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SYNTHESES AND CHEMICAL PROPERTIES OF SULFOXIDES, SULFILIMINES AND SULFOXIMINES CONTAINING PYRIDINE NUCLEI

Naomichi Furukawa, Fujio Takahashi, Keiko Kishimoto, Hiroyuki Morita, and Shigeru Oae*
Department of Chemistry, University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki 305, Japan

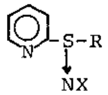
Several 2-pyridyl sulfides, sulfoxides and N-(p-toluenesulfonyl)-sulfilimines were prepared by the usual methods. Hydrolysis of N-(p-toluenesulfonyl)-2-pyridyl-o-tolylsulfilimine with conc. sulfuric acid gave the corresponding N-unsubstituted (free) sulfilimine in a moderate yield. Sulfoximines were obtained by oxidation of the corresponding free sulfilimines derived from the aminosulfonium salts. These free sulfilimines and sulfoximines thus prepared were found to give adducts with few Cu-salts. Methyl 2-pyridyl sulfoxide was found to be a good phase transfer catalyst for some typical nucleophilic reactions.

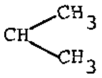
Recently, we found that sulfoximines have strong affinities toward several alkali metal salts.[1] When dimethylsulfoximine was used as solvent in S_N2 and E2 reactions, large rate enhancements were observed like those in common polar aprotic solvents such as DMSO and DMF.[2] The large rate enhancements appear to be due to the increased reactivity of the nucleophilic anion, substantially liberated by chelation of the gegen metal cation by both imino nitrogen and oxygen atoms of the sulfoximine. A remarkable rate-enhancement was observed in the reaction of the sulfoximine with dichlorocarbene generated in situ from chloroform and sodium hydroxide in the sulfoximine.[3] Meawhile, we found that a new adduct is formed between sulfoximines and Cu-salts. The affinity of sulfilimine or sulfoximine toward heavy metal cations will be increased further by substitution of one of alkyl or aryl groups with pyridine nuclei. Thus we have prepared several sulfoxides, sulfilimines and sulfoximines containing pyridine nuclei and explored their characteristic properties and applications for organic reactions.

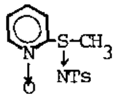
Several 2-pyridyl sulfides and sulfoxides were prepared according to the general procedures.[4] Methyl 2-pyridyl sulfoxide has a strong affinity toward alkali metal cations and hence enhances the nucleophilic reactivity of the gegen anion. Actually, nucleophilic substitution of benzyl bromide with lithium chloride (Finkelstein Reaction) proceeds smoothly in benzene (liquid-solid phase) or benzene-water (liquid-liquid phase) solvent in the presence of a catalytic amount of this sulfoxide. A few other S_N2 type reactions were also found to proceed in benzene or benzene-water solvent in the presence of the sulfoxide. Thus, methyl 2-pyridyl sulfoxide can be employed as a phase tansfer catalyst in two phase-heterogeneous reactions.[5]

Several N-(p-toluenesulfonyl)alkyl-2-pyridylsulfilimines were also prepared by our general procedure.[6] The alkyl-2-pyridylsulfilimines were afforded in moderate yields together with the corresponding sulfoxides. The products obtained were identified by spectroscopic and elemental analyses. Their yields, mps, ir and nmr spectra are summarized in Table I. The absorption bands of ir spectra of the S-N bonds of these 2-pyridylsulfilimines were found to be identical to those of the general alkylaryl- or diarylsulfilimines.[6]

