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STEREOCHEMISTRY IN TRIVALENT NITROGEN COMPOUNDS. 40. TORSIONAL BARRIERS IN N-2,4-DINITROBENZENESULFENYLBENZIMIDAZOLES.[1a,b]

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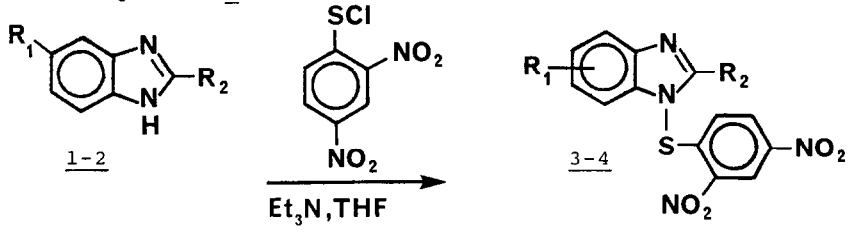
N-2,4-Dinitrobenzenesulfenylbenzimidazoles exhibit substantial barriers to torsion about the sulfur-nitrogen bond (ca 19 kcal/mole).

While there have been numerous investigations of torsional barriers in sulfenamides, there have been no previous reports involving sulfenamides in which the nitrogen atom is part of a heterocyclic ring.[2] Previous attempts to prepare the sulfenyl derivatives of simple indoles were unsuccessful since sulfenylation occurred exclusively at C-3 yielding sulfides.[3] Only when both C-2 and C-3 positions are substituted can N-sulfenyl indoles be prepared by rearrangement of the isomeric indolenines.[4]

In order to avoid the problem of C vs. N sulfenylation, we turned our attention to the sulfenyl derivatives of benzimidazoles.[5] Although such derivatives should be similar to the sulfenyl indoles, C-3 has been replaced by a nitrogen; and reaction at N-1 or N-3 would furnish the same product.

Accordingly, we prepared benzimidazoles 1 and 2 by reaction of o-phenylenediamine (or 4-chlorophenylenediamine for 2) with the corresponding carboxylic acid at 110°-130° C (with HCl catalysis for 2).



1 R_1 = H a R_2 = CH_2CH_3 b R_2 = $CH_2C_6H_5$ c R_2 = CH_2Cl d R_2 = $CH(CH_3)C_6H_5$

2 R_1 = Cl a R_2 = CH_2CH_3 b R_2 = $CH_2C_6H_5$ c R_2 = CH_2Cl

3 R_1 = H

4 R_1 = Cl

Conversion of the benzimidazoles into their derivatives 3 and 4 was easily accomplished by treatment with 2,4-dinitrobenzenesulfenyl chloride and triethylamine in tetrahydrofuran at room temperature.[6]

The room temperature ^{1}H NMR spectra (at 300 MHz) of 3a-c and 4a-c exhibited chemical shift non-equivalence of diastereotopic protons in the prochiral methylene group reflecting torsion about the N-S bond, which was slow on the NMR time scale. Compounds 3b and 3c exhibited AB quartets for the methylene protons while those in 3a appeared as the AB portion of an ABX_3 spin system. Compound 4 exhibited similar spectra but with two AB multiplets of unequal intensities arising from the presence of two constitutional isomers (5- and 6-chloro isomers).

In Compound 3d the prochiral probe group has been replaced by a chiral probe, the phenethyl group. Here the NMR spectrum features two methyl doublets of unequal intensity reflecting the presence of two diastereomers which differ in configuration at the sulfenamide chiral axis.

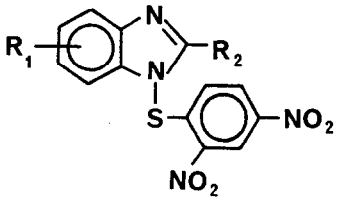
When the temperature was increased, coalescence was observed as torsion became rapid on the NMR time scale. Complete line shape analysis at a number of temperatures in the neighborhood of the coalescence point was carried out to determine the free energy of activation for topomerization. These barriers together with coalescence temperatures, chemical shift differences, melting points, and equilibrium constants are collected in Table 1.

