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51. **Yukiko Tanaka and Yoshimasa Tanaka**: Infrared Absorption Spectra of Organic Sulfur Compounds. I. Studies on S–N Stretching Bands of Benzenesulfonamide Derivatives.

(*Faculty of Pharmaceutical Sciences, Kumamoto University*[*1])

The identification of structural features of organic sulfur compounds by means of infrared absorption spectra has been the subject of a large number of systematic investigations in which the absorption characteristic of many functional groups has been established.[1] Although detailed studies have been made of the infrared spectra of the sulfonamide derivatives, little discussion of the absorption of S–N stretching vibration has appeared. Data only a limited number of compounds have been published by Baxter, *et al.*[2] who already found bands between 1070 and 1100 cm^{-1} usually near 1090 cm^{-1} in several phenylsulfonyl derivatives and assigned them to S–N stretching vibration. From a study of the Raman spectra of benzenesulfonamide, *p*-toluenesulfonamide, 1,1-dithiodipiperidine, potassium nitrilotrisulfonate and aminosulfonic acid, Angus, *et al.*[3] concluded that the characteristic stretching frequency at about 1070 cm^{-1} was S–N mode. In N-methyl *p*-toluenesulfonamide, benzenesulfonamide, *o*- and *p*-toluenesulfonamide, Hadži[4] assigned the bands near 900 cm^{-1} to the S–N stretching vibrations. The S–N bands have also been investigated by Katritzky[5] who noted that in $ArNHSO_2CH_3$, $ArNCH_3SO_2CH_3$, $(CH_3)_2NSO_2CH_3$, $CH_3NHSO_2CH_3$, and $NH_2SO_2CH_3$, two strong bands are found below 1000 cm^{-1}. These are probably the C–S and N–S skeletal stretching modes. Momose, *et al.*[6] reported that RSO_2NH_2 compounds have characteristic frequencies in the region of 919～896 cm^{-1} which may be assigned to S–N stretching vibration. Hofmann, *et al.*,[7] however, indicated that the S–N frequency may be as low as 550 cm^{-1} in the studies of sulfur-nitrogen compounds.

The authors are interested in the absorption of S–N stretching vibration in the organic sulfur compounds. The present investigation of the assignment of S–N stretching vibration was undertaken in order to make a choice between these alternative explanations. In this work, therefore, related compounds were measured and examined systematically concerning the bands in the region near 900 cm^{-1} (band B) and near 1090 cm^{-1} (band A).

[*1] Oe-machi, Kumamoto (田中由紀子, 田中善正).
1) L. J. Bellamy: "The Infrared Spectra of Complex Molecules", 2nd Ed., 351～366 (1958), Methuen and Co., Ltd., London.
2) J. N. Baxter, J. Cymerman-Craig, J. B. Willis: J. Chem. Soc., **1955**, 669.
3) W. Angus, A. H. Leckie, J. I. Williams: Trans. Faraday Soc., **34**, 793 (1938).
4) D. H. Hadži: J. Chem. Soc., **1959**, 847.
5) A. R. Katritzky, R. A. Jones: *Ibid.*, **1960**, 4497.
6) T. Momose, Y. Ueda, T. Shoji: This Bulletin, **7**, 734 (1959).
7) H. J. Hofmann, K. R. Andress: Naturwiss., **41**, 94 (1954).

Results and Discussion

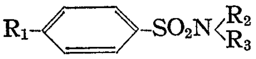
The infrared spectra of 44 kinds of benzenesulfonamide derivatives were measured and the results obtained are shown in Table I. Each spectrum has two bands in 1242~1387 cm^{-1} and in 1135~1175 cm^{-1} regions, corresponding to asymmetric and symmetric SO_2 vibrations respectively.[8] Moreover, a strong band was found near 1090 cm^{-1} region (band A) and medium band near 900 cm^{-1} (band B).

