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Steric Effects of Alkyl Substituents on the N-H Stretching Absorptions and Rotational Isomerism of *N*,*N*′-Dialkylthioureas[1)]

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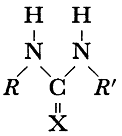
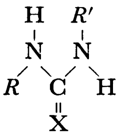
The fundamental N–H stretching absorptions of twenty nine *N*,*N*′-dialkylthioureas were observed in dilute solutions. The observed frequencies were classified into five groups assignable to the *out*, three different types of the *trans*, and the *cis* forms. The steric hindrance between the bulky *t*-butyl group and the thiocarbonyl sulfur, which is larger than for *N*,*N*′-dialkylureas, was suggested to cause the *out* form. Dialkylthioureas of *R*TU*t*B type seem to exist to a great extent in the *trans-out* conformation in solutions. It is suggested that it is not the N–H group with the bulky *t*-butyl group but the N–H group in the opposite part which is out of the skeletal plane. The energy difference between the *out* and the *trans* forms was found to be $\Delta H = 430 \pm 100$ cal mol^{-1}.

A number of studies have been carried out to elucidate the rotational isomerism of secondary amides in solutions in connection with the backbone-structures of polypeptides and proteins.[2),3)] It was disclosed that the steric hindrance between two substituents and the C=X group (X=O or S) plays an important part in the isomerism.

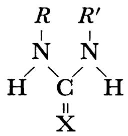
On the other hand, some infrared studies of *N*,*N*′-disubstituted ureas (*R*U*R*′) and -thioureas (*R*TU*R*′) suggested the presence of *trans-cis* isomerism in solutions.[2),4),5)] The isomeric conformations were considered to be the *trans-trans* and the *trans-cis* conformations since the *cis-cis* conformation was unlikely on steric grounds. Nevertheless, percentages of over 50% of the *cis* form[6)] were estimated for the ureas with bulky groups; *s*-D*t*BU[4)] and *s*-DPhU.[2)] For the corresponding thioureas with the sulfur atom larger in effective size than the oxygen atom, *s*-D*t*BTU[5)] and *s*-DPhTU,[2)] the percentages of the *cis* form were estimated to be approximately 50 and 45%, respectively.



trans-trans



trans-cis



cis-cis

In systematic infrared studies on *R*U*R*′ in solutions a correlation was found between the N–H frequencies and *R* and *R*′, the presence of a very small amount of a form differing from the *trans* form in *R*U*R*′ being confirmed with either one *t*-butyl group or two.[7)–10)] From an examination of the infrared spectra of trialkylureas (D*R*U*R*′) in solutions it was suggested that the different form has the N–H group out of the skeletal plane (the *out* form) owing to the steric hindrance between the bulky substituents and the C=O group.[11)] This necessitates a re-examination of the study of *R*TU*R*′.

The purpose of this study is (1) to examine the applicability of our established correlation to *R*TU*R*′, (2) to confirm an increase in the amount of the *out* form caused by the larger steric hindrance in *R*TU*R*′ with a sulfur atom than that in the corresponding *R*U*R*′ with an oxygen atom, and (3) to obtain information on the *out* form.

Experimental

Twenty nine *R*TU*R*′ were prepared by the standard method (addition of *R*CNS to *R*′NH$_2$).[12)] The crude samples were purified by repeated recrystallization from suitable solvents. The purified samples were identified by their melting points and infrared spectra. Each sample was examined as a 10^{-3} M solution in CCl$_4$ (2 cm NaCl cell) and as a 10^{-2} M solution in CS$_2$ and in CHCl$_3$ (2 mm NaCl cell). Solvents of spectroscopic grade were used.

The spectrometer, the experimental conditions in the recording of the spectra, and the calibration of band-positions were the same as given previously.[7)] The spectra at different temperature were obtained with an electrically-heated and beam-transparent box in which the sample and the reference cells were placed and adjusted to each light axis.

Results and Discussion

Two fundamental N–H stretching bands from two N–H links should appear in the infrared spectra of *R*TU*R*′ in the absence of rotational isomerism. However, in some spectra one or two extra bands are observed suggesting the rotational isomerism in solutions (Fig. 1). We examined some possibilities of over- and combination tones, and of Fermi resonance[13)] for the extra bands. It was concluded from observation of the solution spectra of deuterated compounds that the extra bands are really the N–H fundamentals, and from comparison of the solution spectra with the solid spectra that there may be a little or no effect of Fermi resonance in such dilute solution.[14)] We classified the observed bands into five groups, A—E, according to wave number (Table 1).

