDCl_3$) δ 118.3, 124.6, 124.8, 129.1, 131.0, 138.0, 143.8, 150.3, 165.5; MS m/z 203 (M+), 187 (M±O). Anal. calcd. for $C_{11}H_9NOS$: C, 65.00; H, 4.43; N, 6.90. Found: C, 64.83; H, 4.48; N, 6.88.



SCHEME 4



SCHEME 5

Similarly, phenyl 3-pyridyl (**2**), phenyl 4-pyridyl (**3**), and 2-pyridyl *p*-tolyl (**4**) sulfoxides were prepared by oxidation of the corresponding sulfides.

(**2**): Yield 74%; mp 55–56 °C; IR(KBr) 1048 cm^{-1}; ^{1}H-NMR(270 MHz) ($CDCl_3$) δ 7.37(dd, 1H, 5-Py—H, J = 4.6, 8.1 Hz), 7.44–7.48(m, 3H, Ph—H), 7.62–7.66(m, 2H, Ph—H), 7.95(ddd, 1H, 4-Py—H, J = 1.6, 1.6, 8.1 Hz), 8.64(dd, 1H, 6-Py—H, J = 1.6, 4.6 Hz), 8.77(d, 1H, 2-Py—H, J = 1.6 Hz); ^{13}C-NMR($CDCl_3$) δ 124.1, 124.5, 129.5, 131.5, 132.3, 142.3, 144.5, 146.3, 151.8. Anal. calcd for $C_{11}H_9NOS$: C, 65.02; H, 4.43; N, 6.89. Found: C, 64.94; H, 4.47; N, 6.88.

(**3**): Yield 77%; mp 86–87 °C; IR(KBr) 1048 cm^{-1}; ^{1}H-NMR(270 MHz) ($CDCl_3$) δ 7.44–7.55(m, 3H, Ph—H), 7.58(dd, 2H, 3,5-Py—H, J = 1.6, 4.6 Hz), 7.63–7.70(m, 2H, Ph—H), 8.68 (dd, 2H, 2.6-Py—H, J = 1.6, 4.6 Hz); ^{13}C-NMR($CDCl_3$) δ 118.3, 124.9, 129.7, 132.0, 144.2, 150.5, 155.6. Anal. calcd for $C_{11}H_9NOS$: C, 65.02; H, 4.43; N, 6.89. Found: C, 64.79; H, 4.46; N, 6.87.

(**4**): Yield 80%; mp 82–83 °C; IR(KBr) 1046 cm^{-1}; ^{1}H-NMR($CDCl_3$, 270 MHz) δ 2.34(s, 3H, CH_3), 7.25(d, 2H, Ar—H, J = 8.0 Hz), 7.27(ddd, 1H, 5-Py—H, J = 1.0 , 4.9, 7.6 Hz), 7.67(d, 2H, Ar—H, J = 8.0 Hz), 7.87(ddd, 1H, 4-Py—H, J = 1.0, 7.6, 7.8 Hz), 8.05(dd, 1H, 3-py—H, J = 1.0, 7.8 Hz), 8.54(dd, 1H, 6-Py—H, J = 1.0, 4.9 Hz); ^{13}C-NMR($CDCl_3$) δ 21.3, 118.3, 124.5, 125.0, 129.8, 138.0, 140.7, 141.3, 149.7, 165.6; MS m/z 217 (M+), 201 (M±O). Anal. calcd for $C_{12}H_{11}NOS$: C, 66.36; H, 5.07; N, 6.45. Found: C, 66.29; H, 5.13; N, 6.46.

Preparation of 3-Pyridyl 4-Pyridyl Sulfoxide (**5**)

