Table II. ESR Data for C222- and C221-Complexed Potassium 9-Fluorenone Ketyl

	C222			C221
solvent	a_C, G	K	$\Delta H°$,[a] kcal/mol	a_C, G
DME	1.97	9.65	−3.8	3.70
THF	2.20	3.53	−1.7	3.72
MTHF	2.50	1.59	−0.7	3.72
DMTHF	2.86	0.71	*b*	3.80
toluene	3.16	0.33	*b*	3.90
toluene + hexane	3.61	0	*b*	

[a] Enthalpy change for conversion of (C222 K^+ F^-) to (C222 K^+)F^-. [b] The ^{13}C hyperfine splitting is independent of temperature.

space between the $-(CH_2CH_2O)_2CH_2CH_2-$ bridges of C222 permits the ethereal oxygen atom to a considerable extent to approach the sodium ion, although the oxygen atom still behaves as a member of the second sphere of the solvation shell. The extent of this approach depends on the steric factor of ethereal molecules. In (C222 Na^+ F^-), on the other hand, the bridges are packed together more closely, so that the ethereal oxygen atom is squeezed out of the interstitial space. Thus the separation between the sodium ion and solvent molecules is increased from (C222 Na^+)F^- to (C222 Na^+ F^-). The change in the solvation energy of the sodium ion in this process will be of comparable order of magnitude to the aforementioned change in the solvation energy of the F^- ion in aromatic hydrocarbons and should be able to become the dominant factor for the observed changes in the ion pairs.

K–C222 Complexes. The results of ESR studies of the interaction between the C222-complexed potassium ion and the fluorenone anion are summarized in Table II. In analogy with the Na–C222 complex, a large solvent dependence of the ^{13}C splitting can be explained in terms of the equilibrium between (C222 K^+ F^-) and (C222 K^+)F^-. The low-temperature value of the ^{13}C splitting in DME or THF (1.80 G) is identical with that obtained with the C222-complexed sodium keyl in DME or THF at low temperatures. This suggests that in the cryptand-separated ion pair the value of the ^{13}C splitting is independent of alkali metal ion in the cavity. The concentration ratio, K, of (C222 K^+)F^- to (C222 K^+ F^-) was calculated by assuming that the ^{13}C splitting of (C222 K^+ F^-) is 3.61 G which is the value in a 1:1 mixture of toluene and hexane, and the ^{13}C splitting of (C222 K^+)F^- is 1.80 G. In the same solvent, K and $\Delta H°$ values of the potassium complex are of comparable order of magnitude to those for the sodium complex.

K–C221 Complexes. In contrast with the ^{13}C splitting of the C222-complexed sodium or potassium ketyl, that of the cryptand 221-complexed (C221) potassium ketyl exhibits only a small solvent dependence, as listed in Table II, and is independent of temperature in the range +60 to −60 °C. Furthermore, the ^{13}C splitting in the DME or THF solution is even greater than the value assumed for the ^{13}C splitting of (C222 K^+ F^-) (3.61 G). On the basis of these facts, we can conclude that, within the scope of solvent used, the vast majority of the ionic species in solution is a contact ion pair (C221 K^+ F^-) although a slight solvent dependence of the ^{13}C splitting suggests the existence of the equilibrium of (C221 K^+ F^-) and (C221 K^+)F^-. The X-ray study of the crystal structure of C221-complexed potassium thiocyanate[20] has shown that the K^+ ion lies not in the center of the cavity of C221 but between the two $-(CH_2CH_2O)_2CH_2CH_2-$ bridges and the SCN^- ion comes in contact with the K^+ ion. The present results indicate that the structure of the K–C221 complex in the solid will be held in solution and the fluorenone anion can easily approach the potassium ion to form a contact ion pair.

Experimental Section

Optical spectra were obtained on a Shimazu MPS-5000 spectrometer. ESR spectra were obtained on a JES-PE ESR spectrometer. The anion radical was prepared by reduction of 9-fluoroenone with a sodium or potassium mirror in a solution containing an excess of cryptand. All operations were carried out under high vacuum.

Cryptand 222, cryptand 221, and 9-fluorenone containing 90.9% enriched carbonyl ^{13}C were purchased from E. M. Merck and used without further purification. Ethereal and hydrocarbon solvents were used after being dried with sodium hydride or Na–K alloy.

Gear Effect. 9.[1] Steric Anisotropy of Space through "Januslike" Substituents. A Dynamic ^1H and ^{13}C NMR Study of 1,3-Dibenzyl-4,5-diisopropylimidazoline-2-thione

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Contribution from the Division of Organic Chemistry 3, Chemical Center, University of Lund, S-220 07 Lund 7, Sweden, and I.P.S.O.I., Centre Universitaire St. Jérôme, F-13013 Marseilles, France. *Received March 28, 1980*