The trans *N–H Bands.* Although the N–H bands of *R*TU*R*′, as a whole, are lower by about 15 cm^{-1} than those of *R*U*R*′, three of the classified five groups, B, C, and D, correspond to the three groups characteristic of a substituent of the *trans-trans* *R*U*R*′;[7)] the N–H group with a methyl group shows the highest frequency band, the group with other primary alkyl groups exhibits medium one,[15)] and the group with branched alkyl groups shows the lowest one.

In connection with such a correlation it can be understood that, for example, the two bands of MTU*s*B result from two different types of N–H group; the higher com-

TABLE 1. N–H STRETCHING FREQUENCIES OF *N*,*N'*-DIALKYLTHIOUREAS IN CCl_4 SOLUTION (0.001M)

*R*NHCSNH*R'* *R*	*R'*	*R*TU*R'*	Frequency (cm^{-1}) A	B	C	D	E
CH_3–	CH_3–	*s*-DMTU		3445s			3425sh
CH_3–	C_2H_5–	MTUE		3447sh	3436s		3411sh
CH_3–	*n*-C_3H_7–	MTUP			3442s. b		* *
CH_3–	*i*-C_3H_7–	MTU*i*P		3450s		3423s	3400sh
CH_3–	*i*-C_4H_9–	MTU*i*B		3443s			3427sh
CH_3–	*s*-C_4H_9–	MTU*s*B		3450s		3422s	3399sh
CH_3–	*t*-C_4H_9–	MTU*t*B	3468m	3446w		3422s	3398sh
C_2H_5–	C_2H_5–	*s*-DETU			3435s		3414sh
C_2H_5–	*n*-C_3H_7–	ETUP			3435s		3415sh
C_2H_5–	*i*-C_3H_7–	ETU*i*P			3433s	3422s	3400sh
C_2H_5–	*i*-C_4H_9–	ETU*i*B			3436s		3413sh
C_2H_5–	*s*-C_4H_9–	ETU*s*B			3432s	3421sh	3399sh
C_2H_5–	*t*-C_4H_9–	ETU*t*B	3456m			3420s	3399sh
n-C_3H_7–	*n*-C_3H_7–	*s*-DPTU			3435s		3414sh
n-C_3H_7–	*i*-C_3H_7–	PTU*i*P				3422s.b	3401sh
n-C_3H_7–	*i*-C_4H_9–	PTU*i*B			3436s		* *
n-C_3H_7–	*s*-C_4H_9–	PTU*s*B			3431s.b		* *
n-C_3H_7–	*t*-C_4H_9–	PTU*t*B	3458m			3422s	* *
i-C_3H_7–	*i*-C_3H_7–	*s*-D*i*PTU				3422s	3399sh
i-C_3H_7–	*n*-C_4H_9–	*i*PTUB			3431sh	3423s	3402sh
i-C_3H_7–	*i*-C_4H_9–	*i*PTU*i*B			3437sh	3423s	3401sh
i-C_3H_7–	*s*-C_4H_9–	*i*PTU*s*B				3421s	3399sh
i-C_3H_7–	*t*-C_4H_9–	*i*PTU*t*B	3446m			3420s	3399sh
n-C_4H_9–	*t*-C_4H_9–	BTU*t*B	3456m			3423s	* *
i-C_4H_9–	*i*-C_4H_9–	*s*-D*i*BTU			3439s		* *
i-C_4H_9–	*t*-C_4H_9–	*i*BTU*t*B	3467m			3423s	* *
s-C_4H_9–	*s*-C_4H_9–	*s*-D*s*BTU				3421s	3400sh
s-C_4H_9–	*t*-C_4H_9–	*s*BTU*t*B	3446m			3420s	3400sh
t-C_4H_9–	*t*-C_4H_9–	*s*-D*t*BTU	3452s			3418s	* *