The 4-Pyridyl Grignard reagent (4-PyMgBr) was prepared as follows: to a THF solution (60 mL) containing phenyl 4-pyridyl sulfoxide (1.29 g, 6.4 mmol) was added the *p*-tolyl Grignard reagent (10 mL THF solution, 7.0 mmol) with stirring at room temperature for 15 min. Subsequently, 3-pyridyl disulfide (1.08 g, 4.9 mmol) dissolved in 5 mL THF was added to the solution by a syringe and the reaction was allowed to proceed at room temperature for 30 min. After the reaction, 5 mL of water was added and the products were extracted with 30 mL of diethyl ether three times. The ether layers were combined and washed with 10 mL of water. After having been dried over $MgSO_4$, the ether was removed and the crude pyridyl sulfide was purified by silica gel column chromatography using $CHCl_3$ as an eluent (0.79 g, yield 85%). To the sulfide (0.79 g, 4.2 mmol) dissolved in 50 mL of CH_2Cl_2 a solution of *m*-CPBA (0.81 g, 4.2 mmol) dissolved in 20 mL of CH_2Cl_2 was added at −20 °C and the solution was stirred for 2 hr. After the reaction, NH_3 gas was passed through the solution and the salt obtained was removed. The CH_2Cl_2 layer was washed with 10 mL of water and dried over $MgSO_4$. After removal of the solvent, the crude sulfoxide was purified by alumina column chromatography using $CHCl_3$ as an eluent. 3-Pyridyl 4-pyridyl sulfoxide **5** (0.64 g) was obtained in 75% yield; mp, 121–123 °C: IR(KBr) 1055 cm^{-1}; ^{1}H-NMR(500MHz) ($CDCl_3$) δ 7.34(dd, 1H, 5-Py—H, J = 4.8, 7.8 Hz), 7.58(dd, 2H, 3′,5′-Py—H, J = 1.2, 4.2 Hz), 8.01(ddd, 1H, 4-Py—H, J = 1.2, 1.2, 7.8 Hz), 8.67(s, 1H, 2-Py—H), 8.71(dd, 2H, 2′,6′-Py—H, J = 1.2, 4.2 Hz), 8.90(dd, 1H, 6-Py—H, J = 1.2, 4.2 Hz); Anal. calcd for $C_{10}H_8N_2OS$: C, 58.82; H, 3.92; N, 13.73; Found: C, 58.77; H, 3.99; N, 13.57.

Preparation of 3-Pyridyl and 4-Pyridyl Grignard Reagents (3-PyMgBr and 4-PyMgBr)

Reaction of Phenyl 3-Pyridyl Sulfoxide with PhMgBr and then with Benzaldehyde. Phenyl Grignard reagent was prepared from 1.1 mL of bromobenzene (1.0 mmol) and 300 mg of magnesium in 19 mL THF. To phenyl 3-pyridyl sulfoxide (100 mg, 0.49 mmol) dissolved in 15 mL THF, PhMgBr (1.1 mL, 0.54 mmol) was added dropwise with stirring at room temperature for 15 min. Then, benzaldehyde (57 μL, 0.54 mmol) was added to the solution and the stirring was continued for 1 h. After the reaction, 3 mL of water was added and the solution was neutralized with aqueous HCl solution. After extraction of the products with CH_2Cl_2, the organic layer was separated and dried over $MgSO_4$. After removing CH_2Cl_2, the residue was subjected to alumina column chromatography using $CHCl_3$ as an eluent. Diphenyl sulfoxide (94 mg, 95%), mp 70–71 °C (Lit. [11] 71 °C) and phenyl 3-pyridyl-

methyl alcohol (**8**) (80 mg, 88%), mp 55–56 °C (Lit. [12] 56 °C) were obtained. The product was identified by ^{1}H-NMR($CDCl_3$): δ 5.72(s, 1H, CH), 6.98–7.49(m, 6H, 5-Py—H, Ph—H), 7.51–7.80(m, 1H, 4-Py—H), 8.08–8.43(m, 2H, 2,6-Py—H).

Similarly, 3- and 4-pyridyl Grignard reagents were treated with several other electrophiles. The products thus obtained were identified by ^{1}H-NMR, IR, and elemental analyses.

9: mp 134 °C (Lit. [12] 135 °C); ^{1}H-NMR($CDCl_3$) δ 2.80(s, 3H, CH_3), 4.11(b, 1H, OH), 7.01–7.89(m, 7H, 4,5-Py—H, Ph—H), 8.30–8.61(m, 2H, 2,6-Py—H).

10: liq., ^{1}H-NMR($CDCl_3$) δ 1.16–2.30(m, 10H, CH_2), 3.59(b, 1H, OH), 7.04–7.41(m, 1H, 5-Py—H), 7.68–8.00(m, 1H, 4-Py—H), 8.24–8.48(m, 1H, 2-Py—H), 8.56–8.77(m, 1H, 6-Py—H); Ms m/z 177 (M^+).