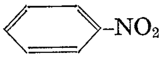
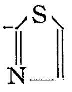
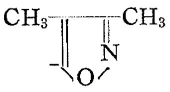
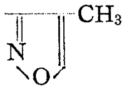
Baxter has already discovered that methanesulfonamide has no absorption between 990 cm^{-1} and 1140 cm^{-1}, and Momose[6] also suggested that phenylsulfone derivatives having no S-N linkage showed the band near 1090 cm^{-1}. In addition, Hadži has pointed out that the 1090 cm^{-1} band is found regularly with sulfonic compounds. In the present work in author's laboratory, this band 1090 cm^{-1} region was actually found in a series of benzenesulfonic derivatives and no characterisic band near 900 cm^{-1} as in Table II.

As shown in Table III a few of the naphthalene sulfonic derivatives were also examined.

As in Fig. 1 a comparison between 8-amino-1-naphthalenesulfonic acid and naphthosultam shows that the former has only band B, however, the latter both of them. Fig. 2 shows that saccharin has two bands, A and B, whereas phthalimide has only band A.

TABLE I. Infrared Spectra of Compounds which include  -SO_2N Linkage


R_1-C_6H_4-$SO_2N\begin{smallmatrix}R_2\\R_3\end{smallmatrix}$

R_1	R_2	R_3	Band A	Band B
H	H	H	1092	901
〃	〃	C_6H_5	1096	927
〃	〃		1091	908
〃	C_2H_5	C_2H_5	1092	938
〃	C_6H_5	C_6H_5	1093	912
NH_2	H	H	1098	898
〃	〃	CH_3	1093	947
〃	〃	C_2H_5	1090	945
〃	〃	C_4H_9	1095	915
〃	〃	C_6H_5	1095	916
〃	〃	$CH_2C_6H_5$	1094	855
〃	〃	$COCH_3$	1092	860
〃	〃		1092	884
〃	〃		1095	873
〃	〃		1091	885

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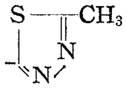
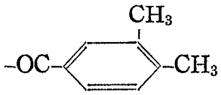
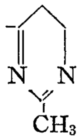
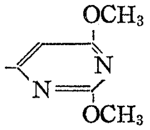
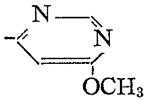
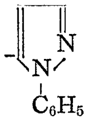
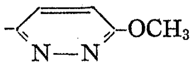
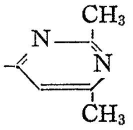
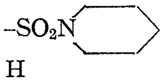
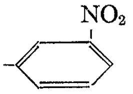
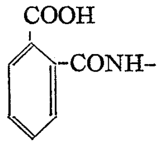
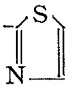
[8] K. Schreiber: Anal. Chem., **21**, 1169 (1949).

NH_2	H		1081	919
〃	〃		1080	865
〃	〃		1080	878
〃	〃		1092	876
〃	〃		1092	895
〃	〃		1093	888
〃	〃		1098	915
〃	〃		1090	855
〃	〃		1091	833
〃	CH_3	CH_3	1092	948
〃	C_2H_5	C_2H_5	1092	938
〃	C_4H_9	C_4H_9	1092	948
〃	H		1095	933
CH_2NH_2	H	H	1097	900
CH_3	〃	〃	1095	907
〃	〃	CH_3	1090	855
〃	〃	NH_2	1091	835
〃	〃	C_6H_5	1093	905
〃	〃	$CH_2C_6H_5$	1062	875
〃	〃		1092	907
〃	〃	$OCH_2C_6H_5$	1087	853
〃	Cl	Na	1095	935
CH_3[a)]	H	H	1072	920
NH_2CO[b)]	〃	〃	1088	894
OH	〃	〃	1095	835
NO_2	〃	C_6H_5	1091	908
CO_2H[b)]	〃	〃	1088	901
〃	C_2H_5	C_2H_5	1083	935
	H		1096	938

