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N-(Arylthio)benzimidazoles. Torsional Barriers and 1,3 Rearrangement[1]

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A series of *N*-[(2,4-dinitrophenyl)thio]benzimidazoles has been prepared by reaction of 2,4-dinitrobenzenesulfenyl chloride with a series of 2-alkylbenzimidazoles and 5(6)-chloro-2-alkylbenzimidazoles. Dynamic NMR spectroscopy was used to measure the torsional barriers about the N–S bonds, which were in the range of ca. 19–20 kcal/mol. In one case, diastereomeric transformation and conventional kinetics were used to obtain an independent measure of the torsional barrier. The kinetics of 1,3 rearrangement of the arylthio group from one nitrogen to another suggested that the rearrangement proceeds via a bimolecular mechanism.

The restriction to torsion about the N–S bond in sulfenamides renders this chemical functionality a unit of axial chirality in compounds that bear different substituents at the sulfenamide nitrogen atom.[3] This axial chirality is manifest in the NMR spectra of sulfenamides that bear prochiral centers incorporating diastereotopic hydrogen atoms or groups of hydrogen atoms. Torsion about the N–S bond results in D → E topomerization,[4] and coalescence of NMR resonances occurs when torsion becomes rapid on the NMR time scale. Dynamic NMR spectroscopy thus affords a convenient method for the determination of sulfenamide torsional barriers, and the free energies of activation for torsion have been measured and reported for a wide variety of sulfenamides bearing alkyl, aryl, and acyl substitutents at nitrogen.

As part of an ongoing study of sulfenamide torsional barriers, we wished to examine topomerization in sulfenyl derivatives of heterocyclic amines. Although derivatives of heterocyclic amines had not been previously examined, we supposed that delocalization of the nitrogen lone pair of electrons would *not* lead to a decrease of the N–S torsional barrier. On the other hand, the planarity of the heterocyclic ring system might lead to higher barriers by increasing the differences in steric interactions between the torsional ground and transition states. Our initial attempt to prepare *N*-arylthio derivatives of simple indoles (and their anions) led to 3-arylthio derivatives instead of the desired sulfenamides.[5] We reasoned either that attack at carbon (C-3) occurred much more rapidly than attack at nitrogen or that initially formed sulfenamides underwent a nitrogen-to-carbon rearrangement of the arylthio moiety. Dmitrienko et al.[6] found that 2,3-disubstituted indoles also favor attack at carbon, yielding 3-(arylthio)-indolenines. Heating these indolenine sulfides to ca. 90 °C yielded the corresponding disulfides and 2,3-disubstituted indoles along with small amounts of the sulfenamide rearrangement products. Dmitrienko argued that since initial attack in 2,3-disubstituted indoles occurred at carbon, sulfides isolated in the previous reactions of simple indoles probably were kinetic products and no N-to-C rearrangement had occurred. In order to avoid the problem of C vs. N sulfenylation we undertook the preparation of a series of benzimidazole sulfenamides[7] and determination of their torsional barriers. In this system both of the α atoms in the heterocyclic ring are nitrogen and attack at either would lead to the same sulfenamide product. The benzimidazole system was also suitable for investigation of the possible 1,3 rearrangement, since we can be sure that the two possible regioisomers in suitably substituted benzimidazoles will be of similar energies. Thus, we avoid

(1) (a) Stereochemistry in Trivalent Nitrogen Compounds. 42. For Part 41, see: Raban, M.; Moulin, C. P.; Lauderback, S. K.; Swilley, B. *Tetrahedron Lett.* **1984**, *25*, 3419. (b) We thank the National Institutes of Health (MBRS) for partial support of this work. (c) A portion of this work appeared in preliminary form: Raban, M.; Chang, H.; Craine, L. *Tetrahedron Lett.* **1984**, *25*, 1337.

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(3) For recent reviews on sulfenamide torsional barriers, see: (a) Raban, M.; Kost, D. *Tetrahedron* **1984**, *40*, 3345. (b) Raban M. In "Organic Sulfur Chemistry"; Freidlina, R. Kh., Skorova, A. G., Eds.; Pergamon Press: Oxford, 1981; pp 141ff.