11: liq., ^{1}H-NMR($CDCl_3$) δ 1.19–2.56(m, 6H, CH_2), 3.57(b, 1H, OH), 5.74(d, 1H, 2-H, J = 10.2 Hz), 6.07(ABX, 1H, 2-H, J = 10.2, 3.0 Hz), 7.06–7.42(m, 1H, 5-Py—H), 7.69–8.03(m, 1H, 4-Py—H), 8.26–8.82(m, 2H, 2,6-Py—H); Ms m/z 175 (M^+).

12: liq., IR($CHCl_3$) 1680 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 3.73(d, 2H, CH_2, J = 7.2 Hz), 4.84(t, 1H, CH, J = 7.2 Hz), 7.03–8.06(m, 12H, 4,5-Py—H, Ph—H), 8.08–8.88(m, 2H, 2,6-Py—H); MS m/z 287 (M^+).

13: mp 39 °C (Lit. [13] 40 °C); IR(KBr) 1660 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 7.30–7.90(m, 6H, 5-Py—H, Ph—H), 8.10(ddd, 1H, 4-Py—H, J = 1.2, 1.2, 7.8 Hz), 8.83(dd, 1H, 6-Py—H, J = 1.2, 4.8 Hz), 9.03(d, 1H, 2-Py—H, J = 1.2 Hz).

14: mp 124 °C (Lit. [12] 125 °C); ^{1}H-NMR($CDCl_3$) δ 3.32(b, 1H, OH), 5.76(s, 1H, CH), 7.15–7.45(m, 7H, 3,5-Py—H, Ph—H), 8.25–8.55(m, 2H, 2,6-Py—H).

15: mp 141 °C; ^{1}H-NMR($CDCl_3$) δ 1.80(b, 1H, OH), 3.77(s, 3H, CH_3), 5.71(s, 1H, CH), 6.71–7.41(m, 6H, 3,5-Py—H, Ar—H), 8.30–8.40(m, 2H, 2,6-Py—H).

16: liq., ^{1}H-NMR($CDCl_3$) δ 4.27(b, 1H, OH), 5.38(d, 1H, CH, J = 6.4 Hz), 6.28(dd, 1H, C=CH, J = 6.4, 16.4 Hz), 6.75(d, 1H, C=CH, J = 16.4 Hz), 7.15–7.54(m, 7H, 3,5-Py—H, Ar—H), 8.38–8.65(m, 2H, 2,6-Py—H); MS m/z 211 (M^+).

17: mp, 145–147 °C (Lit. [12] 146 °C); ^{1}H-NMR($CDCl_3$) δ 2.82(s, 3H, CH_3), 4.23(b, 1H, OH), 7.11–7.43(m, 7H, 3,5-Py—H, Ar—H), 8.23–8.54(m, 2H, 2,6-Py—H).

18: mp 84 °C; ^{1}H-NMR($CDCl_3$) δ 1.02–2.43(m, 8H, CH_2), 3.07(b, 1H, OH), 7.12–7.61(m, 2H, 3,5-Py—H), 8.13–8.66(m, 2H, 2,6-Py—H). Anal. calcd for $C_{10}H_{13}NO$: C, 73.58; H, 8.02; N, 8.58. Found: C, 73.32; H, 8.00; N, 8.40.

19: mp 150 °C; ^{1}H-NMR($CDCl_3$) δ 1.10–2.03(m, 10H, CH_2), 2.70(b, 1H, OH), 7.27–7.53(m, 2H, 3,5-Py—H), 8.37–8.61(m, 2H, 2,6-Py—H).

20: mp, 124 °C; ^{1}H-NMR($CDCl_3$) δ 1.65–3.21(m, 5H, CH_2, OH), 5.78(d, 1H, 2-H, J = 5.6 Hz), 6.16(ABX, 1H, 1-H, J = 5.6, 1.6 Hz), 7.21–7.48(m, 2H, 3,5-Py—H), 8.26–8.60(m, 2H, 2,6-Py—H).

21: mp 113 °C; ^{1}H-NMR($CDCl_3$) δ 1.54–2.35(m, 6H, CH_2), 3.50(b, 1H, OH), 5.70(d, 1H, 2-H, J = 9.6 Hz), 6.08(ABX, 1H, 1-H, J = 9.6, 3.0 Hz), 7.18–7.52(m, 2H, 3,5-Py—H), 8.27–8.72(m, 2H, 2,6-Py—H). Anal. calcd for $C_{11}H_{13}NO$: C, 75.39; H, 7.47; N, 7.99. Found: C, 75.81; H, 7.48; N, 7.47.