Table I The Yields, Mps, Ir and Nmr Spectra of 2-Pyridylsulfilimines



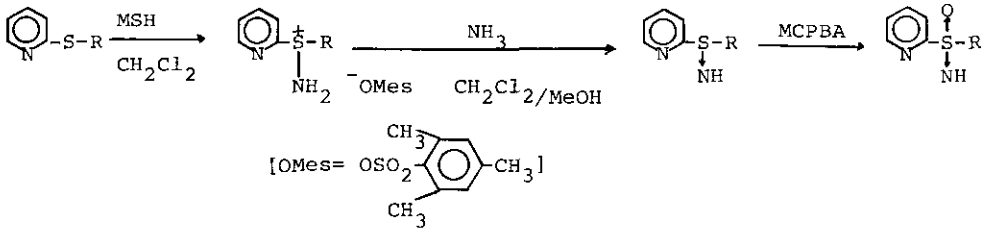
R	X	Yields (%)	Mp (°C)	Ir (S=N)	Nmr (δ-values, ppm)*
CH_3	Ts	31	126-127	955	2.40 (s, 3H, p-CH_3), 2.99 (s,3H, S-CH_3), 7.10-8.72 (m, 8H, Ar-H)
CH_2CH_3	Ts	37	91-92	980	1.19 (t, 3H, J=7.1 Hz, CH_3), 2.40 (s, 3H, p-CH_3), 3.28 (m, 2H, CH_2), 7.14-8.73 (m, 8H, Ar-H)
 $CH(CH_3)_2$	Ts	46	92-93	1000	1.05, 1.26 (dd, 6H, J=6.7 Hz, CH_3), 2.38 (s, 3H, p-CH_3), 3.70 (sept, 1H, J=6.7 Hz, CH), 7.13-8.70 (m, 8H, Ar-H)
$CH_2C_6H_5$	Ts	25	124-125	960	2.34 (s, 3H, p-CH_3), 4.28, 465 (dd, 2H, J=13.4 Hz, CH_2), 6.95-8.75 (m, 13H, Ar-H)
o-$CH_3C_6H_4$	Ts	44	111-112	970	2.33 (s, 3H, p-CH_3), 2.55 (s, 3H, o-CH_3), 7.00-8.69 (m, 12H, Ar-H)

		27	180-181 (decomp)	925	2.40(s, 3H, p-CH_3), 3.10 (s, 3H, S-CH_3), 7.15-8.35 (m, 8H, Ar-H)
o-$CH_3C_6H_4$	H	64	61.5-63	925 3150(NH)	2.52 (s, 1H, NH), 2.58 (s, 3H, o-CH_3), 7.13-8.59 (m, 8H, Ar-H)

* In $CDCl_3$ at 35°C.

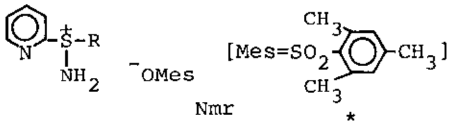
Though the hydrolysis of N-(p-toluenesulfonyl)methyl-2-pyridylsulfilimine in conc. sulfuric acid afforded the corresponding sulfoxide because of the instability of the free sulfilimine, similar treatment of N-(p-toluenesulfonyl)-2-pyridyl-o-tolylsulfilimine afforded the corresponding free sulfilimine in 64% yield which gave an adduct with cupric chloride.

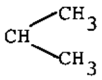
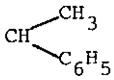
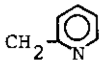
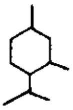
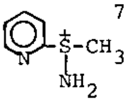
Though a few general methods[7] to prepare the sulfoximine were applied unsuccessfully with the 2-pyridyl sulfoxides, the best preparative method of the sulfoximines containing pyridine nuclei is the in situ oxidation of the corresponding free sulfilimines with such a peracid as MCPBA without isolation.



The free sulfilimines were obtained by treating with ammonia at a low temperature 2-pyridylaminosulfonium salts formed in the reaction of the sulfide with O-mesitylenesulfonylhydroxylamine (MSH).[8] The various 2-pyridylaminosulfonium salts were thus prepared by the reaction of the corresponding sulfides with MSH. The products obtained were identified by spectroscopic and elemental analyses. Amino compounds containing a sulfide linkage was already reported to react with MSH at nitrogen atom but not at sulfur and hence there was no formation of the corresponding aminosulfonium salt.[9] The reactions of several pyridine derivatives and MSH were also reported to complete easily under very mild conditions.[10] In the reactions of alkyl 2-pyridyl sulfides of lower alkyl homologs, e.g., methyl, ethyl, and isopropyl derivatives, the corresponding aminosulfonium salts were undoubtedly obtained since the ^{1}H-nmr spectra of α-protons which are adjacent to the sulfur atom shifted toward the lower fields than that of the sulfides. The results are summarized in Table II together with their yields and mps.