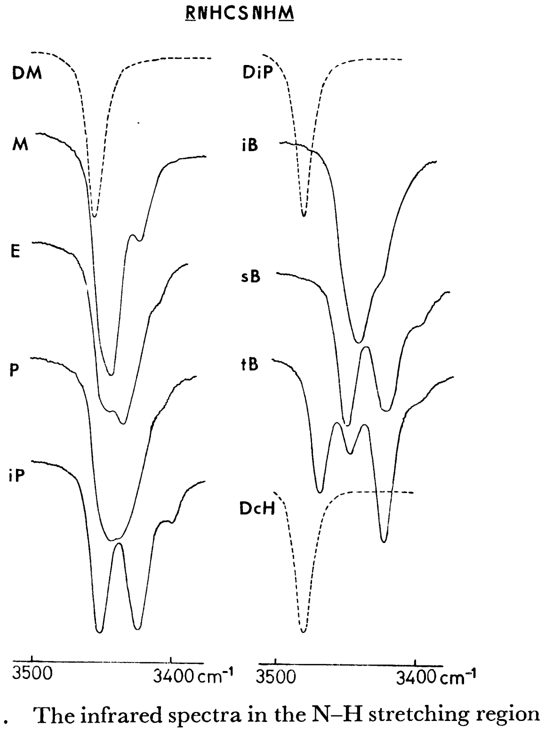


Fig. 1. The infrared spectra in the N–H stretching region of *R*TUM (the solid line) and D*R*TUM (the broken line) in CCl_4. *R*: see the abbreviations in Table 1; *c*H: cyclohexyl.

ponent resulting from the N–H group with the methyl group, and the lower component from the N–H group with the *s*-butyl group. In the case of the *R*TU*R'* showing only one band, the two components from the two different types of N–H group may be closer than those in the above example, or may overlap each other, thus appearing as only one band. This is suggested by the fact that *R*TU*R'* with only slightly different components such as MTUP (combinations of the B and C groups) give a band with lower apparent optical density and with larger half-intensity width than *R*TU*R'* with overlapped components such as *s*-DMTU (combinations of two groups belonging to the same type), as shown in Fig. 1.

It is concluded that these three kinds of bands originate from the *trans* form, and that the established *trans*-correlation for *R*U*R'* is applicable to *R*TU*R'*.

Out N–H Bands. Band A appears at the highest frequency and with medium or strong intensity without exception in *R*TU*R'* with a *t*-butyl group or groups. It probably corresponds to the very weak band at 3469 cm^{-1} of *s*-D*t*BU,[7] to the bands of *R*U*t*B which appear newly when the solvent is changed from CCl_4 to $CHCl_3$,[8] and to the 3478 cm^{-1} band of D*c*HU*t*B, being assignable to the *out* form.[11] It is suggested that the larger X atom of *R*TU*t*B enhances the steric hindrance between substituent and C=X group in comparison with *R*U*t*B since band A of *R*TU*t*B appears always and more strongly than the corresponding band of *R*U*t*B.

Taking into account the N–H frequencies of D*R*U*R*′ higher than those of *R*U*R*′,[11] the spectra of D*R*TU*R*′ (broken lines, Fig. 1) indicate that DMTUM exist completely as the *trans* form, while D*i*PTUM and D*c*HTUM exist completely as the *out* form. It is concluded that the assignment of band A to the *out* form is reasonable from a steric point of view.

Out-of-plane N–H Group. The *out* N–H frequencies seem to be sensitive to the opposite alkyl group, *R*, in *R*TU*t*B; *R*TU*t*B with *R*=M or *i*B being the highest in frequency, *R*=other primary alkyls medium, and *R*= branched alkyls the lowest. The situation was the same for all three solvents.[16] MTU*t*B shows three bands and a shoulder E (Fig. 2). We assign band A=the *out*, B=the *trans* methyl, and D=the *trans* *t*-butyl N–H absorptions. Band B (the *trans* methyl) is considerably weaker than band D (the *trans* *t*-butyl), although in the absence of isomerism the *trans* methyl band of *R*U*R*′[9] and of secondary amides[17] have larger molar extinction coefficients than the other *trans* bands.