Abstract: A molecule has been designed which clearly demonstrates the steric anisotropy of space created by two geared isopropyl groups: 1,3-dibenzyl-4,5-diisopropylimidazoline-2-thione (A). A dynamic ^1H and ^{13}C NMR spectroscopy study of A gives evidence of three rate processes. The high-energy process ($\Delta G^{\ddagger}_{229K}$ = 11.5 ± 0.1 kcal mol^{-1}) has been identified as the exchange of the isopropyl groups between two geared conformations. The two other processes arise from slow rotation of the two benzyl groups, but the magnitudes of the barriers, in this apparently symmetrical (C_{2v}) molecule, are quite unequal, $\Delta G^{\ddagger}_{205K}$ = 10.6 ± 0.1 and 8.5 ± 0.1 kcal mol^{-1}, respectively. The reason for these unequal barriers is found in the geared conformational state of the isopropyl groups in which they have one bulky and one nonbulky face. The comparatively complex exchange system of the benzylic methylene protons, the conformations of the isopropyl and benzyl groups, and the mechanism for the conformational interconversions are analyzed. The implications of these results for other unsymmetrical substituents and for the possible role of such groups in the steric control of the selectivity of enzymes is emphasized.

From a steric point of view, the isopropyl group is very versatile since it can be as bulky as a *tert*-butyl group when it is viewed from the side of the two methyl groups or as small as a methyl group when it is considered from the opposite side. Thus, conformational control of reactivity (and selectivity) may be generated from this "januslike"[2] group depending on its induced confor-

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(1) Part 8: B. Blaive, C. Roussel, J. Sandström, and J. Metzger, *Can. J. Chem.*, in press.

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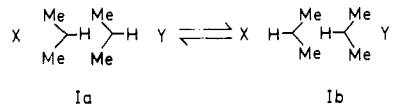
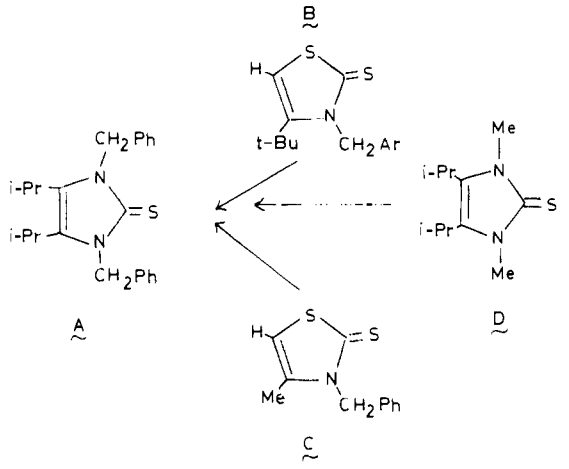
Scheme I



Ia Ib

Scheme II



A B C D

mational state. Furthermore, we have already shown[3,4] that polyhedral substituents like alkyl groups can be involved in a "geared" system when they are in close contact, and several examples are now available in which the interaction of two ortho isopropyl groups leads to a structural block in which the two isopropyl groups act in combination (Scheme I).[5]

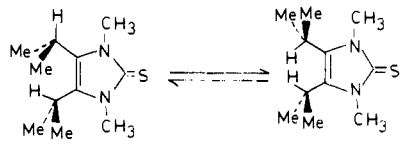
In fact, such a structural block built with two isopropyl groups in a "geared" conformation is also "januslike" since it has a bulky face and a nonbulky one. Thus, in conformation Ia, the flanking substituent X is subjected to the strain of a *tert*-butyl-like substituent, whereas in conformation Ib it is under the influence of a methyl-like one (and vice versa for Y). When X = *Y*, two remote identical substituents in the same molecule should exhibit different dynamical properties, and thus it is possible to illustrate the two extreme conformational states of an isopropyl group in the same molecule.

The purpose of this paper is to show that isopropyl groups involved in a "geared" system can induce large differences in dynamical behavior between apparently symmetrically situated groups, using a very simple model: 1,3-dibenzyl-4,5-diisopropylimidazoline-2-thione (A).

Design of A. This compound must fulfill several conditions to be a useful and convincing model. (a) It must have a time-average C_2 axis with respect to the two isopropyl groups. (b) The two isopropyl groups must be in a geared conformational state. (c) The observed dynamical process must be sensitive to the conformational state of the isopropyl groups. (d) The dynamic process must be accessible to study by DNMR.

The design of A as model compound results from previous work on the dynamic stereochemistry of compounds B–D (Scheme II).

Scheme III



I II

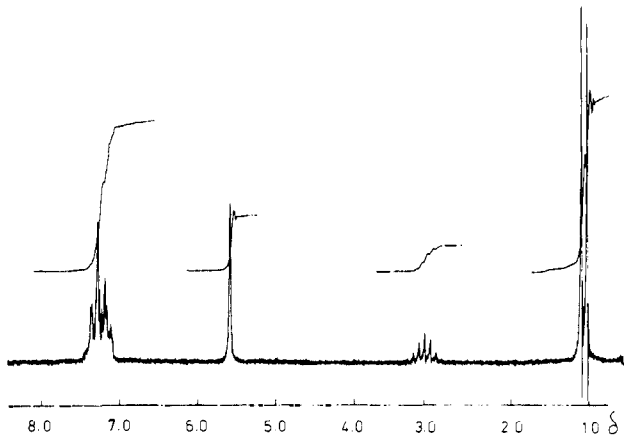


Figure 1. Ambient-temperature 100-MHz ^{1}H NMR spectrum of A in chloroform-*d*.