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a) *ortho* b) *meta*

Table II. Infrared Spectra of Compounds which do not Include SO_2-N Linkage

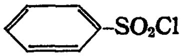
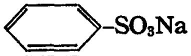
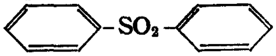
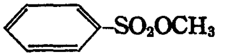
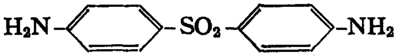
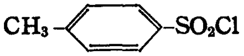
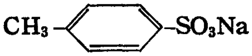
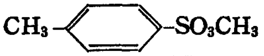
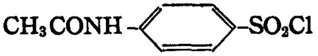
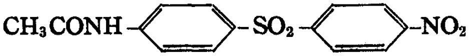
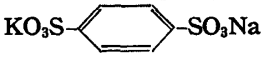
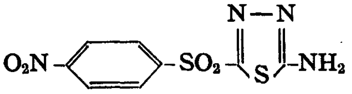
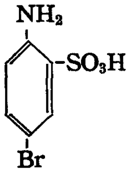
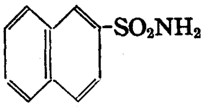
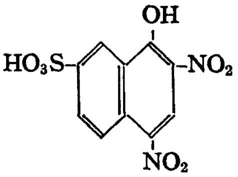
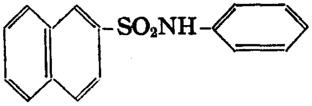
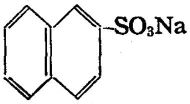
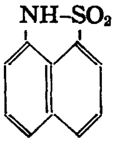
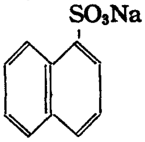
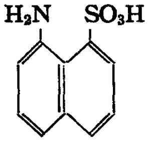
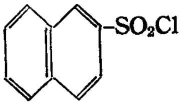
	Band A	Band B
	1083	—
	1135	—
	1107	—
	1096	—
	1098	—
	1108	—
	1080	—
	1135	—
	1098	—
	1083	—
	1104	—
	1135	—
	1097	—
	1108	—

Table III. Infrared Spectra of Naphthalene Derivatives

	Band A	Band B		Band A	Band B
	1080	902		1082	—
	1077	929			
	1110	—		—	840
	1075	—		1082	—
	1072	—			

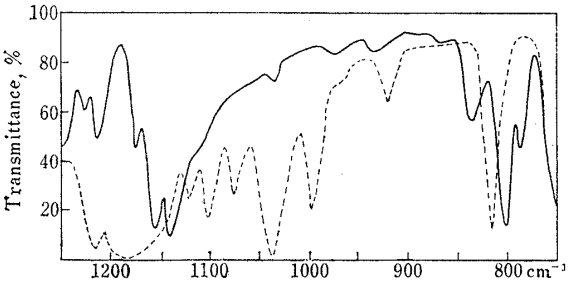


Fig. 1. Infrared Spectra of Naphthosultam (solid line) and 8-Amino-1-naphthalenesulfonic Acid (broken line)

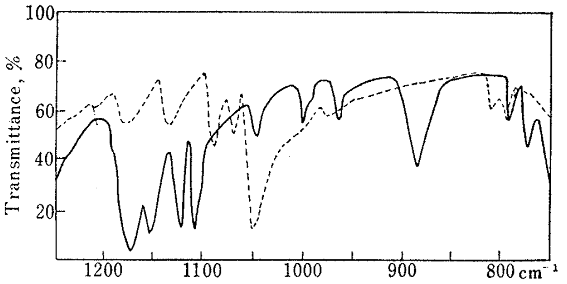
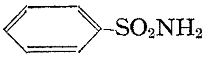
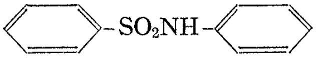
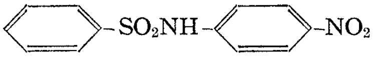
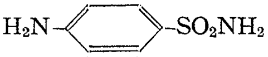
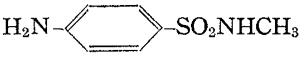
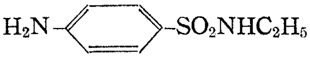
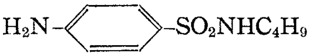
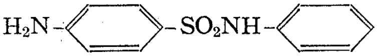
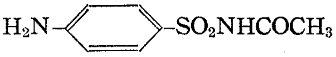
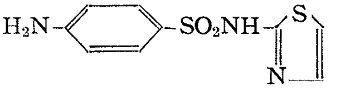
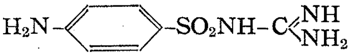
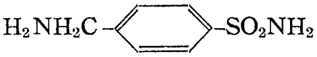
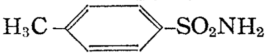
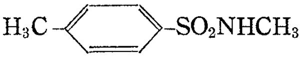
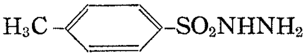
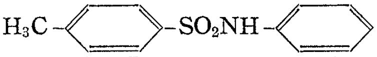
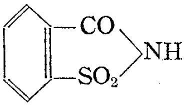
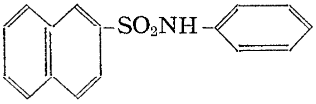
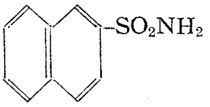


