Slow Rotation around the Nitrogen–Aryl Bond in Ureas†

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MUCH has been reported of the slow rotation, on the ^{1}H n.m.r. time scale, around the nitrogen–aryl bond in *o*-substituted anilides and related compounds,[1] but that for a urea only at very low temperature.[2] We report slow rotation in certain ureas at temperatures up to 180°.

The trisubstituted ureas were prepared by treating the suitable amine with methyl isocyanate,[3] and the disubstituted ureas by treating the amine with potassium cyanate.[4] Attempts to prepare the disubstituted ureas by treating ammonia gas or ammonium hydroxide with the appropriate carbamoyl chloride[3] were not successful. All compounds were purified by repeated crystallization. ^{1}H N.m.r. spectra were measured with a Varian A-60 spectrometer.

The relative free energies of activation (ΔF^*) in the Table were calculated from the exchange broadening[5] (fast exchange limit) of the quartet from the α-protons of the ethyl group in the ureas. A precise signal-shape analysis of the collapse of the ABX_3 pattern was not attempted. The data in the Table were obtained at temperatures where the exchange broadening was the same for all the compounds [except (V)]. The comparison was made when the ratio of heights a : b = 0·3 (see Figure 1). [A slight correction had to be estimated for compound (II) because the NH signals overlapped.] The β-methyl signals were used as internal standards to verify that the spectrometer contribution to broadening was approximately constant. The rotation rate is assumed to be constant when a : b is constant. Values for ΔF^* were calculated for rate constants of 100 and 1000 sec.$^{-1}$; The Table shows that the *relative* values are the same for both rates. The errors in ΔF^* values on an absolute basis are not known. Compound (V) did not clearly resolve into a quartet even at 170°; at 180° it decomposed. However, by comparing the signal shape for (V) at 170° with the shapes obtained for the other

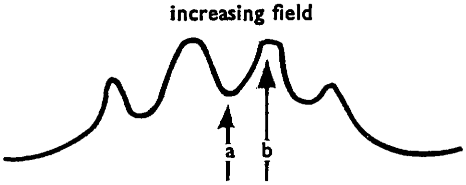

FIGURE 1

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Comparative kinetic data for ureas

Compound		Comparison temperature	ΔF^*, kcal./mol.[a] k = 100 sec.$^{-1}$	k = 1000 sec.$^{-1}$
$\underset{C_6H_4Me\text{-}o}{\mathrm{EtN}}\text{-CO-NHMe}$	(I)	46°	14·3	15·8
$\underset{R}{\mathrm{EtN}}\text{-CO-NHMe}$	(II)	81	16·0	17·6
$\underset{C_6H_4Me\text{-}o}{\mathrm{EtN}}\text{-CO-NH}_2$	(III)	96	16·7	18·4
$\underset{R}{\mathrm{EtN}}\text{-CO-NH}_2$	(IV)	119	17·8	19·6
$\underset{R}{\mathrm{EtN}}\text{-CS-NH}_2$	(V)[b]	190	21·1	23·3
$\underset{C_6H_4Me\text{-}o}{\mathrm{EtN}}\text{-CO-NR}^1\text{R}^2$	*c*	$\leqslant -50$	<10	<10

R = 1-naphthyl.

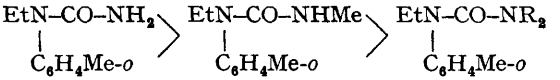
[a] Assumes transmission coefficient of unity. 250 mg. of compound diluted to 1 ml. with *o*-dichlorobenzene.

[b] Obtained from Eastman Organic Chemicals.

[c] Slow rotation is generally not observable for tetrasubstituted compounds dissolved in $CDCl_3$ above about −50°. Qualitative observation is reported for $\text{PhCH}_2\text{-}\underset{o\text{-MeH}_4\text{C}_6}{\text{N}}\text{-CO-}\underset{\text{C}_6\text{H}_4\text{Me-}o}{\text{N}}\text{-CH}_2\text{Ph}$

compounds it could be estimated that at 190°, a : b = 0·3.

The data in the Table, although necessarily approximate, establish that the barrier to rotation around the nitrogen–aryl bond decreases by a typical value of about two kilocalories between members of a series such as



$$\underset{C_6H_4Me\text{-}o}{\mathrm{EtN}}\text{-CO-NH}_2 > \underset{C_6H_4Me\text{-}o}{\mathrm{EtN}}\text{-CO-NHMe} > \underset{C_6H_4Me\text{-}o}{\mathrm{EtN}}\text{-CO-NR}_2$$

Substitution on the other nitrogen atom decreases the barrier to rotation around the nitrogen–aryl bond. This effect is unexpected on simple steric grounds. It would be expected that as the size of other groups in the molecule increased the barrier to rotation would also increase (see Figure 2). It follows that there must be some effect which more than offsets the steric effect of substitution on the other nitrogen atom.

One possible offsetting effect is the double-bond character or stiffness of the nitrogen–carbonyl bonds (amide bonds).[2] The activated state for rotation around the nitrogen–aryl bond may involve at least partial rotation around the amide bond on the same side of the urea molecule. In this manner, overcrowding of the approximate plane, $\rangle\text{N}-\overset{\overset{\text{O}}{\|}}{\text{C}}-\text{N}\langle$ would be avoided. A less-stiff amide bond is to be expected as larger groups are substituted into the urea molecule. The ground state of the molecule should become increasingly non-planar as larger groups are substituted. Since the double-bond character of the amide bond depends on $\cos^2\theta$, where θ is the angle between the plane of the nitrogen atom and its substituents and the plane of the carbonyl group and its substituents, the stiffness of the amide bond must decrease. Thus, it can be seen

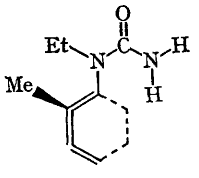


FIGURE 2. *Ground state for compound* (III).

that while the ground and activated states may both be increased in energy, the ground state gains more than the activated state and the barrier to rotation is decreased.

It is also possible that a more subtle effect operates. In general the double-bond character of the amide bond seems to be much less in ureas than in amides.[2] At least two factors may contribute to this. ((1) competitive conjugation between the two amide bonds with the carbonyl bond; (2) steric effects that prevent simultaneous planarity of the carbonyl group with both nitrogen atoms and their substituents; *i.e.* steric competition. Steric competition is most severe in the tetrasubstituted ureas. If one nitrogen atom and its substituents are rotated and the competition reduced, the consequent increase in molecular energy may be largely offset by the increased conjugation permitted to the other nitrogen atom.

A role for the double-bond character of the amide bond in increasing the barrier to rotation around the nitrogen–aryl bond is also indicated from comparison of data for the thioureas with the ordinary ureas in the Table. The amide bond of thio-amides is known to have more double-bond character than in ordinary amides.

The increased barrier for napthalene as compared to *o*-methyl phenyl derivatives demonstrates that rather straight-forward steric factors can be important in these molecules. The rigid fused ring is more effective in slowing rotation than is the methyl group.

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