Tetrahedron Letters,Vol.25,No.24,pp 2549-2552,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

A Convenient Preparation of Bipyridines through Ligand Coupling Reaction with σ-Sulfurane Formed by Treatment of Methyl 2-Pyridyl Sulfoxide with Grignard Reagents

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Summary---6-Substituted 2-methylsulfinyl pyridines react with Grignard reagents to afford 6,6'-disubstituted-2,2'-bipyridines (substituents: MeS, Cl, Br, H) in fair yields.

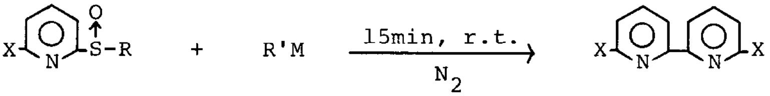
Recently, we have shown that the reaction of benzyl 2-pyridyl sulfoxide with Grignard reagents or organolithium reagents gives intramolecular ligand coupling products within σ-sulfuranes formed incipiently upon nucleophilic attack of the organometallic species on the tricoordinate sulfur compounds1). A number of other coupling reactions between two identical aryl groups have also been found in the treatments of tricoordinate sulfur compounds with either aryllithium or the Grignard reagents2). A similar coupling of two hetero aryl groups was found in the reaction of di-2-pyridyl phenyl phosphine oxide with alkoxide3).

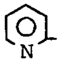
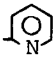
Meanwhile, the reactions of aryl methyl sulfoxide with organolithium compounds or the Grignard reagents have been known to afford various products, derived either through the ligand exchange4), the Pummerer type rearrangement5) or the initial removal of methyl proton6).

We have now found a reaction which involves both the initial ligand exchange and the subsequent ligand coupling between two heteroaryl groups within a σ-sulfurane, namely, the reaction between methyl 2-pyridyl sulfoxide with the Grignard reagents to afford 2,2'-bipyridines in moderate yields.

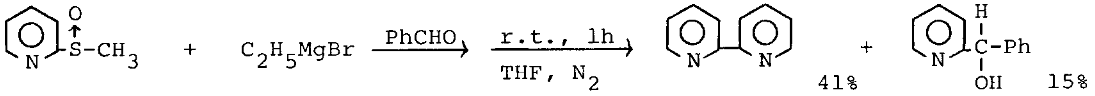
This paper describes a convenient preparation of 2,2'-bipyridine and its derivatives. In a typical run, the reaction was carried out by the following manner, methyl 2-pyridyl sulfoxide (216mg, 1.53mmol) dissolved in 8ml solution of THF was added to EtMgBr (0.8ml, 0.8mmol) in 1.0mmol/1ml THF solution using a 1ml syringe with stirring under nitrogen atmosphere at room temperature. Immediately, the color of the solution changed to yellow and formation of the precipitates was observed. Stirring was continued for 15min, then this reaction mixture was added to water and the aqueous solution was extracted three times with CH_2Cl_2. The combined CH_2Cl_2 layer was washed with water and dried on Na_2SO_4. After the solvent was evaporated, the resulting residue was separated through column chromatography using benzene as an eluent. 2,2'-Bipyridine 68mg was obtained in 57% yield. Similarly, treatment of 6-substituted 2-methylsulfinyl pyridines with 0.5 molar equivalent of EtMgBr in Et_2O instead of THF afforded the corresponding 6,6'-disubstituted-2,2'-bipyridines in moderate yields as shown in the Table 1. When methyl 2-pyridyl sulfoxide was treated with 1 eq. or 0.5 eq. of PhMgBr was obtained 2,2'-bipyridine in good yield together with methyl phenyl sulfoxide as a by-product formed obviously by the initial ligand exchange. When the reaction of methyl 2-pyridyl sulfoxide with 1 eq. of C_2H_5MgBr was carried out in the presence of 1.4 eq. of PhCHO to trap 2-pyridyl magnesium bromide presumed to be formed initially, we obtained phenyl 2-pyridyl methanol in 15% yield beside 2,2'-bipyridine as shown in the following equation.