In 3-(4-methoxybenzyl)-4-*tert*-butylthiazoline-2-thione, B, we have shown that the barrier to rotation of the benzyl group around the N–C bond is 12.1 kcal mol^{-1} and that the transition state corresponds to the aromatic ring passing the molecular plane toward the thiocarbonyl group.[6] In C, the corresponding barrier is 7.2 kcal mol^{-1}, but now the aromatic ring is opposed to the 4-methyl group in the transition state.[7] Thus the simulation of both a methyl and a *tert*-butyl group by the geared assembly of two isopropyl groups should induce, theoretically, a large difference in the dynamic behavior of flanking benzyl groups. Compound D exhibits two conformational states (Scheme III) in which I predominates (65 ± 2% at −110 °C). Previous work on thioamides and amides has shown that an increase of the size of the flanking substituents decreases the stability of conformation II.[4,8] Thus it was expected that the benzyl groups in A instead of the methyl groups in D should induce a conformation analogous to I for the isopropyl groups in A.

Experimental Section

Synthesis. A was prepared according to a previously described route to alkylimidazoline-2-thiones.[9]

Isobutyroin (3.7 g) and *N,N'*-dibenzylthiourea (4.7 g) were refluxed for 18 h in 50 mL of hexanol under azeotropic water elimination conditions. Most of the solvent was then evaporated. The resulting oil was treated with water and crushed ice. White crystals were formed and were recrystallized from ethanol/water (20/80): yield 35%; mp 123–125 °C. Mass spectrum: *m/e* (% relative intensity) 364 (73), 349 (6), 332 (5), 331 (20), 275 (4), 274 (12), 273 (61), 241 (3), 197 (7), 182 (4), 167 (4), 92 (8), 91 (100), 65 (6); mol wt, calcd for $C_{23}H_{28}N_2S$, 364.5. ^{13}C NMR [15.03 MHz, $(CD_3)_2O$, −20 °C]: δ 21.9 (CH_3), 26.1 (CH), 49.5 (CH_2), 127.5, 127.8, 129.2, 130.5 (phenyl), 138.9 (imidazoline ring).

NMR Measurements. The ^{1}H NMR spectra were recorded on a JEOL Model JNM-MH-100 and on a Bruker Model HX-270 NMR spectrometer. The ^{13}C NMR spectra were recorded on a JEOL Model FX-60 spectrometer operating at 15.03 MHz. All spectrometers were equipped with standard variable-temperature equipment. The samples were ca 0.4 M in dimethyl-d_6 ether[10] containing 20% toluene-d_8 and were degassed by three cycles of freeze-thawing under high vacuum before being sealed off. Me_4Si (^{1}H NMR) and $(CD_3)_2O$ (^{13}C NMR) were used

(2) In "Webster's Third International Dictionary", G. C. Merriam Co., 1971, the meaning of "januslike" is described as "acting or looking in opposite or contrasting ways".

(3) C. Roussel, A. Liden, M. Chanon, J. Metzger, and J. Sandström, *J. Am. Chem. Soc.*, **98**, 2847 (1976) and references cited therein.

(4) For a general discussion of the factors affecting the interaction of two isopropyl groups, see: (a) A. Liden, C. Roussel, T. Liljefors, M. Chanon, R. E. Carter, J. Metzger, and J. Sandström, *J. Am. Chem. Soc.*, **98**, 2853 (1976); (b) T. Liljefors and J. Sandström, *Org. Magn. Reson.*, **5**, 276 (1977).

(5) T. T. Tidwell, *Tetrahedron*, **34**, 1855 (1978); H. Forster and F. Vögtle, *Angew. Chem.*, **89**, 443 (1977); A. H. Cowley, R. W. Braun, and J. W. Gilze, *J. Am. Chem. Soc.*, **97**, 434 (1975); J. Bundon and W. B. Jennings, *J. Chem. Soc., Perkin Trans. 2*, 1052 (1976); K. Paxton and T. A. Hamor, *J. Chem. Soc., Dalton Trans.*, 647 (1978); Y. Taheda, T. Matsuda, and T. Tanaka, *Org. Magn. Reson.*, 98, (1977); Y. Taheda, T. Matsuda, and T. Tanaka, *Bull. Chem. Soc. Jpn.*, **51**, 398 (1978); H. M. Hutton, W. E. Hilbert, and V. Mark, *Can. J. Chem.*, 1261 (1978); P. Jennische and R. Hesse, *Acta Chem. Scand.*, **26**, 2799 (1972); F. M. Nicolaisen, *J. Mol. Struct.* 379 (1975); H. Iwasaki, M. Ito, and K. Kosayashi, *Chem. Lett.*, 1399 (1978).

(6) C. Roussel, B. Blaive, R. Gallo, J. Metzger, and J. Sandström, *Org. Magn. Reson.*, **14**, 120 (1980).

(7) Reference 6 and C. Roussel, R. Gallo, J. Metzger, and J. Sandström, *Org. Magn. Reson.*, **14**, 166 (1980).

(8) A. Liden, C. Roussel, M. Chanon, J. Metzger, and J. Sandström, *Tetrahedron Lett.*, 3629 (1974).

