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175. **Yoshihiro Nitta and Noriaki Ando**: Studies on Sulfonylurea Derivatives. III.[*1] The Infrared Spectra of 1-*p*-Tolylthio-3-alkylureas and Corresponding Sulfonyl Compounds.

(*Research Laboratory, Chugai Pharmaceutical Co., Ltd.*[*2])

In a previous paper,[1] *p*-tolylthio-3-alkylureas and the corresponding sulfonyl compounds were prepared and the comparison of these pharmacological activity was reported. In the present paper, the infrared spectra of these compounds are measured, and the difference between the thio and sulfonyl derivatives is discussed, treating mainly with the frequencies due to phenyl group and ureido group.

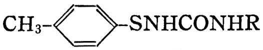
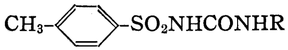
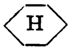
Frequencies due to Phenyl Group

The ring double bond stretching vibrations are normally observed as three bands at 1600, 1580, and 1500 cm^{-1} in benzene derivatives. All of these compounds now studied show two bands near 1600 and 1500 cm^{-1}.

The band near 1600 cm^{-1} for sulfonyl derivatives is stronger in its intensity than that for thio derivatives. On the other hand, the band near 1500 cm^{-1} for sulfonyl derivatives is weaker in its intensity than that for thio derivatives. The intensities of these bands can probably be correlated with the electronic nature of S- and SO_2 groups. Katritzky *et al.*[2] suggested that for *para* disubstituted benzenes the intensity of the band near 1600 cm^{-1} can directly vary as the algebraic difference of the electronic effects of the substituents, and one of the band near 1500 cm^{-1} is always high for electron donor substituents and weak or absent where these are not present. Accordingly, our result is presumedly explained by the electron-donor character of CH_3 and -S- groups and the electron-attracting character of SO_2 group.

All of these compounds now studied show a strong and sharp band at near 800 cm^{-1}. This is clearly due to C-H out of plane deformation mode. The spectral results are summarized in Table I.

Table I. C-H Out of Plane Deformation Frequency

				
	δ_{C-H} (cm^{-1})		δ_{C-H} (cm^{-1})	
R	in KBr	in $CHCl_3$	in KBr	in $CHCl_3$
H	804		814, 818	
CH_3	801		814	
C_2H_5	803	805	814	815
C_3H_7	801	805	808	814
iso-C_3H_7	804	805	812	813
C_4H_9	800	807	817	815
iso-C_4H_9	805	805	817	815
sec-C_4H_9	802	805	814	812
tert-C_4H_9	800	806	819	814
C_5H_{11}	806	805	814	813
	802	805	813	814

[*1] Part II : Yakugaku Zasshi, **82**, 967 (1962).

[*2] TakatAminami-cho, Toshima-ku, Tokyo (新田義博, 安藤憲章).

1) Y. Nitta, N. Ando, Y. Ikeda, M. Koizumi, A. Shioya : Yakugaku Zasshi, **82**, 191 (1962).

2) A. R. Katritzky, *et al.* : Quart. Revs. (London) **13**, 353 (1959).

A sulfonyl group causes a frequency increase of the C–H out of plane deformation mode by about 10 cm^{-1}. This is probably due to the strong electron-attracting effect of the SO_2 group. It is well known that the frequency and intensity of absorption due to C–H out of plane deformation mode for benzene ring are changed by various reasons, and strong electron-attracting substituents decrease the π-electron density of ring to cause the frequency increase in the mode.

Frequencies due to Ureido Group

a) NH Stretching Frequencies

The NH stretching frequencies are expected to occur at 3500~3200 cm^{-1}. Compounds of R=H show four bands near 3400, 3300, 3270, and 3200 cm^{-1}, respectively, in the solid state. These bands may be due to the asymmetrical and symmetrical N–H stretching mode. N-Alkylated compounds show two or more bands at 3500~3100 cm^{-1} in the solid or solution state. These results are summarized in Table II.

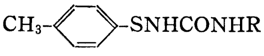
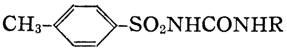
In the spectra in the solution state, thio derivatives show a sharp band at 3390~3365 cm^{-1} (3377±6 cm^{-1}), and in addition to this band also show a relatively weak band at 3190~3170 cm^{-1} (3180±5 cm^{-1}) which disappears upon dilution. The former band remains unchanged upon dilution. These results suggest that the band at about 3180 cm^{-1} is due to the associated molecules, whereas the other at about 3377 cm^{-1} is due to the monomeric molecules. In these compounds, unassociated NH stretching vibration is expected to show absorptions at two frequencies different from each other, because N-alkylated compounds have two NH groups, N_1H group adjacent to the thio group and another N_3H group. However, the unexpected occurrence of only one free NH band in these compounds may be explained as that the two NH groups give absorption at the same frequency.