Table 1



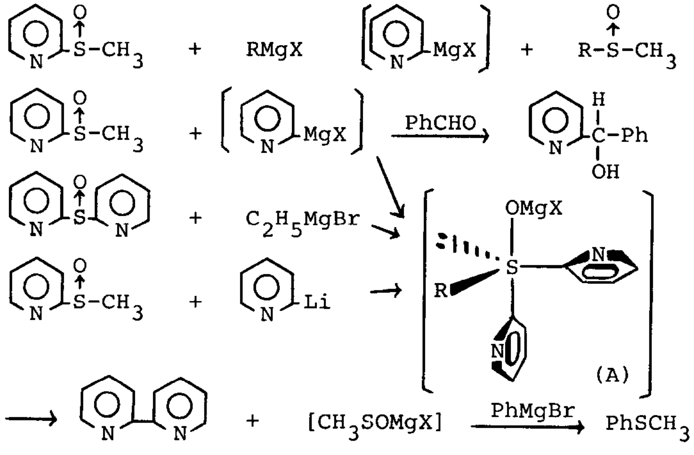
X	R	R'M	Solvent	Time (min)	Yield (%)
H	CH_3	CH_3MgBr[a]	THF	15	73[g]
"	"	C_2H_5MgBr[a]	"	"	57
"	"	"[a]	Et_2O	"	30
"	"	PhMgBr[a]	THF	"	79[c][f]
"	"	"[b]	"	"	78[d][f]
"	"	 - Li[b]	"	"	59[e][f]
"	C_2H_5	C_2H_5MgBr[a]	"	"	55[f]
"	Ph	"[a]	"	"	42[f]
H		C_2H_5MgBr[b]	THF	15	63
Cl	CH_3	CH_3MgI[a]	Et_2O	12h	24[h]
"	"	C_2H_5MgBr[a]	THF	"	33
"	"	"[a]	Et_2O	1h	55
"	"	"[b]	"	"	32
Br	"	"[a]	"	"	50[i]
SCH_3	"	"[a]	"	"	61[j]

a) molar ratio; sulfoxide : R'M = 1 : 0.5 b) molar ratio; sulfoxide : R'M = 1 : 1 c) methyl phenyl sulfoxide was obtained in 36% yield. d) methyl phenyl sulfoxide was obtained in 39% yield. e) at -18°C f) by g.l.c. analysis g) ref.9) h) ref.10) i) ref.11) j) ref.12) *Preparation of starting disubstituted sulfinyl pyridines; ref.13)



The most plausible mechanistic path is thus shown in the Scheme 1.Namely, the initial step of the reaction is the ligand exchange reaction between

Scheme 1

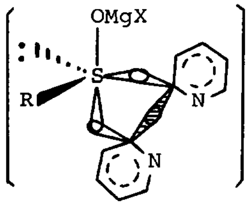


2-pyridyl group and phenyl Grignard reagent to form methyl phenyl sulfoxide and 2-pyridyl magnesium bromide, which in the subsequent step, immediately attacks the sulfinyl sulfur atom of the starting sulfoxide to result in the formation of the σ-sulfurane (A) as the intermediate. Then the ligand coupling reaction within the σ-sulfurane (A) should give 2,2'-bipyridine7). Methanesulfenyl magnesium bromide is considered to be a counter part of this coupling reaction, which was indeed trapped to give thioanisole upon treatment of the reaction mixture with 1 eq. of phenyl magnesium bromide, though the yield was poor (less than 3%)8).

The reaction is quite interesting mechanistically and also convenient procedure for the preparation of the substituted bipyridines.

Reference

1) S.Oae, T.Kawai, and N.Furukawa, Tetrahedron Lett., 25, 69 (1984).
2) a. Y.H.Khim and S.Oae, Bull. Chem. Soc. Jpn., 42, 1968 (1969).
   b. K.K.Andersen and S.A.Yeager, N.B.Peynircioglu, Tetrahedron Lett., 2485 (1970).
   c. B.K.Ackerman, K.K.Andersen, I.Karup-Nielsen, N.B.Peynircioglu, and S.A. Yeager, J.Org.Chem., 39, 964 (1974).
   d. B.M.Trost, R.W.La Rochelle, and R.C.Atkins, J.Am.Chem.Soc., 91, 2175 (1969).
   e. R.W.La Rochelle and B.M.Trost, ibid., 93, 6077 (1971).
   f. B.M.Trost and H.C.Arndt, ibid., 95, 5288 (1973).
   g. S.Oae, T.Yoshimura, and N.Furukawa, Bull. Chem. Soc. Jpn., 45, 2019 (1972).
   h. W.A.Sheppard, J.Am.Chem.Soc., 93, 5597 (1971).
   i. M.Hori, T.Kataoka, and H.Shimizu, Yakugaku-Zasshi, 93, 476 (1973), Chem.Pharm.Bull., 22, 1711, 2004, 2014, 2020, 2030 (1974).
3) G.R.Newkome and D.C.Hager, J.Am.Chem.Soc., 100, 5567 (1978).
4) a. J.P.Lockard, C.W.Schroeck, and C.R.Johnson, Synthesis 485 (1973).
   b. M.Hojo, R.Masuda, T.Saeki, K.Fujimori, and S.Tsutsumi, ibid. 789 (1977).
5) R.Oda and K.Yamamoto, J.Org.Chem., 26, 4679 (1961).
6) G.Tsuchihashi, S.Iriuchijima, and M.Ishibashi, Teterahedron Lett., 45, 4605 (1972).