The spectra of Compound 4c featured two well-separated AB quartets, and it was possible to measure coalescence points and topomerization barriers for both major and minor isomers. However, there was considerable overlap in the spectra of 4a and 4b; and only the barriers of the major isomers could be determined. The presence of separate sharp resonances for the two constitutional isomers of 4 at temperatures well above the coalescence points indicates that coalescence cannot be due to a process which involves cleavage of the N-S bond since this would lead to interconversion of the two isomers as well as topomerization at the prochiral carbon atom.

The data in Table 1 indicate a significant dependence of $\Delta G^{\ddagger}$ on the steric bulk of the R_2 substituent. Thus, the barrier for the phenethyl Compound 3d is somewhat larger than that for the compounds with less bulky substituents. This steric effect on the barrier is comparable to that previously reported in dialkylsulfenamides.[7] There appears to be a small decrease in the barriers in series 4 as compared with those in series 3. Although the differences are comparable to experimental errors, we note that the trend is consistent with the positive ρ value observed for N-arylsulfonyl-N-2,4-dinitrobenzenesulfenamides.[8]

The torsional barriers reported here are among the highest yet observed for torsion about sulfenamide bonds, although the presence of the sulfenamide nitrogen in a five-membered ring leads to an increase in CNS angles which should lessen steric interactions somewhat. Nevertheless, we may attribute these exceptionally high barriers to two factors which can exhalt steric effects on the torsional barriers. It must be noted that steric deceleration

TABLE 1[a]



Compounds	R_1	R_2	Mp(°C)	$\Delta\nu$[b] (Hz)	R[c] (22°)	$\Delta\nu_c$ (Hz)	T_c(°C)	k_c	$\Delta G^{\ddagger}$[d] (kcal/mol)
3a	H	CH_2CH_3	189-191	45.9		43.5	101	74.0	18.85
3b	H	$CH_2C_6H_5$	185-187	100.1		70	120.5	180	19.14
3c	H	CH_2Cl	158-160	25.8		4.3	74	3.1	19.6
3d	H	$CH(CH_3)C_6H_5$	174-185	28.2	6.25	17.5	89	10.5	19.6
4a	Cl	CH_2CH_3	145-150	47.1	1.85	46.1	97	80	18.62
4b	Cl	$CH_2C_6H_5$	160-173	102.9	1.4	69	118.5	180	19.07
4c(major)	Cl	CH_2Cl	150-158	26.0	1.5	4.7	80	12	19.0
4c(minor)				23.5		4.3	75	5.0	19.3

a) All spectra were measured on solutions in toluene-d_8 at 300 MHz.

b) Chemical shift differences measured at ambient temperature (21-23°C).

c) The value for 3d is the equilibrium constant for the two diastereomers which differ in configuration at the S-N chiral axis. The values for Compounds 4 correspond to the ratio of regioisomers. Preliminary experiments suggest that this is an equilibrium ratio.

d) Free energies of activation were obtained by complete lineshape analysis at several temperatures near the coalescence point. The barriers for 3a,b and 4a,b are considered accurate to ±0.1 kcal/mol based on assumed accuracy of ±1°C in the temperature. The standard deviations from the mean $\Delta G^{\ddagger}$ on these compounds were ≤0.05 kcal/mol. We consider the barriers for 3c,d and 4c to be less accurate (±0.2 kcal/mol) because of uncertainties introduced by the large value for R (in 3d) and the small and highly temperature-dependent chemical shift differences in 3c and 4c.

of torsion about the N-S bond depends not solely on steric hindrance in the transition state but on the difference in steric interactions between the ground and transition states. First, planarity at nitrogen decreases ground state steric interactions by increasing the CSNC dihedral angle (to ca. 90°). In addition, it maximizes the transition state energy by insuring that the geometry for maximum steric interaction coincides with the geometry of maximum overlap between p lone pairs on sulfur and nitrogen (four-electron interactions). Second, while interaction with the peri hydrogen on the phenyl ring can involve substantial steric hindrance in the torsional transition state, it would not lead to significant destabilization in the torsional ground state. This differential steric interaction with the peri hydrogen can lead to greater enhancement of the torsional barrier than interaction with a more bulky group which also occasions substantial interaction in the ground state. Finally, we may point out that this study demonstrates that substantial conjugation of the sulfenamide nitrogen does not lead to greatly decreased barriers, consistent with the previous observation of a substantial barrier in an N-sulfenylaniline.[2]

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