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Generation of Sulfenate Salts via Ipso-substitution of Azaheterocyclic Sulfoxides. First Preparation and Characterization of Sodium 2-Pyridinesulfenate

Naomichi FURUKAWA,* Yasuo KONNO, Masayuki TSURUOKA, Hisashi FUJIHARA, and Satoshi OGAWA
Department of Chemistry, University of Tsukuba, Tsukuba, Ibaraki 305

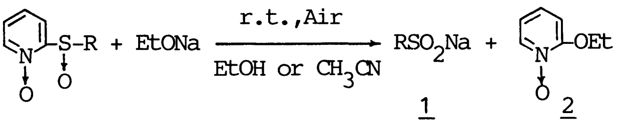
2-Alkyl- or 2-aryl-sulfinylpyridine N-oxides undergo ipso-substitution reaction with sodium ethoxide to afford sodium sulfenates which were converted soon to the corresponding sulfinates upon contact with oxygen. Sodium 2-pyridinesulfenate was prepared and characterized by FT-IR as the first example of stable sulfenate.

Sulfenic acids are generated either by pyrolysis of sulfoxides1) or oxidation of thiols2) but are extremely unstable to dimerize soon to thiolsulfinates. Therefore, only a few stable sulfenic acids have been prepared and determined their structures in which the SOH group should be protected either by bulky substituents or the functional groups capable of hydrogen bonding to prevent the facile dimerization.3) On the other hand, only a few procedures have been reported to detect sufenate anions. For example, the alkaline hydrolysis of the sulfenate derivatives involving esters, sulfenyl halides and disulfides provides sulfenate anions as reactive intermediates.4) However, no sulfenate salts have been isolated. Recently, numerous 2-sulfonyl-substituted azaheterocycles have been found to undergo facile ipso-substitution to afford the corresponding sulfinic acids.5) This ipso-substitution also provides for preparation of sulfenates. In order to find a convenient method for preparation of sulfenate salts and investigate their natures, we tried to react 2-sulfinylpyridine N-oxides with alkali and found that the sulfenate salts could be generated but they were too highly sensitive to oxygen to be isolated even in Ar or N_2 atmosphere but their formation can be detected by converting them to the sulfoxides upon treatment with MeI. Interestingly, after careful treatment of the reaction mixture under rigorous exclusion of oxygen and work-up in N_2 stream, sodium 2-pyridinesulfenate was isolated as pale yellow crystals which were identified by FT-IR, ^{1}H-NMR, and elemental analysis. This paper reports the generation and reactions of several sodium sulfenates together with first isolation of sodium 2-pyridinesulfenate from the ipso-substitution of 2-alkyl-(and 2-aryl)sulfinylpyridine N-oxides and benzothiazole with EtONa in CH_3CN or EtOH.

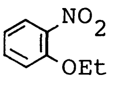
2-Alkyl-(and 2-aryl)sulfinylpyridine N-oxides were prepared from the reaction of 2-mercaptopyridine N-oxide with appropriate alkyl iodides or bromides followed by oxidation with m-chloroperbenzoic acid(mcpba), whereas 2-aryl, t-butyl or 2-

adamantylsulfinyl groups were introduced by using 2-methanesulfonylpyridine N-oxide with the correspodning thiols under alkaline condition.[5)] 2-Alkyl- or 2-aryl-sulfinylpyridine N-oxides were then subjected to react with sodium ethoxide in CH_3CN or EtOH under air for 0.5 h. After the reaction, 2-ethoxypyridine as an ipso-substitution product was obtained in 70-90% yield. The sodium sulfenates as a counter part of this ipso-substitution were generally dissolved in this solvent. Removal of the solvent under air, however, gave no sodium sulfenates but sodium sulfinates were obtained in 50-60% yields except 2-t-butylsulfinylpyridine N-oxide which was recovered quantitatively. Apparently, these results indicate that the sodium sulfenates would be generated but the salts were converted soon by oxidation upon contact with oxygen in air to result in the formation of sulfinates. The sensitivity of the sulfenates to oxygen was checked by bubbling of air or oxygen to the solution, which resulted in the immediate formation of coloreless precipitates of the corresponding sulfinates. Therefore, the formation of sulfenates was confirmed indirectly by adding MeI to the solution under N_2 stream. When the reaction was carried out in the presence of excess MeI under the reaction conditions, methyl aryl(or alkyl) sulfoxides were obtained in moderate yields together with the corresponding sulfones. The results are summarized in Tables 1 and 2.

