Proton Magnetic Resonance Studies of Rotational Isomerism around the 2-Propyl–Nitrogen Bond in Some Thionamides

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Slow rotation around the 2-propyl–nitrogen bond in five N,N-di-2-propyl thionamides was studied by proton magnetic resonance (pmr). The barrier (ΔF^*) to this rotation in N,N-di-2-propyl thionacetamide is *ca.* 14 kcal/mol. The pmr signal sets were all assigned to specific rotational isomers and to *cis* and *trans* 2-propyl groups within each isomer.

We have previously reported evidence for slow rotation around the *sec*-alkyl–nitrogen bond in some N,N-di-*sec*-alkyl amides.[1] This evidence was in some cases indirect and in others depended on proton magnetic resonance (pmr) spectra that were necessarily of poor quality because of the complex molecules and low temperatures required to demonstrate the effect. However, when sulfur replaces oxygen, rotation slows around the (thio)carbonyl–nitrogen (amide) bond[2-9] and stiffens the amide framework. The more rigid framework and the larger size of the sulfur atom should work together to increase rotational barriers and to make the effects more readily observable. This paper reports a study of rotation in five N,N-di-2-propyl thionamides, $CH_3C(S)N(2\text{-}Pr)_2$ (I), $PhCH_2C(S)N(2\text{-}Pr)_2$ (II), 2-propyl $C(S)N(2\text{-}Pr)_2$ (III), $CH_3CH_2C(S)N(2\text{-}Pr)_2$ (IV), and cyclohexyl-$C(S)N(2\text{-}Pr)_2$ (V).

Experimental Section

Spectra were obtained at 60 MHz with a Varian A-60 and a Varian HR-60 spectrometer. Decoupling was done by strongly irradiating the methine protons and observing the methyl doublet collapse. Complete decoupling was obtained in all cases. Samples for signal shape analysis were sealed under nitrogen.

The thionamides were prepared in the conventional manner[10] by treating the corresponding amides in boiling xylene with a 100% excess of P_2S_5. Initial purification was obtained by vacuum distillation. Small quantities of unconverted amides usually distilled with the thionamide but were easily removed by crystallization of the distilled product. Methylcyclohexane was the best and most convenient solvent for this purpose. Pure white crystals were obtained, which tended to yellow on standing. Purity and identity were confirmed by pmr and infrared (ir) spectra and by elemental analysis.

Signal Shape Analysis.—Signal shape analyses to provide rotational rate data is complicated for these compounds because of the necessity for treating exchanging multiplets and because two types of rotational processes are involved.[1] However, an approximate treatment was developed and applied to the simplest of the molecules studied, $CH_3C(S)N(2\text{-}Pr)_2$. This treatment is described briefly below.

Signal shape analysis to obtain rotational barriers was based on the Gutowsky–Holm equation.[11] Nakagawa's[12] formulation of this equation was used to calculate spectra for exchanging carbonyl methyl groups [$CH_3C(S)$ singlets]. For exchanging β-methyl groups (CH_3CHCH_3, doublets), the signal shapes for two sets of two exchanging singlets were superimposed. For exchanging methine protons (CH_3CHCH_3, septets), seven sets of two exchanging singlets were superimposed. Calculated spectra were then matched with observed spectra to obtain exchange times. This type of superposition procedure has already been used and reported.[13] Further details of our application of this method here will be reported elsewhere.

Signal shape analysis gave $\Delta F^* = 19$ kcal/mol at 105° for the rotational barrier around the amide bond and 14 kcal/mol at −13° for the barrier to 2-propyl rotation.

Results

Description of the Spectra (See Figure 1). $CH_3C(S)N(2\text{-}Pr)_2$ (I).—At high temperature (>130°), the β-methyl protons give one doublet, the $CH_3C(S)$ protons one singlet, and the methine protons one septet, as would be expected for rapid rotation around all relevant bonds. Below this temperature, the methine signals split into two broad sets of signals of equal intensity. The expected two doublets for β-methyl protons do not at first appear; the splitting into two doublets, very closely spaced, is observable only below 70°. The doublet at higher field is very much broader than the doublet at lower field. With deuteriotoluene as the solvent, separate doublets are observable even at 100°. The near degeneracy of β-methyl signals is removed in this solvent. However, the signals are reversed—the broadened doublet comes to lower field.