(9) G. Kjellin and J. Sandström, *Acta Chem. Scand.*, **23**, 2879 (1969).

(10) Deuterated dimethyl ether was prepared as previously described.[4a]

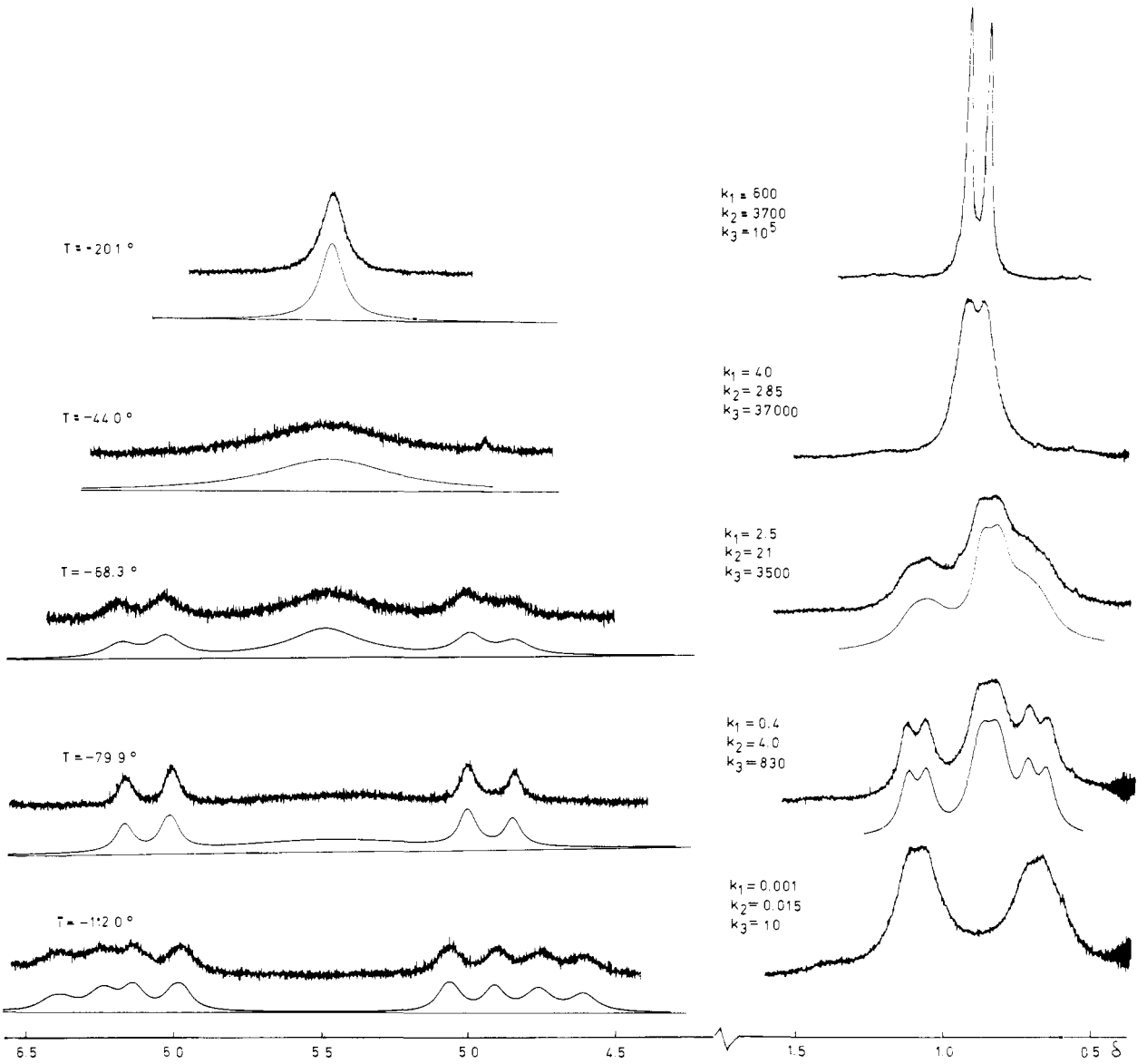


Figure 2. Experimental (100-MHz) and calculated spectra of the benzylic methylene protons and isopropyl methyl protons at various temperatures (solvent dimethyl-d_6 ether).

for the internal lock. Two drops of acetone were added to serve as resolution standard in the ^1H NMR experiments. Measurement of the temperature and T_2 was performed as previously described.[4]

The rate constants were evaluated by visual bandfitting of experimental to calculated spectra. The exchange-broadened $^{13}C\{^1H\}$ signals of the benzylic methylene groups were simulated by a simple symmetrical exchange doublet.[11] The ^1H resonances of the *i*-Pr methyl groups were simulated by superposition of the appropriate number of such doublets, suitably displaced to account for couplings to the methine protons and to differences in chemical shifts. Scaling factors were used to simulate second-order effects due to the couplings.