(4) We recognize three kinds of topomerizations based upon the stereotopic relationships without and with averaging: E → H (enantiotopic to homotopic), D → E (diastereotopic to enantiotopic), and D → H (diastereotopic to homotopic). Only the latter two types result in coalescence phenomena in NMR spectra.

(5) Raban, M.; Chern, L.-J. *J. Org. Chem.* **1980**, *45*, 1688.

(6) Dmitrienko, G. L.; Friesen, R. W.; Carson, L.; Vice, S. F. *Tetrahedron Lett.* **1982**, *23*, 821.

(7) (a) Chizhevskaya, I. I.; Shupskaya, R. V.; Karitanovich, A. N. *Zh. Org. Khim.* **1968**, *4*, 1497; *J. Org. Chem. USSR (Engl. Transl.)* **1968**, *4*, 1441. (b) Parfenov, E. A.; Fomin, V. A. *Zh. Obshch. Khim.* **1981**, *51*, 1129; *J. Gen. Chem. USSR (Engl. Transl.)* **1981**, *51*, 947.

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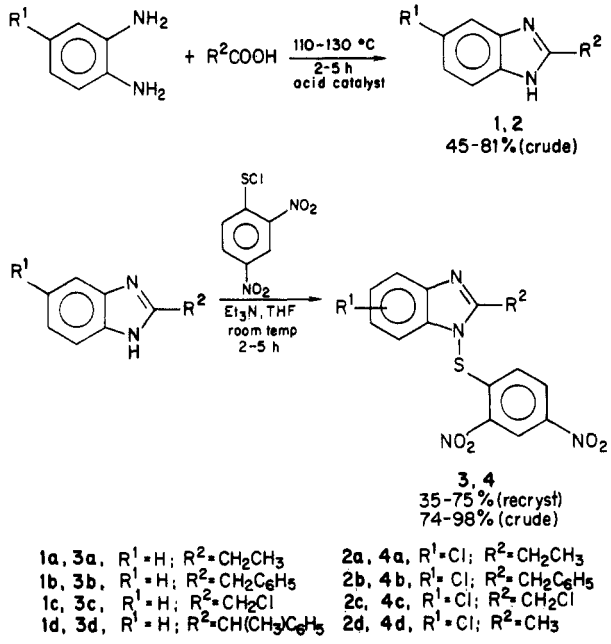
Scheme I. Synthesis of N-[(2,4-Dinitrophenyl)thio]benzimidazoles



1a, 3a, R^1 = H; R^2 = CH_2CH_3 2a, 4a, R^1 = Cl; R^2 = CH_2CH_3
1b, 3b, R^1 = H; R^2 = $CH_2C_6H_5$ 2b, 4b, R^1 = Cl; R^2 = $CH_2C_6H_5$
1c, 3c, R^1 = H; R^2 = CH_2Cl 2c, 4c, R^1 = Cl; R^2 = CH_2Cl
1d, 3d, R^1 = H; R^2 = $CH(CH_3)C_6H_5$ 2d, 4d, R^1 = Cl; R^2 = CH_3

a system where one isomer might so dominate the equilibrium that the minor component would not be detectable.

In this paper we report the N–S torsional barriers in a series of benzimidazole sulfenamides. In addition, we have examined the 1,3 nitrogen-to-nitrogen rearrangement of the arylthio moiety and can offer evidence relevant to possible mechanisms.

Results and Discussion

Measurement of torsional barriers in benzimidazole sulfenamides requires the incorporation of a prochiral or chiral probe group into the benzimidazole moiety. Accordingly, we prepared a series of benzimidazoles (**1a–c**) with prochiral substituents (ethyl, benzyl, and chloromethyl) at the 2-position, by reaction of *o*-phenylenediamine with the corresponding carboxylic acids at 110–130 °C with either excess carboxylic acid or mineral acid catalyst (Phillips reaction)[8] (Scheme I). We also prepared a chiral benzimidazole (**1d**) by reaction with 2-phenylpropanoic acid (hydrotropic acid). In order to investigate the possibility of nitrogen-to-nitrogen rearrangement, we needed to desymmetrize the benzimidazole, and for this purpose, we chose to incorporate a β-chlorine atom in the nonheterocyclic ring. Although we prepared a series of compounds with the same prochiral probe groups (**2a–c**) we settled on the 2-methyl substituent (**2d**) as the most convenient for kinetic studies. Benzimidazoles **1** and **2** could be conveniently converted into their sulfenyl derivatives **3** and **4** by treatment with 2,4-dinitrobenzenesulfenyl chloride and triethylamine in dry tetrahydrofuran.