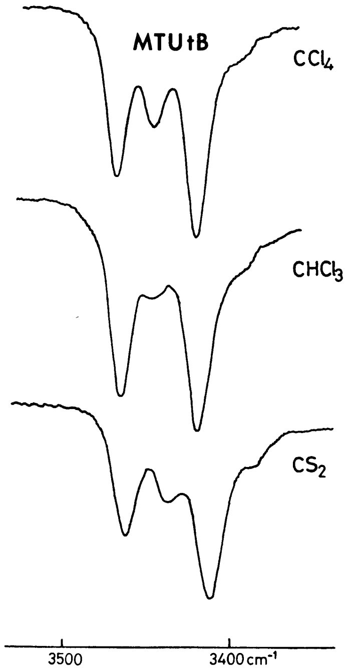


Fig. 2. Solvent effects on the infrared spectra of MTU*t*B.

By changing the solvent from CCl_4 to $CHCl_3$ the intensity of band A seems to increase at the expense of the weak band B (Fig. 2). The two bands were observed to be temperature dependent but in the opposite direction to each other. Other *R*TU*t*B with *R*=E, P, *i*B, and B were expected to show bands C and D. However, band C did not appear even as a shoulder. The component of band C is considered to be weakened by the appearance of band A.

From the facts mentioned above it is suggested that it is not the N–H group with the bulky *t*-butyl group but the N–H group in the opposite part that is predominantly out of the skeletal plane, though this seems to be unlikely. However, the suggestion may have validity if we consider that it is not the bulkiness of the substituent attached to the one N–H group, *R*′, but that of the opposite substituents, D*R*, in D*R*U*R*′ that plays an important role in the rotational isomerism.[11] This can be interpreted in terms of the steric hindrance between the *t*-butyl group and the sulfur atom, and of the stronger electron-releasing inductive effect of the *t*-butyl group. The hindrance may weaken the resonance effect of the skeleton. While the inductive effect, which would be expected to increase the electron density on the nitrogen atom, may strengthen the double-bond character on the N–C link with the *t*-butyl group more strongly than that on the other N–C link. Accordingly, these effects would make only the N–H link with the *R* group out-of-plane (the *trans-out* conformation).

The amount of the *trans-out* conformation was roughly estimated from band-intensity data; (*R* in *R*TU*t*B, %) M or *i*B, 60%; E, P, or B, 70%; *i*P or *s*B, 75%; and *t*B (=*s*-D*t*BTU), 90%.

Energy Difference. We carried out the analysis on the *trans-out* equilibrium using the 3452 (the *out*) and 3418 cm^{-1} (the *trans*) bands of *s*-D*t*BTU in CCl_4 (15.5—85.3 °C). Each band-intensity curve was in good agreement with the corresponding Lorentz curve calculated for bands A and D except for a slight deviation on the lower frequency side of band D. The presence of band E (O. D. <0.05) and the slope of the overtone band near 3150 cm^{-1} (O. D. <0.02 at 3400 cm^{-1}) were analyzed to give the deviation. The energy difference between the *out* and the *trans* forms was found to be $\Delta H=430\pm100$ cal mol^{-1} from area-intensity data ($\Delta H=380\pm100$ cal mol^{-1} from peak-intensity data). The ΔH value is consistent with the value 500 ± 200 cal mol^{-1} of Rao *et al.*[5] for the *cis-trans* forms estimated in the first N–H overtone region.

Band E. Most of the spectra of *R*TU*R*′ have this band as a shoulder. By examining the solution spectra at different temperatures and concentrations, band E was confirmed to be no associated band, being assignable to the N–H vibration from a certain form in a rotational isomer, probably the *cis* form. Despite some uncertainty in frequency the band of *R*TU*R*′ with both primary alkyl groups is slightly higher than that of the other *R*TU*R*′.

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15) Here, isobutyl and other primary alkyl groups will be treated as one type, C, though the N–H group with an isobutyl group shows a slightly higher-frequency band than the group with other primary alkyl groups (Ref. 7).

16) The data in the $CHCl_3$ and CS_2 solutions are omitted: The change of solvent from CCl_4 to CS_2 lowered band A by 6—8 cm^{-1} and bands B—D by 10—12 cm^{-1}, and the difference of lowering made bands A and B in MTU*t*B more distinguishable (Fig. 2). The spectra in the $CHCl_3$ solution gave similar data to those in the CCl_4 solutuon.

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