As the temperature is lowered below 100°, the high-field methine set sharpens and can be resolved into the expected septet. On the other hand, the low-field methine set broadens at first as the temperature is lowered. A sharp septet is not obtained until *ca.* −20°. At this point, the high-field methine signals obviously consist of *two* or more septets. The high-field set of signals is more intense than the low-field septet (*ca.* 1.6:1).

Below room temperature, the β-methyl doublets broaden but finally emerge as four doublets at −20° with intensity 3:1:3:1 (high field → low field) for $CDCl_3$, 1.5:1:1.5:1 for C_7D_8; 1.3:1:1.3:1 for CH_3OH; and 1.4:1:1.4:1 for deuterioacetone. At the same temperature the signal for $CH_3C(S)$ splits into two signals of the same ratios for the respective solvents.

No further changes in any signals were observed down to −80°, the lowest temperature obtainable without precipitation in a 50:50 mixture of $CDCl_3$–$CFCl_3$ (except for some preferential broadening of the doublet of triple intensity at higher field).

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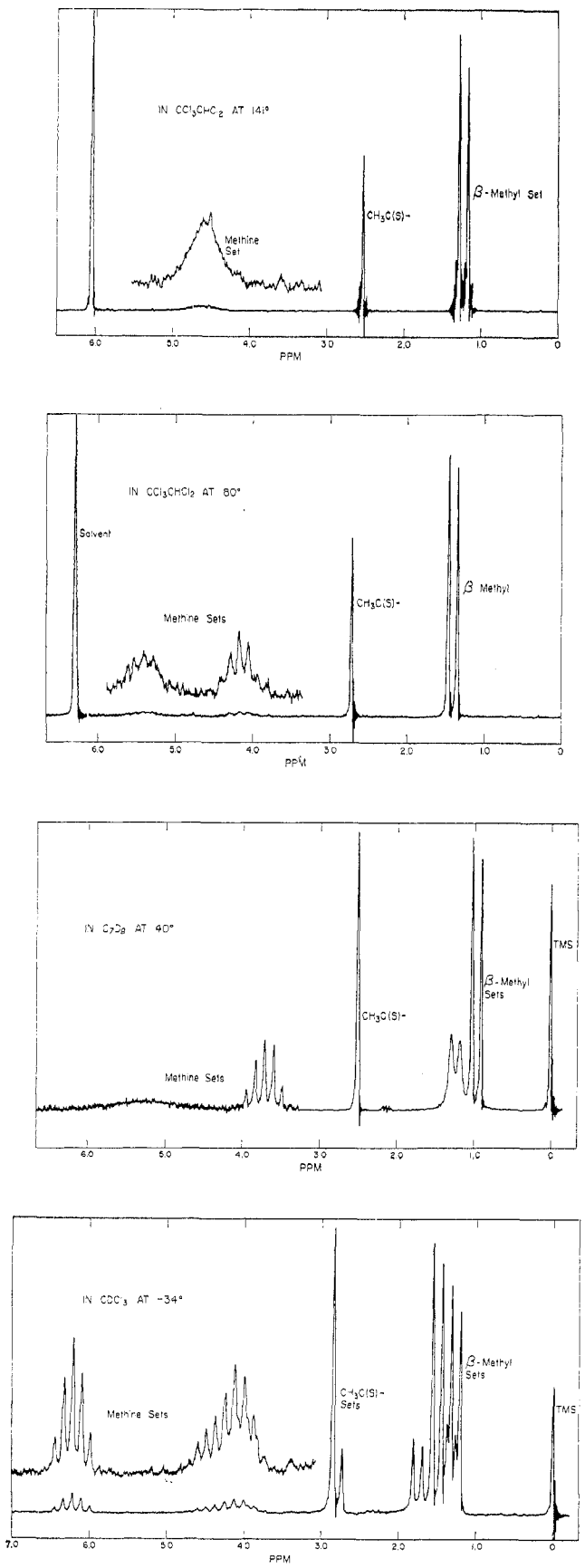

Figure 1.—The pmr spectra of $CH_3C(S)N(2\text{-}Pr)_2$.

We interpret the changes on coming down to *ca.* 80° as being due to the slowing of rotation around the thiocarbonyl–nitrogen (amide) bond (except for the selective broadening of one doublet). The barrier, 19 kcal/mol, is normal for rotation around this bond. Corresponding changes take place in N,N-di-2-propyl acetamide, but at *ca.* 70° lower temperature. An increase of 2–6 kcal in the barrier to rotation around the amide bond is to be expected in going from the amide to the thionamide.