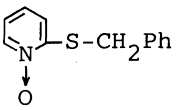
Table 1. Reactions of 2-Sulfinylpyridine N-oxides with Sodium Ethoxide under Air



R	Solvent	Yield/% 1	Yield/% 2
Ph	EtOH	74	85
o-$NO_2C_6H_4$[a)]	EtOH	57	71
2-Pyridyl	CH_3CN	60	95
$PhCH_2$[b)]	EtOH	50	71
t-Bu[c)]	CH_3CN	0	0
2-Adamantyl	CH_3CN	49	45

a)


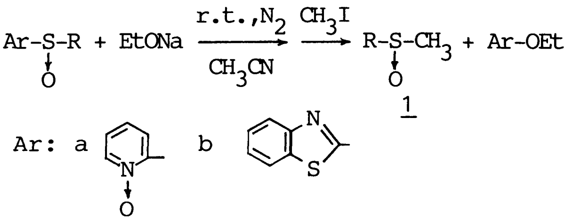
9%

b)


26%

c) recovery 70%

Table 2. Reactions of 2-Sulfinylazaheterocycles with Sodium Ethoxide under N_2



Ar	R	1 Yield/%
a	p-Tol	trace
a	Ph	54
a	o-$NO_2C_6H_4$	55
a	2-Pyridyl	94
a	4-Pyridyl	53
a	Mesityl	trace
a	2-Adamantyl	21
b	2-Pyridyl	89
b	2-Benzothiazolyl	61

As shown in Tables 1 and 2, 2-sulfinylpyridine N-oxides are convenient sources for preparation of sulfenate salts except t-butylsulfoxide which did not react under the present conditions. By this procedure the sulfenates having strong electron withdrawing substituents such as o-nitro group or 2-pyridyl group are possibly prepared as stable salts if one could exclude air rigorously during and after the reactions. Other sulfenates thus generated are extremely labile to oxygen and unable to be isolated as solid sulfenates in the air.

In order to isolate and characterize sodium sulfenate, 2-(2-pyridinesulfinyl)-pyridine N-oxide was treated with EtONa in CH_3CN under N_2-atmosphere. After the reaction, the work-up procedures were carried out in a dry-box by rigorously excluding air and moisture. After removing the solvent, the residual products were washed with anhydrous ether to remove ipso-substitution product, 2-ethoxypyridine N-oxide. Pale yellow powder was obtained in more than 80% yield. This compound showed a strong IR-absorption at 870 cm^{-1}. However, the solid contaminated 2-ethoxypyridine N-oxide even upon repeated washing with ether. Therefore, we switched the substrate for the reaction from the sulfinylpyridine N-oxide to 2-(2-pyridinesulfinyl)benzothiazole[6] which was treated with an equimolar amount of EtONa in CH_3CN similarly as described above. This sulfoxide also reacted readily with EtONa in CH_3CN at room temperature for 0.5 h. After evaporating the solvent under N_2 stream, the residue was washed with anhydrous ether in a dry-box. Pale yellow crystalline materials were obtained in 90% yield. Mp. 157-161 °C(decomp). Anal. Calcd for C_5H_4NOSNa: C, 40.27; H, 2.70; N, 9.39%. Found C, 39.81; H, 2.76; N, 9.45%. ^{1}H-NMR(CD_3CN) δ 8.07-8.17(m, 1H, 6-Py), 6.42-7.17(m, 3H, 3,4,5-Py). KBr disk for measurement of FT-IR was prepared in N_2 stream. The FT-IR absorption spectrum of this compopund is shown in Fig. 1. A strong absorption band appears at 870 cm^{-1} which is assigned as S-O stretching vibration. On exposure to the air of this KBr disk of the sodium sulfenate IR spectrum was gradually changed and finally converted completely to that of sodium 2-pyridinesulfinate which was prepared authentically. The SO-band due to the sulfenate disappeared and appeared new bands corresponding to the sulfinate at 1050, 1040, 990 cm^{-1}. The spectrum of the sulfinate is shown in Fig. 2. If one stored this sulfenate under N_2 or Ar atmopsphere, the compound was stable even at room temperature and