7) 

The coupling mode of the ligands in the sulfurane (A) is not known well. However, the following model proposed by Trost[2e] in the coupling reactions of the aryl sulfonium salts with organolithium compounds would be also applied in our reaction. The detailed description of the molecular orbitals used in this coupling reactions including our former publication[1] is presented soon in a full paper.

8) D.N.Harpp, S.M.Vines, J.P.Montillier, and T.H.Chan, J.Org.Chem., 41,3987 (1976).

9) 2,2'-Bipyridine was identified as follows, : mp 69.5-71°C ; lit.69.7°C, Merck Index 9, 3367.

10) 6,6'-Dichloro-2,2'-bipyridine : mp 216-217°C, ^{1}H-NMR (60MHz, $CDCl_3$, TMS) δ 7.35 (dd, 5-pyrH, J=8,1Hz, 2H), 7.77 (t, 4-pyrH, J=7Hz, 2H), 8.36 (dd, 3-pyrH, J=7,1Hz, 2H) ; lit. mp. 218-219°C, S.Ogawa and S.Shiraishi, J.Chem. Soc.Perkin Trans. 1., 2527 (1980).

11) 6,6'-Dibromo-2,2'-bipyridine : mp. 228-229°C, ^{1}H-NMR (60MHz, $CDCl_3$, TMS) δ 7.48 (dd, 5-pyrH, J=8,2Hz, 2H), 7.68 (t, 4-pyrH, J=8Hz, 2H), 8.38 (dd, 3-pyrH, J=7,2Hz, 2H) ; lit. mp 221-223°C, 226-227°C, J.E.Parks, B.E.Wanger, and R.H.Holm, J.Organometallic Chem., 56, 53 (1973).

12) 6,6'-Dimethylthio-2,2'-bipyridine : mp 130-131°C, ^{1}H-NMR (60MHz, $CDCl_3$, TMS) δ 2.67 (s, SCH_3, 6H), 7.17 (dd, 5-pyrH, J=8,1Hz, 2H), 7.61 (t, 4-pyrH, J=8Hz, 2H), 8.17 (dd, 3-pyrH, J=7,1Hz, 2H), $C_{12}H_{12}N_2S_2$; C, 58.03; H, 4.87; N, 11.27, Found; C, 57.78; H, 4.48; N, 11.14 .

13) Methyl 2-pyridyl sulfoxide : bp 117°C/6mmHg, N.Furukawa, F.Takahashi, T.Kawai, S.Ogawa, and S.Oae, Phosphorus and Sulfur, 16, 167 (1983).
2-Chloro-6-methylsulfinyl pyridine : mp 66-66.5°C, N.Furukawa, S.Ogawa, T.Kawai, and S.Oae, J.Chem.Soc.Perkin Trans. 1., in press.
2-Bromo-6-methylsulfinyl pyridine : mp 76.5-77.0°C, ^{1}H-NMR (60MHz, CCl_4, TMS, δ 2.74 (s, $S(=O)CH_3$, 3H), 7.25-7.86 (m, 3,4,5-pyrH, 3H), C_6H_6BrNOS ; C, 32.74; H, 2.74; N, 6.36, Found; C, 32.90; H, 2.67; N, 6.38 .
2-Methylthio-6-methylsulfinyl pyridine : bp 134-137°C/4mmHg, ^{1}H-NMR (60MHz, $CDCl_3$, TMS) δ 2.54 (s, SCH_3, 3H), 2.86 (s, $S(=O)CH_3$, 3H), 7.16-7.31 (m, 3-pyrH, 1H), 7.65-7.77 (m, 4,5-pyrH, 2H), $C_7H_9NOS_2$; C, 44.89; H, 4.84; N, 7.47, Found; C, 44.85; H, 4.88; N, 7.59 .

(Received in Japan 10 February 1984)