We interpret the further sequence of changes on down to *ca.* −20° as the slowing of rotation around the 2-propyl–nitrogen bonds. Two rotational isomers exist on the pmr time scale. Each isomer is a separate and distinct molecule with a complete set of signals. These sets are assigned to the isomers in Table I. One isomer (major isomer) is about three times as abundant as the other (minor) in $CDCl_3$, 1.4:1 in $CD_3C(O)CD_3$, 1.3:1 in CH_3COH, and *ca.* 1.5:1 in toluene. Either one of these apparent isomers represents the average of two rapidly interchanging isomers, or one of the three expected isomers is missing.[1]

A few spectra of $CH_3CH_2C(S)N(2\text{-}Pr)_2$ (IV) were also obtained. These closely paralleled those for I. An isomer ratio of 3:1 was obtained at low temperature in $CDCl_3$. The degeneracy of the β-methyl doublets at higher temperature was also observed. Because of this close parallel, IV was not investigated further.

$PhCH_2C(S)N(2\text{-}Pr)_2$ (II).—The change of the pmr spectrum of this compound with temperature closely resembles that of the acetamide (I). The β-methyl doublets, however, are well separated at all temperatures. This, in part, may reflect the effect of the anisotropic field of the benzene ring. The chief difference between the compounds is that the isomer abundance apparently is reversed. The isomer with methine signals at low field is now the minor isomer with only one third the abundance of the major isomer in $CDCl_3$.

$2\text{-}PrC(S)N(2\text{-}Pr)_2$ (III).—This compound exhibits the spectra characteristic of slow, intermediate, and rapid rotation around the amide bond. No signals are obtained that could be ascribed to rotational isomerism. However, the low-field methine signal set is selectively broadened over a wide temperature range (−10 to 70°) in a manner reminiscent of the oxygen analog at lower temperature.[1] The high-field set is sharp throughout this range and downward. This behavior suggests that one isomer (with low-field methine) predominates highly at low temperature, but that a small amount of a second isomer is present in the region of intermediate exchange at higher temperature.

Almost precisely the same behavior was obtained in preliminary work with cyclohexyl-$C(S)N(2\text{-}Pr)_2$ (V). For that reason V was not investigated in further detail.

Decoupling Experiments.—In both the major and minor isomers of I, the low-field methine proton was coupled to the high-field methyl group. The same results were obtained in $CDCl_3$ and in C_7D_8. The same coupling behavior, low methine to high methyl, was observed for II and III.

Discussion

The behavior of these thionamides can be rationalized within the framework of hypotheses utilized to explain the behavior of related amides.[1] The symbolism of the previous study[1] is repeated here to aid in the discussion.

This symbolism can be visualized with the aid of Figure 2. It is assumed that the angle θ for the methine

TABLE I

PROTON SIGNALS[a] AT −20°

Compd[b]	Solvent	β-Methyl		Methine		R-C(S)-	
		Minor	Major	Minor	Major	Minor	Major
$CH_3C(S)N(2\text{-}Pr)_2$	$CDCl_3$	1.32, 1.76[c]	1.27,[c] 1.52	~4.0,[c] 4.36	4.12, 6.21[c]	2.76	2.84
	$C_6D_5CD_3$	0.73, 1.68[c]	0.85,[c] 0.90	~3.4,[c] 3.80	3.39, 6.32[c]	2.40	2.53
	CH_3OH	1.27, 1.67	1.20, 1.43	Overlap	~4.1, 6.12	2.63	2.72
	$CD_3C(O)CD_3$	1.30, 1.70	1.18, 1.47	~4.0, 4.53	4.12, 6.19	2.65	2.73
$PhCH_2C(S)N(2\text{-}Pr)_2$	$CDCl_3$	1.32,[c] 1.46	0.95, 1.76[c]	6.2[c]	3.83,[c] 4.3	4.37 (CH_2); only one signal; 7.34 (complex) (aromatic)	
	70% C_7D_8–30% $CDCl_3$	1.07,[c] 1.11	0.59, 1.70[c]	3.53, 6.3[c]	3.37,[c] 4.06	4.24 (CH_2); only one signal; 7.2 (complex) (aromatic)	
$2\text{-}PrC(S)N(2\text{-}Pr)_2$	$CDCl_3$	*d*	1.23,[c] 1.50		4.10, 6.32[c]	3.37 (methine)	1.33 (β-methyl)
	$C_6D_5CD_3$		0.88,[c] 1.08		3.48, 6.42[c]	3.07	1.33

