

A CONVENIENT PREPARATION OF SULFINIC ACIDS BY THE REACTION OF 2-SULFONYLPYRIDINES AND THEIR N-OXIDES WITH NUCLEOPHILES

Naomichi Furukawa*, Masayuki Tsuruoka, and Hisashi Fujihara
Department of Chemistry, Tsukuba University, Sakura-mura,
Niihari-gun, Ibaraki 305, Japan

Abstract- Ipso-substitution reaction of 2-sulfonylpyridines and their N-oxides with alkoxide or thiolate anion afforded the sodium salts of sulfinic acids together with the corresponding substitution products in high yields. This procedure becomes a convenient and versatile method for preparation of various sulfinic acids.

It has been demonstrated that substitution reaction on azaheteroaromatic compounds with various nucleophiles i.e., 2-halogenopyridine with ethoxide ion takes place more readily than that on simple benzene system to afford the corresponding ipso-substitution product.^{1,2} Interestingly, in the ipso-substitution reaction on heteroaromatics, the sulfur functional groups such as sulfinyl and sulfonyl groups work as good leaving groups.³ Even a sulfenyl group attached to the 2-position of a pyridinium salt is displaced readily. Thus, this procedure has been successfully utilized for preparation of thiols.⁴ The reactions of the sulfoxides with nucleophiles give both the ipso-substitution and reduction products, whereas 2-sulfonylpyridines and their N-oxides react with nucleophiles to afford the corresponding ipso-substitution products in almost quantitative yields.³ We examined the fate of the sulfonyl moieties in these ipso-substitution reactions and found that 2-sulfonylpyridines and their N-oxides afforded quantitatively the corresponding salts of sulfinic acids together with the ipso-substitution products. This paper describes an alternate and convenient synthetic method of sulfinic acids by using ipso-substitution reactions of 2-sulfonylpyridines and their N-oxides.

The starting materials employed in this investigation were 2-sulfonylpyridines 1 and the corresponding N-oxides 2 and also 4-phenylsulfonylpyridine N-oxide. Both

sulfones 1 and 2 were prepared according to the known procedure starting from the corresponding sulfides⁶ which were oxidized to the sulfones upon treatment with an appropriate oxidant such as m-chloroperbenzoic acid(mCPBA) or H₂O₂. The sulfones 1 and 2 thus obtained were treated with an equimolar or slightly excess amount of NaOEt in EtOH. After the usual work-up process, sodium sulfinates were isolated by filtration and their structures were identified by ¹H-nmr in D₂O and IR spectroscopy. Furthermore, the sulfinates were also identified by converting them to the corresponding sulfones. The results obtained are summarized in Table 1 and 2.

Table 1

$\text{Pyridine ring with SO}_2\text{R at position 2} \quad + \quad \text{EtONa} \xrightarrow[\text{EtOH}]{\text{reflux}}$		$\text{RSO}_2\text{Na} \quad + \quad \text{Pyridine ring with OEt at position 2}$	
<u>1</u>		<u>3</u>	
R	Ratio ^{I)}	Time(h)	Yield(RSO ₂ Na,%)
a) CH ₃	1 : 3	0.25	58 ^{II)}
c) i-Pr	1 : 1	1	no reaction
c) i-Pr	1 : 2.5	48	38
e) PhCH ₂	1 : 3	0.25	52
f) Ph	1 : 3	0.25	65
f) Ph	1 : 1	19	92 ^{III)}

I) Ratio = sulfone : EtONa II) The yield of 2-ethoxypyridine was 52%.

III) PhSO₂Na + MeI → PhSO₂Me (73%)

Inspection of the results provides us the following features for the reactions. 1) The reactions of 1 bearing primary alkyl,benzyl and phenyl groups with EtONa in refluxing EtOH gave the sodium salts of sulfinic acids in good to moderate yields. On the other hand, the sulfone 1c gave 3c in low yield and in order to increase the yield was needed more drastic reaction condition, such as higher base concentration and prolonged reaction time. 2) In contrast to the reaction of 1, the sulfones of pyridine N-oxides 2 gave the sulfinates 3 having primary, secondary and even tertiary alkyl groups under mild condition in almost quantitative yields, as show in Table 2.