On the other hand, sulfonyl derivatives in the solution state also show a sharp band at 3375~3355 cm^{-1} (3368±6 cm^{-1}), and an additional weak band appears broadly at 3200~3120 cm^{-1}. However, both bands does not vary upon dilution, the reason of this behavior being noteworthy to study further. A sulfonyl group causes a frequency lowering of the free NH stretching mode by ca. 10 cm^{-1}. The N_1–H bond will be weaker than the N_1–H bond in the thio derivatives because of the electron migration towards the adjacent sulfonyl group, which causes a great acidity increase of NH group. This seems to be the reason why the free NH frequency of the sulfonyl derivatives is lower than that of the thio derivatives.

In the solid spectra, three bands appear. The first band appears at 3340~3295 cm^{-1} (3313±8 cm^{-1}) for thio derivatives, and at 3360~3290 cm^{-1} (3341±17 cm^{-1}) for sulfonyl derivatives. The second band appears at 3285~3240 cm^{-1} (3261±9 cm^{-1}) for thio derivatives, and at 3235~3145 cm^{-1} (3183±22 cm^{-1}) for sulfonyl derivatives. The third band appears at 3125~3040 cm^{-1} (3090±16 cm^{-1}) for thio derivatives, and at 3140~3060 cm^{-1} (3091±18 cm^{-1}) for sulfonyl derivatives. The difference in the spectral position between the first and second bands is approximately 50 cm^{-1} for the thio derivatives, and 160 cm^{-1} for sulfonyl derivatives. The third band which may include the absorption due to benzene ring occurs in the same position in both derivatives. From the above result, it is clear that the second band for sulfonyl derivatives shows a greater shift to lower frequency than that for thio derivatives. This fact may be explained by considering that sulfonyl derivatives possess hydrogen bonding to a larger extent than thio derivatives, because of the strongly electron-attracting nature of the sulfonyl group.

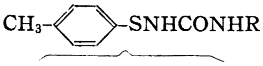
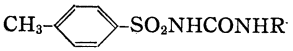
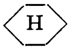
An additional evidence for the explanation is the fact that the free NH vibration of sulfonyl derivatives also absorb at appreciable lower frequencies than that of thio derivatives in the solution spectra, as described above.

Table II. Absorption Frequencies due to NH Group

R										
	ν_{NH}					ν_{NH}				
	in KBr			in $CHCl_3$		in KBr			in $CHCl_3$	
CH_3	3310 s	3250 s	3100w			3335 s	3175sh	3095m		
C_2H_5	3315 s	3260 s	3095w	3385m	3190w	3310 s	3205 s	3140sh	3375m	3120~3200w
C_3H_7	3315 s	3285 s	3105w	3390m	3190w	3355 s	3175sh	3110 s	3375m	3120~3200w
iso-C_3H_7	3325 s	3270 s	3125w 3075w	3370m	3180w	3290 s	3235 s	3075w	3360m	3120~3200w
C_4H_9	3320 s	3270 s	3095w	3375 s	3170w	3355 s	3180sh	3095 s	3375m	3135b-w
iso-C_4H_9	3310 s	3250 s	3090sh	3365 s	3180w	3335 s	3150sh	3090 s	3375m	3120b-w
sec-C_4H_9	3300 s	3265 s	3070w	3375m	3180 v w	3355 s	3145sh	3085 s	3355m	3115b-w
tert-C_4H_9	3340 s	3275 s	3040w	3375m	3180w	3360 s	3225 s	3060w	3365m	3120b-w
C_5H_{11}	3305 s	3240 s	3120w	3385m	3180 v w	3355 s	3175sh	3110m	3370m	3120b-w
	3295 s	3250 s	3080w	3375m	3180w	3355 s	3160sh	3100 s	3365m	3120b-w