Fig. 2. Infrared Spectra of Saccharin (solid line) and Phthalimide (broken line)

Table IV. Shifts of Infrared Absorptions by Deuteration

	Band A		Band B	
	H	D	H	D
	1092	1090	901	848
	1096	1094	927	852
	1083	1093	905	843
	1098	1095	898	852
	1093	1092	947	892
	1090	1090	945	890
	1095	1094	915	880
	1095	1097	916	835
	1092	1093	860	803
	1092	1095	884	841
	1091	1093	833	783
	1097	1095	900	862
	1095	1092	907	858
	1090	1090	855	788
	1091	1088	835	760
	1093	1095	905	845
	1062	1062	875	842
	1122	1122	898	798
	1077	1076	929	865
	1080	1079	902	860

On the basis of these data, absorption appearing near 900 cm^{-1} region in benzenesulfonamide derivatives can be reasonably assigned to S-N stretching vibration.

The deuteration work of 14 kinds of benzenesulfonamide derivatives, in which hydrogen is directly attached to nitrogen, were undertaken to afford confirmatory proof. The NH or NH_2 bands shifted to lower wave number on deuteration.[9] Moreover, the C-N bands similarly shifted to the lower wave number in the same deuterated compounds.[10] Similarly in those compounds including S-N linkage, when the hydrogen atom attaching to nitrogen atom directly changed to deuterium, some effect might be expected to occur to the S-N band. Hadži reported that the S-N band of N-methyltoluenesulfonamide at 839 cm^{-1} shifted to 791 cm^{-1} on deuteration. In this work, the S-N bands (band B) shifted to lower wave number on deuteration about 100~38 cm^{-1} (Table Ⅳ, Fig. 3).

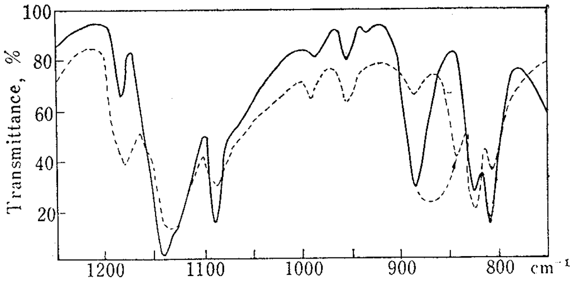


Fig. 3. Infrared Spectra of Sulfanilamide (solid line) and Sulfanilamide-D (broken line)

In comparison with N-Methylsulfonamide and N,N-dimethylsulfonamide and N-ethylsulfonamide and N,N-diethylsulfonamide, the S-N bands of N-monosubstituted compounds shifted -45 cm^{-1}, while the S-N bands of N-disubstituted compounds did not move on deuteration, as shown in Fig. 4. Further, little or no shift has been observed in the absorption near 1090 cm^{-1} region (band A). These facts suggest that the bands near 900 cm^{-1} region (band B) is S-N stretching vibration.