22: mp 94 °C; IR($CHCl_3$) 1680 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 3.72(d, 2H, CH_2, J = 7.2 Hz), 4.81(t, 1H, CH, J = 7.2 Hz), 7.08–8.05(m, 12H, 3,5-Py—H, Ph—H), 8.27–8.72(m, 2H, 2,6-Py—H). Anal. calcd for $C_{20}H_{17}NO$: C, 83.59; H, 5.96; N, 4.87. Found: C, 83.33; H, 6.00; N, 4.84.

23: mp 71 °C (Lit. [14] 72 °C); IR(KBr) 1650 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 7.35–7.85(m, 7H, 3,5-Py—H, Ph—H), 8.74(dd, 2H, 2,6-Py—H, J = 1.2, 4.8 Hz).

*Preparation of (S)-(+) 3-Pyridyl p-Tolyl Sulfoxide (**6**)*

Phenyl Grignard reagent (0.75 M solution) was prepared as described above. To the sulfoxide (**2**) (1.2 g, 5.9 mmol) dissolved in 12 mL THF was added PhMgBr solution (8.7 mL, 6.5 mmol) dropwise with stirring for 15 min at room temperature. Then, (S)-(+) ℓ-menthyl p-toly/sulfinate (1.9 g, 6.5 mmol) in 10 mL THF was added dropwise and the reaction mixture was stirred for 1 h at room temperature. After the reaction, water (1 mL) was added and the solution was neutralized with aqueous HCl solution. The aqueous solution was extracted with CH_2Cl_2 and the organic layer was dried over $MgSO_4$. After removal of the solvent, the residue was separated by silica gel column chromatography using $CHCl_3$ as an eluent. The solid was recrystallized from benzene-hexane (1:1). (S)-(+)-3-Pyridyl p-tolyl sulfoxide (1.0 g) was obtained in 80% yield. Enantiomeric excess, determined by using chiral shift reagent [Eu(tfc)$_3$], was found to be ca. 100%; mp 68–69 °C; IR(KBr) 1050 cm^{-1}; ^{1}H-NMR(270 MHz) ($CDCl_3$) δ 2.36(s, 3H, CH_3), 7.28(d, 2H, Ar—H, J = 8.1 Hz), 7.38(dd, 1H, 5-Py—H, J = 4.7, 7.9 Hz), 7.53(d, 2H, Ar—H, J = 8.1 Hz), 7.96(ddd, 1H, 4-Py—H, J = 1.4, 2.2, 8.1 Hz), 8.64(dd, 1H, 6-Py—H, J = 1.4, 4.7 Hz), 8.75(d, 1H, 2-Py—H, J = 2.2 Hz); ^{13}C-NMR($CDCl_3$) δ 21.3, 124.1, 124.8, 130.2, 132.3, 141.3, 142.2, 142.4, 146.4, 151.7. Anal. calcd for $C_{12}H_{11}NOS$: C, 66.36; H, 5.07; N, 6.45. Found: C, 66.23; H, 5.14; N, 6.43; $[\alpha]_D$ = +85° (c = 2.0, $CHCl_3$).

Similarly, (S)-(+) 4-pyridyl p-tolyl sulfoxide (**7**) was prepared in 77% yield; mp 112–113 °C; IR(KBr) 1048 cm^{-1}; ^{1}H-NMR(270 MHz) ($CDCl_3$) IR(KBr) 1048 cm^{-1}; ^{1}H-NMR(270 MHz) ($CDCl_3$) δ 2.36(s, 3H, CH_3), 7.27(d, 2H, Ar—H, J = 7.8 Hz), 7.50(dd, 2H, 3,5-Py—H, J = 1.6, 4.6 Hz), 7.54(d, 2H, Ar—H, J = 7.8 Hz), 8.68(dd, 2H, 2,6-Py—H, J = 1.6, 4.6 Hz); ^{13}C-NMR($CDCl_3$) δ 21.5, 118.3, 125.3, 130.4, 141.0, 142.7, 150.4, 155.9. Anal. calcd for $C_{12}H_{11}NOS$: C, 66.36; H, 5.07; N, 6.45. Found: C, 66.35; H, 5.09: N, 6.39; $[\alpha]_D$ = +134° (c = 2.0, $CHCl_3$), ee 100%.