s : strong w : weak sh : shoulder m : medium v : very b- : broad

Table III. Absorption Frequencies due to Ureido Group

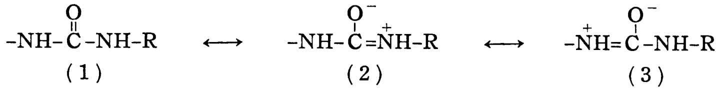
R								
	Amide I		Amide II		Amide I		Amide II	
	KBr	$CHCl_3$	KBr	$CHCl_3$	KBr	$CHCl_3$	KBr	$CHCl_3$
H	1683		1617		1709sh, 1667		1631	
CH_3	1641		1582		1699, 1658		1564	
C_2H_5	1638	1676	1558	1523	1690	1703, 1686	1538	1541
C_3H_7	1639	1675	1560	1523	1663	1703, 1688	1543	1542
iso-C_3H_7	1639	1673	1546	1513	1668	1699, 1683	1559	1533
C_4H_9	1636	1675	1561	1525	1657	1706, 1690	1551	1545
iso-C_4H_9	1653	1678	1547	1514	1664	1706sh, 1688	1547	1546
sec-C_4H_9	1641	1673	1552	1518	1659	1701sh, 1683	1532	1542, 1533
tert-C_4H_9	1652	1673	1546	1524	1670	1708, 1691	1543	1537
C_5H_{11}	1642	1678	1558	1523	1663	1703, 1687	1545	1539
	1642	1659	1554	1515	1654	1703, 1683	1534	1542, 1533

b) Amide I and II Bands

The spectra of all compounds show a very strong absorption at 1700~1650 cm^{-1}, the region normally regarded as characteristic for the carbonyl vibration in ureido compounds. In addition to this absorption, they show a strong band at 1600~1500 cm^{-1} which is assigned to ureido absorption (amide II band). These results are summarized in Table III.

The positions of these bands can be expected to correlate with the electronic nature of S- and SO_2 groups. Variations in the ureido-alkyl group have little effect on the position and intensity of the carbonyl and Amide II band, except that in several series of compounds the methyl derivatives absorbs at appreciably higher frequencies than the others in Amide II. The Amide I band for sulfonyl derivatives was observed at a higher frequency than for thio derivatives. This result can be explained as due to the difference between the thio and sulfonyl derivatives in the electronic state of the urea structure. Although more work is necessary in this field, it is assumed that the structure of thio derivatives involve resonance between three structures of (1), (2), and (3), as shown in Chart 1, which are not essentially different from that of simple urea.

In the case of sulfonyl derivatives, the polar structure of (3) must make little contribution to the resonance hybrid, because of the migration of lone pair of nitrogen



$$\underset{(1)}{-NH-\overset{O}{\overset{\|}{C}}-NH-R} \longleftrightarrow \underset{(2)}{-NH-\overset{O^-}{\overset{|}{C}}=\overset{+}{N}H-R} \longleftrightarrow \underset{(3)}{-\overset{+}{N}H=\overset{O^-}{\overset{|}{C}}-NH-R}$$

Chart 1.

atom to the adjacent SO_2 group. Accordingly, the increase in the bond order of the carbonyl linkage of sulfonyl derivatives is explained from the consideration described above. The Amide I and II bands considerably change their positions in the spectra according to the state of aggregation in which the substance is measured. These changes can be explained as due to the changes in hydrogen bonding and in the electronic state of the urea structure. Amide I band for thio derivatives in the solution state has been displaced to high frequency by ca. 25 cm^{-1} when compared with the values in the solid state. And this is accompanied by decrease of ca. 40 cm^{-1} in frequency of Amide II absorption. This is explained from the fact that the contribution of the polar resonance structure described above increases on going from solution to solid state. This spectral change from solid to solution state is in good agreement with the assignment to the amide bands, as well known. Furthermore, this fact and the data observed for the N-H vibration described above certainly conclude that the molecular association of 1-*p*-tolylthio-3-alkylureas are caused through the hydrogen bond (NH...O=C). However, it is interesting to find that Amide I band for sulfonyl derivatives in the solution state is displaced upwards by ca. 20 cm^{-1} when compared with that in solid state, whereas there is no appreciable change of Amide II frequencies in both states. The change of Amide I band is similarly explained from the change in contribution of various structures (i.e., mainly (1) and (2)). However, the reason for no change of Amide II band is not clear.

Comparing the Amide I and II absorptions of the thio derivatives the effects produced by their N-substituents appear closely parallel to the effects produced by similar substituents in the sulfonyl derivatives.

Experimental

All the IR spectral studies were performed in a Hitachi EPI-2 Spectrophotometer using sodium chloride optics. All the samples were measured in 5~7% solution in $CHCl_3$ and in KBr discs. The experimental details of the preparation of these compounds were reported in the previous paper.[1]

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Summary

The infrared absorption spectra of eleven 1-*p*-tolylthio-3-alkylureas and the corresponding sulfonyl compounds were recorded. Comparison of the thio and sulfonyl derivatives is made with respect to the influence exerted by the S or SO_2 group on their respective frequencies due to phenyl and ureido groups. The variations of the absorption positions depend on the electronic nature of each groups. The nature of the alkyl group has relatively little effect on the position of these bands.

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