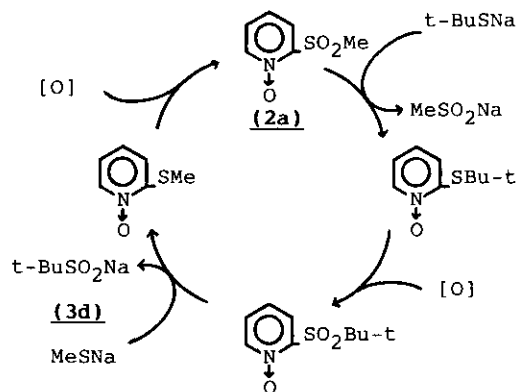
Use of CH₃CN as a solvent instead of EtOH was recommended since the sulfinates salts 3 were found to precipitate in this solvent and could be separated easily from the substitution products by filtration. Furthermore, the sulfone 2a was found to be used as a starting material for preparation of various sulfonylpyridines which were synthesized by treatment of 2a with thiol under alkaline condition and subsequently with oxidants. For example, the sulfone 2d

Table 2

$ \begin{array}{c} \text{C}_5\text{H}_4\text{N} \text{ ring with } \text{SO}_2\text{R} \text{ at position 2 and } \text{N-O} \end{array} + \text{EtONa} \xrightarrow[\text{EtOH}]{\text{reflux}} \text{RSO}_2\text{Na} + \begin{array}{c} \text{C}_5\text{H}_4\text{N} \text{ ring with } \text{OEt} \text{ at position 2 and } \text{N-O} \end{array} $			
<u>2</u>		<u>3</u>	
R	Time(min)	Yield(RSO ₂ Na, %)	Yield(RSO ₂ Me, %) ^{I)}
a) Me ^{II)}	10	quant.	-
b) n-Oct	30	quant.	83
c) i-Pr	15	quant. ^{III)}	-
c) i-Pr ^{II)}	15	quant.	-
d) t-Bu	15	quant.	-
e) PhCH ₂	15	quant.	79
f) Ph	15	89	68
f) Ph ^{IV)}	15	69	-

I) $\text{RSO}_2\text{Na} + \text{MeI} \longrightarrow \text{RSO}_2\text{Me}$ II) The yield of 2-ethoxypyridine N-oxide was 95%. III) In CH_3CN at room temperature. IV) 4-phenylsulfonylpyridine N-oxide in CH_3CN at room temperature.

which is hardly prepared by an ordinary procedure was obtained by the present ipso-substitution of 2a with t-BuSNa following by oxidation of the sulfide in high yield. The sulfone 2d upon treatment with MeSNa resulted in the sulfinate 3d and 2-(methylthio)pyridine N-oxide which was oxidized to the starting sulfone 2a. This result indicates that the sulfone 2a works as a mediator for the preparation of various kinds of sulfinic acids. The reaction cycle is shown in the



Scheme-Reaction Cycle

scheme. In comparison with the known methods, this procedure for preparation of 3 has advantages such as; 1) no tedious processes are required during experiments. 2) 2a can be prepared readily starting from commercially available 2-mercaptopyridine N-oxide and be used as a starting material for the synthesis of various sulfones 2 from which the desired sodium salts of sulfinic acids are obtained by treating with an appropriate nucleophiles.

REFERENCES

1. G. Illuminati, Adv. Heterocycl. chem., 1964, 4, 285.
2. J. March, Advanced Organic Chemistry : Reactions, Mechanisms and structure (McGraw-Hill, London, 1968) pp. 498.
3. G. B. Barlin and W. V. Brown, J. Chem. Soc. (B), 1967, 568, 648, 954.
 G. B. Barlin and A. C. Young, J. Chem. Soc. (C), 1969, 921.
 D. J. Brown and R. V. Foster, Aust. J. Chem., 1966, 19, 1487, 2322.
 N. Fukawa, S. Ogawa, T. Kawai, and S. Oae, J. Chem. Soc. Perkin I, 1984, 1833.
4. M. Yamada, Y. Watabe, T. Sakakibara, and R. Sudoh, J. Chem. Soc. Chem. Commun., 1979, 179.
 M. Yamada, K. Sotoya, T. Sakakibara, T. Takamoto, and R. Sudoh, J. Org. Chem., 1977, 42, 2180.
 P. Molina, A. Alajaran, M. Vilaplana, and A. R. Katritzky, Tetrahedron Lett., 1985, 26, 469.
5. Preparation of sulfinic acids has been reported in the following literatures.
 K. K. Andersen, " Comprehensive Organic Chemistry " D. N. Jones Ed., (Pergamon Press, Oxford, 1979) Vol. 3. pp. 317-330 (1979).
 Houben-Weyle EII, 614 (1985).
 Y. Ueno, A. Kojima, and M. Okawara, Chem. Lett., 1984, 2125.
6. N. Furukawa, F. Takahashi, T. Kawai, K. Kishimoto, S. Ogawa, and S. Oae, Phosphorous and Sulfur, 1983, 16, 167.

Received, 30th May, 1986