Reaction of Optically Active 3-Pyridyl p-*Tolyl Sulfoxide* (**6**) *with PhMgBr*

To (S)-(+) sulfoxide (**6**) (70 mg, 0.33 mmol) dissolved in 15 mL THF were added PhMgBr (0.66 mL, 0.33 mmol) and subsequently 1-naphthalenecarbaldehyde (66 mg, 0.42 mmol). After the usual work-up procedure, (S)-(−) phenyl *p*-tolyl sulfoxide (62 mg, 91% yield), mp 47–48 °C (Lit. [7] 49 °C) and 1-naphthyl 3-pyridylmethyl alcohol (61 mg, 80% yield) were obtained. Optical rotations of these products were measured in $CHCl_3$ giving $[\alpha]_D = -23°$ (c = 1.24, for phenyl *p*-tolyl sulfoxide) and 0° (1-naphthyl 3-pyridylmethyl alcohol). The optical rotation of (R)-(+) phenyl *p*-tolyl sulfoxide was $[\alpha]_D = +23°$ [7].

In the case of the reaction with chalcone, the addition product was found to be racemic. Similarly, (S)-(+) sulfoxide (**7**) was treated with PhMgBr as described above.

Reaction of Phenyl 2-Pyridyl Sulfoxide (**1**) *with* p-*Tolyl Grignard Reagent*

p-Tolyl Grignard reagent (*p*-TolMgBr) was prepared from 1.1 mL of *p*-bromotoluene (1.0 mmol) and 300 mg of magnesium in 19 mL THF. To phenyl 2-pyridyl sulfoxide (203 mg, 1.0 mmol) dissolved in 20 mL THF, *p*-TolMgBr (2.2 mL, 1.1 mmol) was added dropwise with stirring at −90 °C for 2 h. After the reaction, 3 mL of water was added and the solution was neutralized with aq ^{1}N-HCl solution. The products were extracted with CH_2Cl_2 and the organic layer was dried over $MgSO_4$. After removal of CH_2Cl_2, the products were separated by means of silica gel column chromatography using $CHCl_3$ as an eluent to give a mixture of aryl 2-pyridyl sulfoxides (69% yield) and diaryl sulfoxides (14% yield). Both mixtures were separated and the ratios of the corresponding sulfoxides were determined by gas chromatography. The ratio of phenyl 2-pyridyl and 2-pyridyl *p*-tolyl sulfoxides was 20:80 and the ratio of diphenyl, phenyl *p*-tolyl, and di-*p*-tolyl sulfoxides was 7:57:36. Similarly, 2-pyridyl *p*-tolyl sulfoxide (**4**) was treated with phenyl Grignard reagent as described above. Phenyl 2-pyridyl and 2-pyridyl *p*-tolyl sulfoxides were obtained in 55% total yield and the ratio was 24:76. Diaryl sulfoxides were obtained in 17% total yield and the ratio was 18:65:18, respectively.

When the reaction of phenyl 2-pyridyl sulfoxide and *p*-TolMgBr was carried out at −90 °C to −20 °C, 2-phenylpyridine, 2-*p*-tolylpyridine and 2,2′-bipyridyl were obtained. They were separated and purified by silica gel column chromatography using $CHCl_3$ as an eluent and then by preparative liquid chromatography.

2-Phenylpyridine: Yield 7%; ^{1}H-NMR($CDCl_3$) δ 7.11–7.98(m, 8H, 3,4,5-Py—H, Ph—H), 8.55–8.69(m, 1H, 6-Py—H); MS m/z 155(M^+).

2-*p*-Tolylpyridine: Yield 6%; ^{1}H-NMR($CDCl_3$) δ 2.35(s, 3H, CH_3) 7.11–7.88(m, 7H, 3,4,5-Py—H, Ar—H), 8.55–8.69(m, 1H, 6-Py—H); MS m/z 169(M^+).

2,2′-Bipyridyl: Yield 30%; mp 73 °C (Lit. [15] 73 °C); ^{1}H-NMR($CDCl_3$) δ 7.11–7.48(m, 2H, 5,5′-Py—H), 7.60–8.02(m, 2H, 4,4′-Py—H), 8.24–8.45(m, 2H, 3,3′-Py—H), 8.50–8.85(m, 2H, 6,6′Py—H); MS m/z 156(M^+).