The methylene protons undergo a more complex exchange (see Figure 3) which may be described by four coupled AB cases, and the band shape had to be treated by the density matrix formalism. We used a slightly modified version of a previously described program, placed at our disposal by Nilsson and Carter.[12] The free energies of activation were derived according to the classical Eyring equation in the form of eq 1.

$$\Delta G^{\ddagger} = (4.575 \times 10^{-3})T[10.319 + \log (T/k)] \text{ kcal mol}^{-1} \quad (1)$$

Results

The ambient temperature 100-MHz ^1H NMR spectrum of compound A (0.4 M in $CDCl_3$) is shown in Figure 1. This spectrum is in agreement with a molecule that maintains C_{2v} symmetry as assumed for A under time averaged conditions.

At temperatures below −20 °C, the CH_2N and $CHMe_2$ resonances broadened. The methine proton resonance and the aromatic multiplet also showed minor temperature dependence, but the low-temperature spectrum was not resolved.

At −70 °C the CH_2N resonance appeared as one AB quartet (δ 4.93 and 6.17, J_{AB} = 16.7 Hz) *and* one broad ($\Delta\nu_{1/2}$ = 26 Hz) unresolved signal (δ 5.46; Figure 2). At still lower temperatures, the AB quartet further *sharpened* while the broad band inside the quartet *broadened* and completely disappeared in the base line at −90 °C. At −110 °C a new AB quartet (δ 4.60 and 6.46, J = 15.5 Hz) appeared.

However, as shown on the 270-MHz spectrum at −110 °C (Figure 3), these two AB quartets are actually made up of two AB quartets *each*, the high-field parts of which coincide pairwise and the low-field parts of which are separated by the value of ca. one coupling constant giving rise to triplets. Consequently, the CH_2N protons appear as four AB quartets at −110 °C.

The isopropyl methyl signals underwent a corresponding change. At lower temperatures, the doublet decoalesced and reappeared (at −80 °C) as three doublets at δ 0.72 (J = 6.7 Hz), 0.90 (J = 6.2 Me), and 1.16 (J = 6.7 Hz) with the intensity ratio 1:2:1. At still lower temperatures, the central, high-intensity doublet broadened and split into two new doublets, which essentially

(11) H. M. McConnell, *J. Chem. Phys.*, **28**, 430 (1958).
(12) B. Nilsson, P. Martinsson, K. Olsson, and R. E. Carter, *J. Am. Chem. Soc.*, **95**, 5615 (1973).