The room-temperature ^1H NMR spectra (300 MHz) of **3a–c** and **4a–c** exhibited chemical shift nonequivalence of the diastereotopic methylene protons attached to the prochiral carbon atom. This reflects the axial chirality of the sulfenamide S–N bond, which is manifest when torsion is slow on the NMR time scale. Compounds **3b** and **3c** exhibited AB quartets, while the methylene protons in **3a** appeared as the AB portion of an ABX_3 spin system. Compounds **4a–c** exhibited similar spectra but with two AB multiplets of unequal intensities due to the presence of the two constitutional isomers (5-chloro and 6-chloro isomers).

In compound **3d** the prochiral probe group has been replaced by a chiral probe group, the 1-phenylethyl group. Here the NMR spectrum features spectral doubling arising from the presence of two diastereomers that differ in configuration at the sulfenamide chiral axis. Integration of signals from the two diastereomers indicates a ratio of 6.25:1, corresponding to a significant biasing of the configuration at the stereolabile sulfenamide configurational unit by the stereostable asymmetric carbon atom (thermodynamic asymmetric induction).[9]

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 energies of activation for topomerization. The chemical shift differences at the coalescence point ($\Delta\nu_c$) were estimated by extrapolating plots of observed chemical shift vs. temperature below the region of coalescence. Matching of calculated and observed spectra was used for more accurate estimation of $\Delta\nu_c$. All of the compounds exhibited decreases in the chemical shift differences as the temperature was increased. This was especially marked for the chloromethyl compounds **3c** and **4c**. Here the chemical shift dropped from ca. 25 Hz at room temperature (21–23 °C) to less than 5 Hz at the coalescence point. In these cases, the determination of k_c was less accurate, and we assign a higher error range (±0.2 kcal/mol) to these compounds.

Accurate determination of the barrier for topomerization in the compound with the chiral probe group (**3d**) was difficult because of the large thermodynamic asymmetric induction observed. The signal due to the major isomer underwent little change in signal shape in the region of coalescence; the major broadening was observed for the much less intense peak belonging to the minor isomer. As a result, there was greater uncertainty in the matching of calculated and experimental spectra. In this case too, we regard the assigned value as having an uncertainty of ±0.2 kcal/mol.

For the remaining compounds, **3a,b** and **4a,b**, we based our estimates of the barriers on at least three separate spectra in the neighborhood of T_c and obtained good agreement in separate determinations. In these cases, we regard uncertainty in the temperature (±1 °C) as the main source of error and regard the measured free energies of activation to be within a range of ±0.1 kcal/mol. The NMR data and torsional barriers are collected in Table I.

The presence of the chiral probe in **3d** provided an additional way to measure the barrier. Crystallization of **3d** occurs with diastereomeric transformation,[10] and the solid is composed of a single diasteromer, the major isomer. When the solid was dissolved in toluene-d_8 at low temperature and the NMR spectrum taken at temperatures below ca. −35 °C, *without allowing warming of the sample*, only the C-methyl doublet of the major isomer was observed. When the temperature was raised to −21 °C, the growth of the peaks corresponding to the minor isomer could be observed as the sample composition relaxed toward the equilibrium composition of diastereomers. Because the minor isomer is not very prominent at equilib-

(8) (a) Phillips, M. A. *J. Chem. Soc.* **1928**, 172. (b) Wright, J. B. *Chem. Rev.* **1951**, *48*, 397. (c) Preston, P. N. *Chem. Rev.* **1974**, *74*, 279.

(9) (a) Raban, M.; Carlson, E. H. *Isr. J. Chem.* **1977**, *15*, 106. (b) Raban, M.; Moulin, C. P.; Lauderback, S. K.; Swilley, B. *Tetrahedron Lett.* **1984**, *25*, 3419.