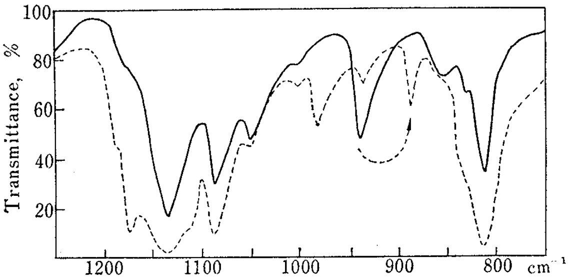


Fig. 4a. Infrared Spectra of N-Ethylsulfonamide (solid line) and N-Ethylsulfonamide-D (broken line)

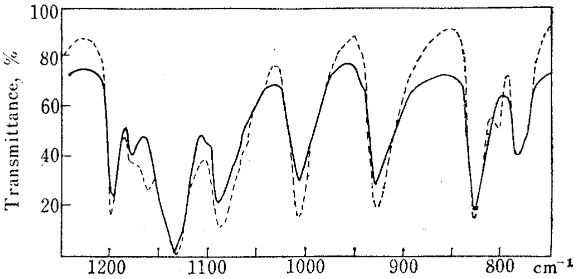


Fig. 4b. Infrared Spectra of N,N-Diethylsulfonamide (solid line) and N,N-Diethylsulfonamide-D (broken line)

Experimental

Almost all of the sulfonamide derivatives for medical use were used after recrystallization. The other samples were synthesized in the author's laboratory.

Spectroscopic technic : The IR spectra were measured with a Nihon Bunko Model DS-301 Spectrometer and for the region 4000~600 cm^{-1}. Solid Specimens were measured as tablets of potassium bromide. N-deuterated species were prepared by the recrystallization with deuterium oxide and methanol in N_2 gas. Usually CH_3OD or CD_3OD is to be employed at first, but these were difficultly available and instead CH_3OH was used in the present deuteration work. Of course, this work was not done to completion, but the aim to examine the shift of the S-N band by this way was accomplished. The deuterated samples usually were measured in Nujol, but the authors measured them as KBr tablets because KBr tablets were more stable and less susceptible to change from D to H in a short time.

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Summary

The infrared spectra of 44 kinds of benzenesulfonamide derivatives and a few naphthalenesulfonamide derivatives were measured and compared with the benzenesulfonic acid derivatives. The sulfonamide derivatives showed two characteristic bands near 900 cm^{-1} and 1090 cm^{-1} regions, but the latter didn't show the bands near 900 cm^{-1} region. The infrared spectra of deuterated benzenesulfonamide derivatives were examined. In the compound in which nitrogen atom is directly attached to hydrogen, the band near 900 cm^{-1} region shifted about $38\sim100$ cm^{-1}. However, in case of the compounds where nitrogen atom is not attached to hydrogen, the band near 900 cm^{-1} region did not shift on deuteration work. These facts suggest that the band near 900 cm^{-1} region can be ascribed to S–N vibration.

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52. **Keiji Sekiguchi and Keiji Ito**: Studies on the Molecular Compounds of Organic Medicinals. I. Dissolution Behavior of the Molecular Compound of Sulfanilamide and Sulfathiazole.[*1]

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Up to the present, many organic systems have been investigated by thermal analysis, and it was widely recognized that molecular compounds were often formed between organic medicinals. Also, there have appeared in literatures a number of reports[1~3] concerning complex or molecular compound formation in solution with the intention of finding effective solubilizers for insoluble drug substances. These solubility studies, however, have been confined to the interactions at equilibrium, and none of them inferred the dissolution process before the system attained solution equilibrium. Moreover, the molecular compound isolated has never been employed as the starting material for investigation.

Since information obtained from these method of approach indicates little or nothing on the therapeutical efficacy of the molecular compound itself, it would be natural that only a few of them have been adopted for therapeutical purposes.

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1) L. Irrera: Gazz. chim. ital., **61**, 614 (1931); C. A., **26**, 642 (1932).

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