[a] In parts per million from tetramethylsilane. [b] 100 mg + 0.5 ml of solvent. [c] Assigned *cis* to sulfur. [d] No observable minor sets for this compound.

proton of a 2-propyl group (a tetrahedron) may assume multiples of 60° with respect to the amide frame (a trigonal plane on the pmr time scale) to produce minima of rotational energy. Since six such minima exist for each 2-propyl group, there are 36 combinations or conformations. These can be symbolized as C_iT_j, where the index 1 corresponds to $\theta = 30°$, 2 to $\theta = 90°$, etc., C represents the 2-propyl group *cis* to sulfur and T, *trans* to sulfur. However, six of these conformations (where $j = i + 3$) ought to have lower energy than the rest; these six minimize the repulsion between β-methyl groups. Figure 2 represents one of these conformations.

The six isomers exist as three *dl* pairs: C_1T_4, C_6T_3; C_2T_5, C_5T_2; and C_3T_6, C_4T_1. The spectrometer does not respond to the *dl* distinction within a pair. A maximum of three complete signal sets are to be expected. However, since these isomers are asymmetric molecules, the β-methyl groups within a 2-propyl radical are nonequivalent and could give separate signals, provided that interconversion of *d* and *l* forms (racemization) is slow on the pmr time scale. Similar nonequivalence would be expected for all other geminal pairs or other appropriate arrays.[14]

All transitions between the six isomers are accomplished *via* synchronous (or immediately sequential) rotation of 2-propyl groups. Rotation of one 2-propyl group at a time produces one of the 30 remaining high-energy conformations ($j \neq i + 3$). Of these 30 the conformation(s) that is appropriate might serve as the transition state between the favored six isomers, the C_iT_j with $j = i + 3$. Rotation into a transition state does not of itself complete an isomer (or proton site) interchange, but must be followed by rotation of the other group.

Signal Assignments for I (See Table I).—The C_1T_4, C_6T_3 *dl* pair is responsible for the low-field methine signal. The *cis* methine proton for this pair is close to the thiocarbonyl group and therefore deep into the magnetic field that surrounds the amide frame. The average value of θ_C in this pair (see Figure 2) may be smaller than 30° because the methine proton is smaller than the β-methyl groups. This places the methine protons near the amide plane. Positions both near to the amide plane and near to the (thio)carbonyl group

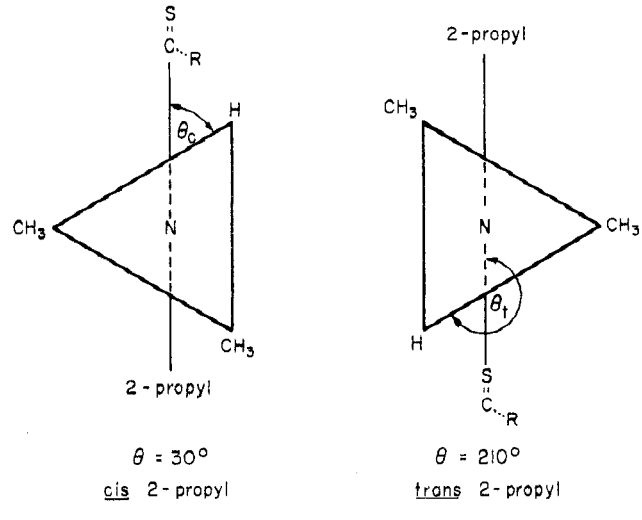

Figure 2.—Conformation C_1T_4.

are known to be very much deshielded.[15–20] The *trans* methine proton, while near the amide plane, is turned away from and is remote from the amide field, and resonates at higher field.

In the solvent toluene, the high-field methine signal of the major isomer is shifted 0.7 ppm upfield from its position in $CDCl_3$, but the low-field methine signal is shifted downfield by 0.11 ppm. This behavior is consistent with the assignment of the high-field methine signal to the *trans* methine proton.[21]

From the decoupling experiments, the high-field major doublet (in $CDCl_3$) is assigned to the β-methyl protons of the *cis* 2-propyl group of the major isomer. This doublet is shifted upfield in toluene, but not so much so as the other (*trans*) doublet. This, too, is consistent with the assignment.[21]

For the minor isomer, the low-field β-methyl doublet is assigned *cis*. This doublet shows the smallest shift

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(almost no shift) of the four doublets. This would be expected for the *cis* β-methyl groups of the C_3T_6, C_4T_1 *dl* pair. For this pair the *cis* β-methyl groups are very close to the sulfur atom and therefore not affected by solvent.