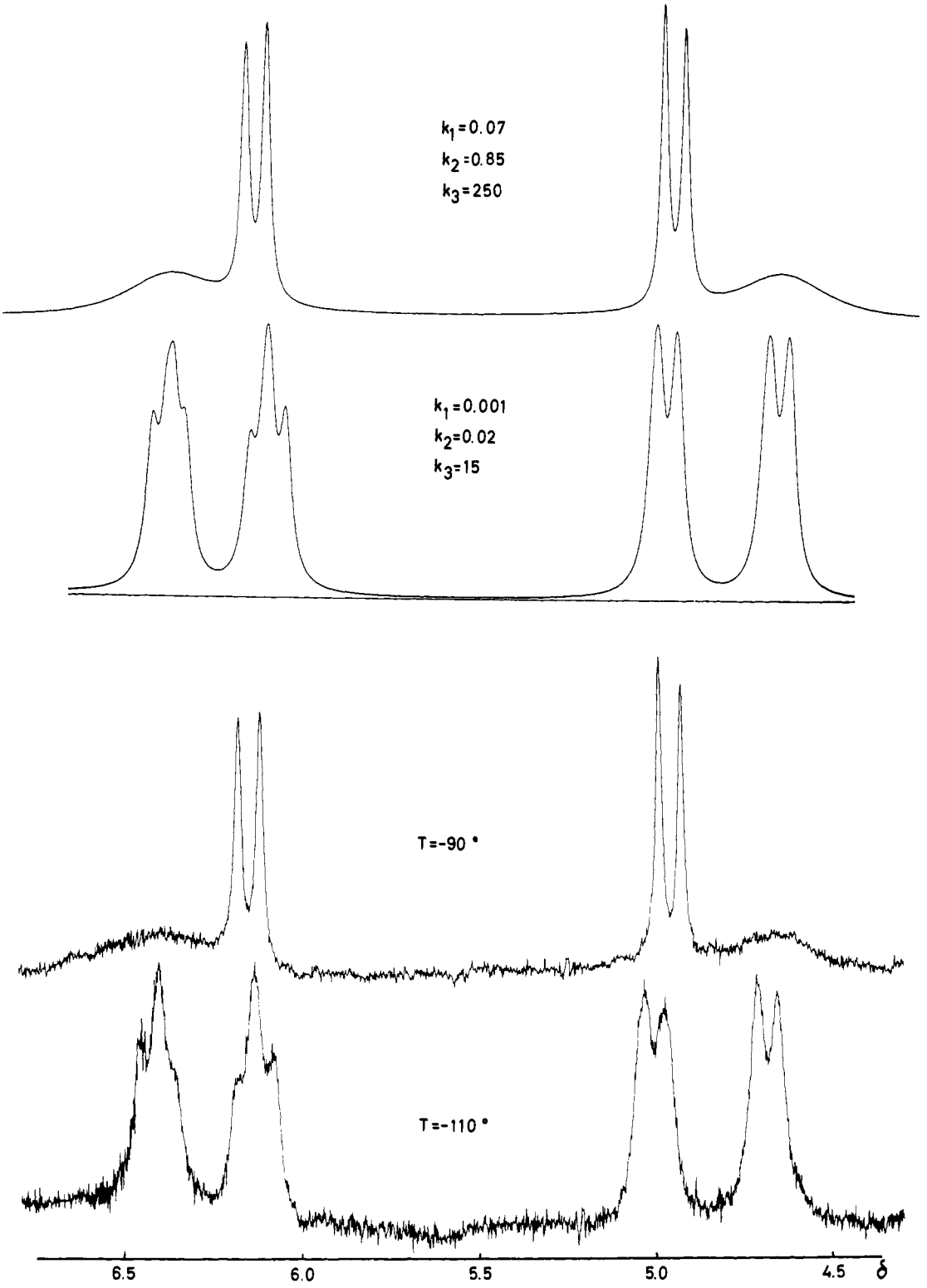


Figure 3. Experimental (270-MHz) and calculated spectra of the benzylic methylene protons at various temperatures (solvent dimethyl-d_6 ether).

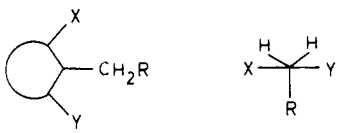
coincided with the remaining two. At −110 °C (270 MHz), the two high-field doublets were separated by ca. 16 Hz, whereas the low-field ones overlapped.

The ambient-temperature ^{13}C NMR spectrum of A was also consistent with the symmetry considerations mentioned above. At lower temperature each of the CH_2N and imidazolinic carbon signals decoalesced to symmetrical doublets ($\Delta\delta$ = 0.27 and 0.07). Likewise, the phenylic carbons gave four signals at ambient temperature, which were split into seven signals, and the isopropyl methyl carbon singlet changed to a broad 3:1 doublet at −90 °C. Surprisingly enough, no splittings due to the benzyl rotations were observed down to −135 °C.

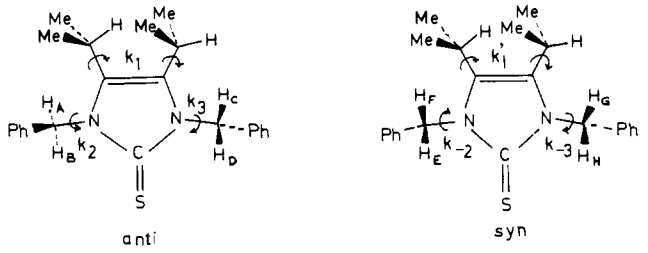
An examination of the spectra between −20 and −90 °C reveals that more than one rate process must be involved in the decoalescence features. The following analysis of the spectral features attempts to clearly demonstrate that the two benzyl groups of A have very unequal barriers to rotation around the CH_2–N bond and to determine these barriers, as well as that of the isopropyl group rotation.

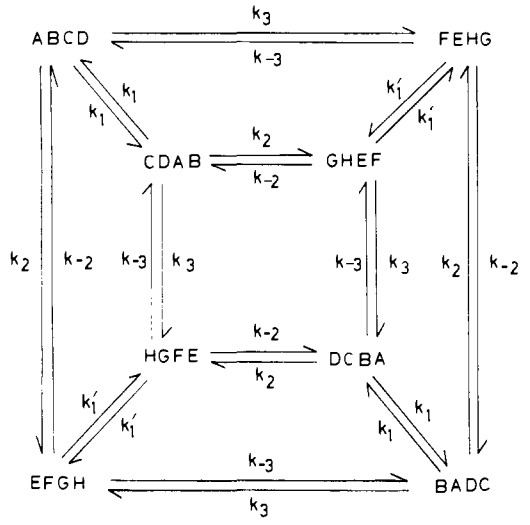
Initially, it should be noted that neither ^1H nor ^{13}C NMR spectra gave credence to the existence of conformation II (Scheme III) in any appreciable amount. Furthermore, ^{13}C NMR spectra can be used to study the isopropyl rotation alone, without the influence of the other rotational processes. Thus, the splitting

Chart I



Scheme IV





of the $^{13}CH_2N$ signal is unaffected by the benzyl group rotation whatever the magnitude of this barrier (vide infra).

The conformational properties of primary alkyl groups such as ethyl, benzyl, isobutyl, and neopentyl attached to an sp^2-hybridized framework are rather well established. It turns out that in all cases studied, the alkyl group takes up an essentially perpendicular arrangement with respect to the sp^2 framework[6,7,13-16] (Chart I). The interchange between the two perpendicular orientations has been studied by DNMR and molecular mechanic calculations. According to both experiment and calculation, the alkyl group has two nonequivalent pathways over the energy maxima in which the CH_2–R group is near the plane of the sp^2 framework. The energies of the maxima are essentially determined by the steric requirements of the flanking substituents X and Y. Thus, compound A may exist in two diasteromeric pairs of enantiomers with the benzyl groups in an anti or a syn relation to each other.