Similarly, 2-pyridyl *p*-tolyl sulfoxide (**4**) was treated with phenyl Grignard reagent as described above. The yields of the corresponding coupling products, 2-phenylpyridine, 2-*p*-tolyl-pyridine and 2,2′-bipyridyl were 12, 3 and 16%, respectively.

Preparation of α-Substituted 2-Pyridyl Sulfoxide (**1a$_1$**, **1a$_2$** and **1a$_{1'}$**, **1a$_{2'}$**) *and Reaction with the Grignard Reagent*

Lithium diisopropylamide (LDA) was prepared from isopropyl amine (1.35 mL, 9.6 mmol) and butyllithium (6.0 mL, 9.6 mmol) in 50 mL of THF at −20 °C. To this solution was added phenyl 2-pyridyl sulfoxide (1.50 g, 7.4 mmol) dissolved in 10 mL of THF by a syringe at −90 °C and stirred for 15 min. Then acetophenone (1.33 g, 11.0 mmol) was added and the solution was stirred for 60 min at this temperature and then 30 min at 0 °C. After general work-up, products were separated and purified by silica gel column chromatography using ethyl acetate/n-hexane (1:1) as an eluent. Each diastereoisomer **1a$_1$** as a first solute (1.27 g, 3.93 mmol) and **1a$_2$** as a second solute (0.75 g, 2.31 mmol) was obtained in 84% total yield. To 30 mL of THF solution containing NaH (117 mg, 5.07 mmol) was added diastereomer **1a$_1$** (1.27 g, 3.93 mmol) dissolved in 20 mL of THF with stirring at 0 °C for 30 min and was added subsequently MeI (0.48 mL, 7.77 mmol) for 1 h. After the reaction and usual work-up, the product was purified as described above and the ether **1a$_{1'}$** (1.25 g, 3.71 mmol) was obtained in 95% yield. Similarly, isomer **1a$_2$** was converted to the ether **1a$_{2'}$** in 95% yield. The ether **1a$_{1'}$** (250 mg, 0.74 mmol) was dissolved in 20 mL of THF and to this solution was added 0.5 m *p*-TolMgBr (1.9 mL, 0.95 mmol) at −40 °C and the solution was stirred for 10 h. After the usual work-up, the products were separated and purified by the same column chromatography procedure described above. The ether **1a$_1$** was recovered in 41% yield and the ether **2a$_{2'}$** was obtained in 21% yield and they contained no other diastereomer.

1a$_1$: mp 193–194 °C; IR(KBr) 1020 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 1.96(d, 3H, CH_3), 5.91(b, 1H, OH), 7.17–7.72(m, 11H, 5-Py—H, Ph—H), 7.82(dd, 1H, 4-Py—H, J = 1.2, 7.2 Hz), 8.50(dd, 1H, 6-Py—H, J = 1.2, 4.8 Hz). Anal. calcd for $C_{19}H_{17}NO_2S$: C, 70.59; H, 5.26; N, 4.33. Found: C, 70.91; H, 5.10; N, 4.09.

1a$_2$: mp 219–220 °C; IR(KBr) 1040 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 1.93(d, 3H, CH_3), 6.15(b, 1H, OH),

7.19–7.29(m, 11H, 5-Py—H, Ph—H), 7.79(dd, 1H, 4-Py—H, J = 1.8, 7.8 Hz), 8.56(dd, 1H, 6-Py—H, J = 1.8, 4.8 Hz). Anal. calcd for $C_{19}H_{17}NO_2S$: C, 70.59; H, 5.26; N, 4.33. Found: C, 70.31; H, 5.49; N, 4.01.

1a$_1$': mp 175 °C; IR(KBr) 1040 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 2.07(s, 3H, CCH_3), 3.22(s, 3H, OCH_3), 7.07–7.73(m, 12H, 4,5-Py—H, Ph—H), 8.62(dd, 1H, 6-Py—H, J = 1.8, 4.2 Hz).

1a$_2$': mp 191 °C; IR(KBr) 1040 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 1.82(s, 3H, CCH_3), 2.89(s, 3H, OCH_3), 7.20–7.57(m, 11H, 5-Py—H, Ph—H), 7.78(dd, 1H, 4-Py—H, J = 1.8, 7.8 Hz), 8.72(dd, 1H, 6-Py—H, J = 1.8, 4.8 Hz).