From the decoupling experiments the high-field minor methine signals are assigned *cis*. This methine proton is close to the amide plane, but remote (in the C_3T_6, C_4T_1 pair) from the amide field, while the *trans* methine proton is deeper in this field. The *trans* signal is, therefore, found downfield. This signal also has the larger solvent shift of the two minor methine signals.

There is one apparent contradiction in these assignments. They require that methine protons close to sulfur have downfield shifts relative to methine protons remote to sulfur, but that β-methyl signals be upfield for β-methyl groups near to sulfur. We believe that this contradiction is not real and that it can be explained on the basis of whether the proton(s) in question is rotated nearly into the amide plane or well out of this plane. The amide field is deshielding in and near to the amide plane but shielding out of plane.[15-20]

As pointed out, for all of the C_1T_4, C_6T_3, C_4T_1, C_3T_6 isomers and for both *cis* and *trans* positions, the methine protons probably lie close to the amide plane—closer than 30°. The minimum energy for all these isomers requires a distortion from rigid 60° intervals. Such a distortion places the methine protons, with their much smaller bulk, near the amide plane and the methyl groups as much out of this plane as possible. *A major factor in setting any amide conformation must be the need to exclude as much as possible from this crowded plane.*

Our assignments also ignore the C_2T_5, C_5T_2 *dl* pair. We have in our discussion so far proceeded as though this isomer did not exist in significant abundance. Actually, the two signal sets could be assigned in any of several ways: (A) major (1)–minor (3); (B) major (1)–minor (2); or (C) any of a family of combinations of major (1 + 2 or 3)–minor (2 or 3) (the numbers designate the *dl* pair according to the lower C index occurring in the pair, *i.e.*, C_1T_4, C_6T_3 = 1). The only straightforward and certain requirement is that 1 make the major contribution to the major signal set. We have chosen to exclude B, since the barrier between the *d* and *l* isomers within the pair 2 ought to be exceptionally large. Racemization within this pair would involve a maximum transfer of β-methyl groups across the amide plane. However, there is no direct evidence for such a slow racemization. For 1 and 2 pairs only, one methyl group at a time needs to be transferred across the plane, and racemization might be fast, as is observed. Also the effects of toluene seem to exclude B. There is no obvious argument to exclude C; C might very well have been included in our discussion, but was not, since its inclusion would not alter the substance of the discussion substantially but would certainly complicate it.

Assignment for II.—The low-field methine signal set is assigned to the *cis* methine proton C_1T_4, C_6T_3 by the same arguments as for I. Since the high-field minor doublet is coupled to this methine, it too must be assigned *cis* in this *dl* pair. The rest of the assignments are also the same as for I from the decoupling experiments and the effects of toluene. No separate minor CH_2 signal is observed.

Assignment for III.—There is only one signal set for this compound and therefore either only one rotational isomer (1 = C_1T_4, C_6T_3) or a rapidly exchanging mixture of 1 + 2 or 3 that is dominated by 1. The selective signal broadening of the low-field methine signal suggests that there is a mixture at high temperature that approaches pure 1 at low temperature.

This picture is, of course, too simple, since now there is a third 2-propyl group and therefore good reason to believe that a triple designation—$C_iT_jS_k$—is required, where S designates the 2-propyl group that is attached to the thiocarbonyl group. The resulting array of 216 possible isomers leads to all sorts of possible complications.

However, one consideration may still limit the real situation to the original six likely ground states. If the 2-propyl groups are indeed so much interacting as to be interlocked, then specification of the rotational state of one group sets the conformation of the other two; thus C_1 requires T_4 and S_1. The sulfur atom may be regarded as the spatial buffer that prevents direct interaction of C (2-propyl) with S (2-propyl).

The close correspondence of chemical shifts for III with the major isomer of I suggests that the dominant isomer of III is C_1T_4, C_6T_3 for the N-2-propyl groups. Subject to the consideration of the paragraph immediately above, the full designation must be $C_1T_4S_1$, $C_6T_3S_6$.

Future Work.—Further experimental work is required to adequately test this model of interlocking tetrahedral rotors rotating against a trigonal frame. In particular, it would be desirable to improve isomer signal assignments to establish whether mixtures of isomers or a single isomer produced observed signals.

We have also not attempted to deal with the question of relative isomer abundance. There are observable differences in these abundances, and plausible explanations, but we have not yet enough data to construct a systematics or a theory to predict such abundances.

Registry No.—I, 23264-07-5; II, 23264-08-6; III, 23264-09-7.

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