Table II The Yields, Mp and Nmr Spectra of 2-Pyridylaminosulfonium Salts

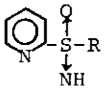


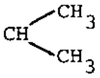
R	Yield (%)	Mp (°C)	Nmr (δ-values, ppm)*
CH_3	80	94-95	2.29 (s, 3H, p-CH_3), 2.48 (s, 6H, o-CH_3), 333 (s, 3H, S-CH_3), 6.72 (s, 2H, C_6H_2), 6.90-7.16 (brs, 2H, NH_2), 7.12-8.56 (m, 4H, C_5H_4N)
CH_2CH_3	67	118-119	1.41 (t, 3H, J=7.2 Hz, CH_3), 2.19 (s, 3H, p-CH_3), 2.53 (s, 6H, o-CH_3), 3.66 (m, 2H, CH_2), 6.63-6.78 (br.s, 2H C_6H_2), 6.93-7.16 (br.s, 2H, NH_2), 7.33-8.63 (m, 4H, C_5H_4N)
 $CH\begin{matrix}CH_3\\CH_3\end{matrix}$	75	93-94	1.36 (t, 6H, J=6.5 Hz, CH_3), 2.20 (s, 3H, p-CH_3), 2.58 (s, 6H, o-CH_3), 3.97 (sept, 1H, J=6.5 Hz, CH), 6.68-6.78 (br.s, 2H, C_6H_2), 6.88-7.10 (br.s, 2H, NH_2), 7.49-8.66 (m, 4H, C_5H_4N)
$CH_2C_6H_5$	68	unstable	2.18 (s, 3H, p-CH_3), 2.44 (s, 6H, o-CH_3), 4.90, 497 (dd, 2H, J=13.4 Hz, CH_2), 6.56-6.75 (br. s,2H, C_6H_2), 6.91-8.55 (m, 11H, NH_2, C_6H_5, C_5H_4N)
 $CH\begin{matrix}CH_3\\C_6H_5\end{matrix}$	52		unstable
	88		unstable
*** 	52	159-161 (decomp.)	0.74-2.13 (m, 18H, Alkyl), 2.19 (s, 3H, p-CH_3), 2.61 (s, 6H, o-CH_3), 3.90 (m, 1H, S-CH), 6.78 (br.s, 2H, C_6H_2), 7.25-8.20 (m, NH_2, C_5H_4N)
	79	155-156**	2.04 (s, 3H, p-CH_3), 2.35 (s, 6H, o-CH_3), 3.26 (s, 3H, S-CH_3), 6.64 (br.s, 2H, C_6H_2), 6.75 (br.s, 2H, NH_2), 7.55-8.58 (m, 4H, C_5H_4N)

*In $CDCl_3$ at 35°C. ** In DMSO-d_6. ***$[\alpha]_D^{25°}$=+41.7°(c 2.130 chloroform)

Since aminosulfonium salts of benzyl, 1-phenylethyl 2-pyridyl sulfides and bis(2-pyridylthio)methane were found to be unstable, their accurate nmr spectra were not measured. 2-Pyridylsulfoximines thus prepared in moderate yields were methyl, ethyl, and isopropyl derivatives, respectively. The products obtained were identified by their spectroscopic and elemental analyses. The results are summarized in Table III.

Table III The Yields, Mp, Ir and Nmr Spectra of 2-Pyridylsulfoximines

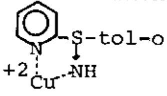


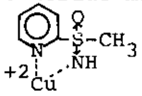
R	Yield (%)	Mp (°C)	Ir (O=S=N)	(NH)	Nmr (δ-values, ppm)*
CH_3	65	64.5-66	1010 1225	3250	2.80 (br.s, 1H, NH), 3.28 (s, 3H, CH_3), 7.40-8.87 (m, 4H, C_5H_4N)
CH_2CH_3	43	**	990 1210	3300	1.29 (t, 3H, J=7.2 Hz, CH_3), 2.95 (s, 1H, NH) 3.47 (m, 2H, CH_2), 7.38-8.90 (m, 4H, C_5H_4N)
 $CH\langle^{CH_3}_{CH_3}$	36	65-66.5	950	3250	1.30, 1.36 (dd, 6H, J=7.2 Hz, CH),7.48-8.88(m, 4H, C_5H_4N)

* In $CDCl_3$ at 35°C. ** Oil.

The chemical shifts of α- and β-protons of these sulfoxides, sulfilimines and sulfoximines appeared at higher fields as compared with those of the sulfides. These seem to be due to the anisotropic effects of pyridine ring or S-O, S-N bonds.[11]

The ir absorption band of the S-N bond of the adduct of 2-pyridyl-o-tolylsulfilimine with cupric chloride (mp, 185-192°C) was found to have a lower wave number, υ_{SN}=900 cm^{-1}, as compared to that of the sulfilimine, υ_{SN}=930 cm^{-1}. Furthermore, methyl 2-pyridyl sulfoximine afforded also a 1:1 adduct with cupric chloride, mp, 181-182°C. Anal. Calcd. for $C_6H_8Cl_2NOSCu$; C, 24.79, H,2.77, N, 9.46; Found, C, 25.33, H, 3.33, N, 9.39, ir(cm^{-1} KBr); 1230, 1090, 1015(O=S=N). These results indicate that the basic nitrogen atoms of the sulfilimine and the sulfoximine form a rather strong chelation with copper atom. Thus, the structures of the adducts with cupric chloride may be formulated as shown below.





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