In the light of these remarks the complete exchange scheme for the benzylic methylene protons may be constructed. In the anti conformation these protons give rise to four sites, ABCD, and by rotating the CH_AH_B benzyl group ca. 180°, we obtained one syn conformer with four new sites, EFGH. With this notation of the sites, eight different configurations of the four protons may be obtained by any suitable combination of rotations of the isopropyl groups and the benzyl groups. The complete scheme for the configurational interconversions is shown in Scheme IV.

Table I. Barriers to Rotation of 1,3-Dibenzyl-4,5-diisopropylimidazoline-2-thione, A, in Dimethyl-d_6 Ether Solution

exchange process[a]	resonance obsd	T/°C	k/s^{-1}	$\Delta G^{\ddagger}$/kcal mol^{-1}
k_1	CH_2N[b]	−44.0	40	11.5 ± 0.1
k_1	CH_2N[c]	−20.1	600	11.5 ± 0.2
k_2	$(CH_3)_2CH$[c]	−68.3	21	10.6 ± 0.1
k_2	CH_2N[c]	−44.0	2850	10.7 ± 0.2
k_3	CH_2N[c]	−90.0	250	8.5 ± 0.1
k_3	CH_2N[c]	−68.3	3500	8.5 ± 0.1

[a] Notations according to Scheme IV. [b] ^{13}C NMR experiment. [c] ^1H NMR experiments.

Since the syn and anti conformations are diastereomerically related to each other, they have in principle different energies. The energy difference may be obtained by band shape fitting of the 270-MHz spectrum at −110 °C (Figure 3). The fractional populations at this temperature were estimated to be 0.54 and 0.46 ($\Delta G° \approx 50 \pm 15$ cal mol^{-1}), but the assignment of the syn and anti forms was not possible. We have arbitrarily chosen the anti conformation as the most populated one, but this has no influence on the conclusions. If the syn conformer is actually the most populated one, the following mutual exchanges must be made: A ⇌ F, B ⇌ E, C ⇌ G and D ⇌ H. If our assumption is correct, the chemical shifts and coupling constants of all eight sites, A–H, may be unequivocally determined: δ_A 5.01, δ_B 6.10, δ_C 4.69, δ_D 6.42, δ_E 6.15, δ_F 5.00, δ_G 4.68, and δ_H 6.38; $J_{AB} = J_{CD}$ = 16.7 Hz and $J_{EF} = J_{GH}$ = 15.5 Hz.

These assignments are in agreement with the known strong deshielding effect of the thiocarbonyl group and with the anticipated van der Waals' shift of the proton close to the isopropyl methyl groups.

Although the NCH_2 proton NMR spectra are affected by all three rate processes, the corresponding rate constants cannot be extracted from the band shapes of the NCH_2 proton signals alone with acceptable accuracy. Thus, in the temperature interval −30 to −70 °C the band shape is affected by all the processes, but the covariance of the rate constants is considerable. Furthermore, the small chemical shift difference between the NCH_2 groups induced by the isopropyl groups (~0.02 ppm at −110 °C) makes the determination of k_1 (isopropyl rotation) uncertain. However, as stated above, this rate constant can be measured from the ^{13}C NMR spectra at −40.4 to −56.2 °C with acceptable accuracy. Strictly speaking, a mean value of the two rate constants for syn and anti conformations is obtained, but the difference between these rate constants is very small or maybe even nonexistant at these temperatures. The isopropyl groups thus undergo the process Ia ⇌ Ib. The free-energy barrier is 11.5 ± 0.1 kcal mol^{-1} (T_c = 223.6 K, $\delta\nu$ = 13.0 Hz). The mechanism of the process, i.e., synchronous or stepwise rotation of the two isopropyl groups, has been dealt with previously in several similar systems. Both experimental and theoretical (molecular mechanics calculations) results suggest that the interconversion takes place by rotation of one isopropyl group at a time.[3,4] In one case, methyl-*N*,*N*-diisopropyldiselenocarbamate,[4b] this mechanism has been unequivocally proven. In A the most reasonable alternative is a two-step process via an intermediate conformation of type II (Scheme III).

The experimental spectra in the temperature range −40 to −110 °C can only be understood if *two quite different barriers are assumed for the benzyl group rotations*. The slower of these rotations can be studied between −40 and −70 °C on the CH_2N signals and between −60 and −75 °C on the isopropyl methyl signals. Finally, the fast benzyl group rotation may be studied below −60 °C on the CH_2N resonances. The data are summarized in Table I. The temperature intervals within which accurate rate constants could be derived were too limited to allow for the evaluation of reliable enthalpies and entropies of activation.

(13) C. A. Cupas, J. M. Bollinger, and H. Haslangar, *J. Am. Chem. Soc.*, **90**, 5592 (1968).
(14) B. Nilsson, P. Martinsson, K. Olsson, and R. E. Carter, *J. Am. Chem. Soc.*, **96**, 3190 (1974).
(15) J. Peeling, J. B. Rowbotham, L. Ernst, and T. Schaefer, *Can. J. Chem.*, **52**, 2414 (1974).
(16) U. Berg, M. Grimaud, and J. Sandström, *Nouv. J. Chim.*, **3**, 175 (1979).