2a$_2$': mp 196 °C; IR(KBr) 1040 cm^{-1}; ^{1}H-NMR($CDCl_3$) δ 1.81(s, 3H, CCH_3), 2.34(s, 3H, $ArCH_3$), 2.91(s, 3H, OCH_3), 7.07–7.66(m, 11H, 4,5-Py—H, Ar—H), 8.63(dd, 1H, 6-Py—H, J = 1.8, 4.8 Hz).

*Reaction of 3-Pyridyl 4-Pyridyl Sulfoxide (**5**) with* p-*TolMgBr*

To 3-pyridyl 4-pyridyl sulfoxide (203 mg, 1.00 mmol) dissolved in 20 mL THF, *p*-TolMgBr (1.4 mL, 0.7 mmol) was added dropwise with stirring at −78 °C for 1 h. After the reaction, 3 mL of water was added and the solution was neutralized with aq ^{1}N-HCl solution. The products were extracted with CH_2Cl_2 and the organic layer was dried over $MgSO_4$. After removal of CH_2Cl_2, the products were separated by silica gel column chromatography using ethyl acetate/hexane (1:1) as an eluent to give 3- and 4-pyridyl *p*-tolyl sulfoxides (216 mg, 61% yield) as a mixture and the recovered sulfoxide (71 mg, 35% yield). The ratio of 3-pyridyl and 4-pyridyl sulfoxides was determined to be 1:1.24 from the integral value of the pyridyl protons at the 2- and 6-positions by ^{1}H-NMR(500 MHz).

^{1}H-NMR(500 MHz); 3-pyridyl *p*-tolyl sulfoxide: δ 2.38(s, 3H, CH_3), 7.29(d, 2H, 3,5-Ph—H, J = 7.3 Hz), 7.40(dd, 1H, 5-Py—H, J = 4.9, 8.2 Hz), 7.56(d, 2H, 2,6-Ph—H, J = 7.3 Hz), 7.98(ddd, 1H, 4-Py—H, J = 1.5, 1.7, 8.2 Hz), 8.66(dd, 1H, 6-Py—H, J = 1.5, 4.9 Hz), 8.78(d, 1H, 2-Py—H, J = 1.7 Hz); 4-pyridyl *p*-tolyl sulfoxide: δ 2.38(s, 3H, CH_3), 7.29(d, 2H, 3,5-Ph—H, J = 7.3 Hz), 7.53(dd, 2H, 3,5-Py—H, J = 1.5, 4.5 Hz), 7.56(d, 2H, 2,6-Ph—H, J = 7.3 Hz), 8.69(dd, 2H, 2,6-Py—H, J = 1.5, 4.5 Hz).

Similarly, a mixture of phenyl 3-pyridyl (**2**) (203 mg, 1.00 mmol) and phenyl 4-pyridyl sulfoxides (**3**) (203 mg, 1.00 mmol) was treated with *p*-TolMgBr (0.60 mmol). Phenyl *p*-tolyl sulfoxide (125 mg) was obtained in 29% yield. Sulfoxides (**2**) and (**3**) were recovered as a mixture in 71% yield (288 mg) and the ratio was determined in 1.40:1 by the integral value of the pyridyl protons at the 2- and 6-positions by ^{1}H-NMR(500 MHz).

^{1}H-NMR(500 MHz); Phenyl 3-pyridyl sulfoxide (**2**): δ 7.41 (dd, 1H, 5-Py—H, J = 5.0, 7.9 Hz), 7.48–7.52(m, 3H, 3,4,5-Ph—H), 7.65–7.72(m, 2H, 2,6-Ph—H), 8.00(ddd, 1H, 4-Py—H, J = 1.5, 1.8, 7.9 Hz), 8.68(dd, 1H 6-Py—H, J = 1.5, 5.0 Hz), 8.80(d, 1H, 2-Py—H, J = 1.8 Hz); Phenyl 4-pyridyl sulfoxide (**3**): δ 7.48–7.52(m, 3H, 3,4,5-Ph—H), 7.54(dd, 2H, 3,5-Py—H, J = 1.5, 4.5 Hz), 7.65–7.72(m, 2H, 2,6-Ph—H), 8.71(dd, 2H, 2,6-Py—H, J = 1.5, 4.5 Hz).

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