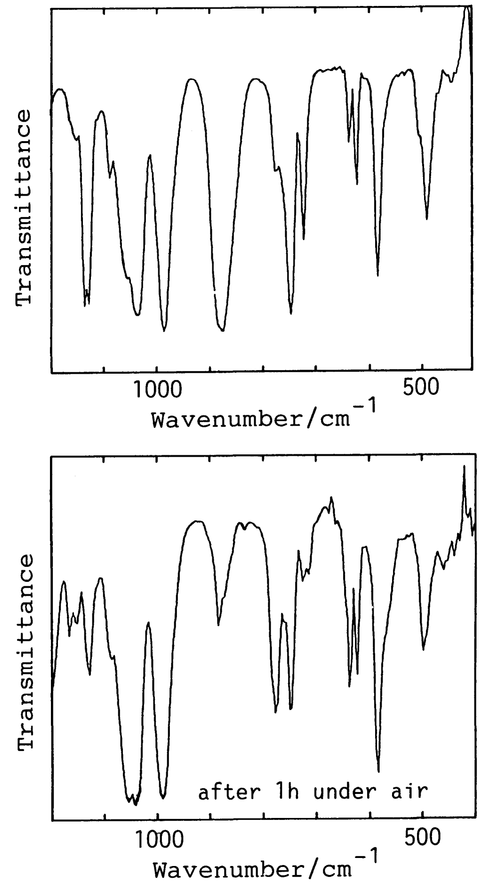


Fig. 1. FT-IR spectra of sodium 2-pyridinesulfenate.

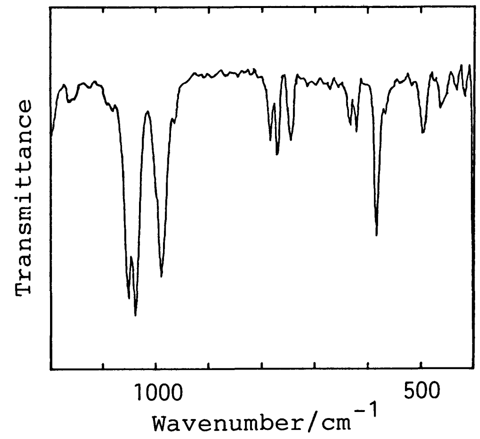
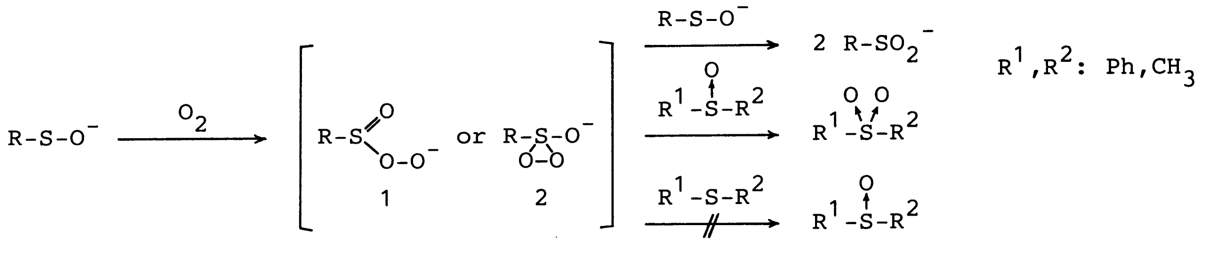


Fig. 2. FT-IR spectra of sodium 2-pyridinesulfinate.

did not disproportionate after standing for one month. Therefore, the result indicates that the sulfenate salts would be unstable in the air and converted soon to the sulfinates even in the solid state. This is the first example of isolation and characterization of the sodium salt of sulfenic acid. As for the mechanism for this oxidation reaction we postulate the formation of persulfenate anion 1 by direct nucleophilic attack of the sulfenyl sulfur atom to the oxygen molecule as shown in Scheme 1.



Scheme 1.

The formation of persulfinate anion seems to be supported by the following fact; when the reaction was carried out in the presence of methyl phenyl or diphenyl sulfide, the corresponding sulfoxide was not obtained at all, while in the presence of methyl phenyl or diphenyl sulfoxide, the corresponding sulfone was obtained in moderate yield. The sulfoxide was not oxidized at all with oxygen in the absence of sulfenates.

Thus, the present procedure is simple and convenient for preparation of unstable sodium sulfenates. Further studies for preparation and reactions of other sulfenates are in progress in this laboratry.

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