Discussion

Three dynamic processes are thus in evidence in this apparently symmetrical molecule. The one with the highest barrier ($\Delta G^{\ddagger}$ = 11.5 kcal mol^{-1}) is the rotation of the two isopropyl groups between two geared conformational states. The second is the rotation of one of the two benzyl groups ($\Delta G^{\ddagger}$ = 10.5 kcal mol^{-1}), and the third is the rotation of the second benzyl group ($\Delta G^{\ddagger}$ = 8.5 kcal mol^{-1}). The first process is the cornerstone of the study: a lower barrier to rotation for the isopropyl groups than for the benzyl groups would have hidden any experimental evidence for a difference in the benzyl group rotations whether the conformational state was geared or not. On the other hand, it is clear that an ungeared conformation as in II (Scheme II) would have preserved the symmetry of the molecule, leading to identical barriers to rotation for both benzyl groups. The more important point is that a geared conformation is in operation and that the experimental evidence for the resulting steric anisotropy of space is possible due to the barrier heights.

During the lifetime of a geared state, the benzyl group which is subject to the steric effect of the bulky face has time to rotate ca. 10 times whereas the opposite benzyl group rotates ca. 2000 times. Actually the ratio of about 200/1 is large enough to demonstrate that the structural block composed of two isopropyl groups behaves as a januslike substituent, but it must be stressed that this ratio has little to do with the difference in effective size of the two faces. The two transition states corresponding to the benzyl rotations are different. For the high-energy benzyl rotation (k_2), the transition state is reached when the phenyl group passes the thiocarbonyl group, whereas for the low-energy benzyl rotation (k_3), the transition state is reached when the phenyl group passes the methine proton of the isopropyl group. Thus, roughly speaking, this 200/1 ratio is the difference in steric effect between the thiocarbonyl group and the methine proton of the isopropyl group, and the effective difference in size of the two faces of the januslike substituent is certainly much higher. Furthermore, replacement of the sulfur atom by a larger group would most likely increase the ratio, and a limit should be attained when the benzyl group rotation will be on one side toward the two methyl groups and on the opposite face toward the methine group. In contrast, the replacement of sulfur by a smaller group would result in a decrease of the ratio, and a limit should be reached when both the transition states of the benzyl groups correspond to the interaction of the phenyl groups with this small substituent. This lower limit of the ratio would correspond to the secondary steric effect of the different isopropyl groups on the different methylenes in the transition states.

Comparison of these barriers with those measured in the model compounds B and C is instructive. The barrier to rotation of a benzyl group in the 4-*tert*-butyl derivative B was found to be 12.2 kcal mol^{-1}, whereas the barrier in the 4-methyl analogue C was equal to 7.2 kcal mol^{-1}.[6] We observed that the barrier is smaller on the side of the *tert*-butyl-like isopropyl face, i.e., 10.5 compared to 12.2 kcal mol^{-1}, which may be partly ascribed to geometry changes in the ring itself.[17] On going from an imidazoline to a thiazoline ring, the intracyclic C–N bond is shorter than the intracyclic C–S bond. These geometry effects result in a closer proximity of the thiocarbonyl, benzyl, and 4-substituents in the thiazole ring than in the imidazole ring. The difference in ring geometry is compensated for in the low-energy process in A (8.5 kcal mol^{-1}) compared to C (7.2 kcal mol^{-1}) by both the localization of the methine group in the plane of the ring and the buttressing angular deformation which results in a closer proximity of the methyl-like face of the diisopropyl group to the rotating benzyl group. We consider the increase of the low-energy barrier and the decrease of the high-energy barrier on going from C and B to A as a confirmation of the two postulated transition states.

More generally, geared isopropyl groups are a good simulation of both *tert*-butyl and methyl groups depending on from which side they are considered. This is also true for a single isopropyl group which possesses both the character of a *tert*-butyl and of a methyl group depending on its induced conformational state. We propose that such an induced conformational state may also play an important role in the steric control of the selectivity in the hydrophobic zone of enzymes.[18]

Our results are relevant to the current interest in conformational aspects of steric effects of substituents and provide a clear-cut example of the two extremes of the steric behavior of a nonsymmetrical group.[19]

Januslike substituents, $-CH(X)_2$, lead to a steric anisotropy of space. This concept can be easily extended to asymmetric januslike substituents, $-*CH(X,Y)$, for which, apart from the steric anisotropy of space, an asymmetric anisotropy of space is superimposed, which will be more or less pronounced depending on which side is considered.

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(17) J. Sandström and C. Roussel, unpublished results.

(18) A. Fersht in "Enzyme Structure and Mechanism", W. H. Freeman, San Francisco, Calif., 1977.

(19) M. Charton, *J. Org. Chem.*, **43**, 3995 (1978); J. E. Dubois, J. A. Macphee, and A. Panaye, *Tetrahedron Lett.*, 4099 (1978); T. Fujida, C. Takayama, and M. Nakayama, *J. Org. Chem.*, **38**, 1623 (1973); A. Heynes and J. Jacques, *Ann. Chim. (Paris)*, 555 (1968); A. Babadjamian, M. Chanon, R. Gallo, and J. Metzger, *J. Am. Chem. Soc.*, **95**, 3807 (1973).