(10) (a) Raban, M.; Carlson, E. H. *J. Am. Chem. Soc.* **1971**, *93*, 685. (b) Raban, M.; Lauderback, S. K. *J. Am. Chem. Soc.* **1971**, *93*, 2781.

Table I. Torsional Barriers and NMR Data for N-[(2,4-Dinitrophenyl)thio]benzimidazoles[a]

compd	R^1	R^2	mp, °C	$\Delta\nu$,[b] Hz	R[c]	$\Delta\nu_c$,[d] Hz	T_c, °C	k_c	$\Delta G^\ddagger$, kcal/mol
3a	H	CH_2CH_3	189–191	45.9		43.5	101	74.0	18.9
3b	H	$CH_2C_6H_5$	185–187	100.1		70	120.5	180	19.1
3c	H	CH_2Cl	158–160	25.8		4.3	74	3.1	19.6
3d	H	$CH(CH_3)C_6H_5$	211–213	28.2	6.25[e]	17.5	89	10.5	19.6, 20.7[f]
4a	Cl	CH_2CH_3	145–150	47.1	1.85	46.1	97	80	18.6
4b	Cl	$CH_2C_6H_5$	160–173	102.9	1.4	69	118.5	180	19.6
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] At 22 °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] Chemical differences at the coalescence point were obtained by extrapolation of chemical shift vs. temperature data and spectral simulation. [e] The temperature-dependent equilibrium constant was determined to be 4.8 in the region of the coalescence point by matching of stimulated and experimental spectra. [f] Since topomerization involves interconversion of diastereomers, two free energies of activation are involved; the higher corresponds to conversion of the major isomer to the minor isomer and is the appropriate one for comparison with the barrier obtained by conventional kinetics at −21 °C, viz. 21.5 kcal/mol.

rium (only ca. 13.5%), it was difficult to carry out very accurate kinetic measurements. Nevertheless, we obtained an estimate of the first-order rate constant: 7.7×10^{-7} s^{-1}. This corresponds to a free energy of activation of 21.5 kcal/mol for conversion of the major to the minor isomer, which was in fair accord with the value obtained by complete line shape analysis.

The spectra of **4c** featured two well-separated AB quartets for the chloromethyl group. It was possible to measure coalescence points and topomerization barriers for both the major and minor constitutional isomers. However, there was considerable overlap in the spectra of **4a** and **4b**, and only the barriers corresponding to the major isomers could be measured. 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 that 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. This experiment also indicated that the isomerization (nitrogen-to-nitrogen migration of the arylthio moiety) could not be investigated by NMR line shape methods because the process would be too slow on the NMR time scale at accessible temperatures. The investigation by standard methods is discussed in a subsequent section of this paper.

The data in Table I indicate a significant dependence of $\Delta G^\ddagger$ on the steric bulk of the R^2 substituent. Thus the barrier for the 1-phenylethyl compound **3d** is somewhat larger than those for compounds with less bulky substituents. The thermodynamic asymmetric induction provides an indication that steric interaction between the 1-phenylethyl group and the 2,4-dinitrophenyl ring also takes place in the ground state. These steric effects on the barrier and on the thermodynamic asymmetric induction seem comparable in magnitude to those previously observed in dialkyl sulfenamides and *N*-alkyl-*N*-arylsulfonyl sulfenamides.[11] There appears to be a small decrease in the barriers in series **4** as compared with those in series **3**. Although the differences are not much larger than experimental uncertainities, we note that the trend is consistent with the positive ρ value observed for *N*-(arylsulfonyl)-2,4-dinitrobenzenesulfenamides.[12]

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. We may attribute these exceptionally high barriers to two factors that can exalt steric effects on torsional barriers.

Steric deceleration of torsion about the N–S bond does not depend only on steric hindrance in the transition state but on the *difference* in steric interactions between the ground and transition states. Therefore, we must consider structural factors that lessen steric interactions in the ground state as well as those that increase interactions in the transition state. 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 ensuring that the overlap between p lone pairs on sulfur and nitrogen is at a maximum (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 steric interaction in the ground state. The observation that conjugation of the sulfenamide nitrogen does not lead to greatly decreased barriers is consistent with the previous observation of a substantial barrier in an *N*-sulfenyl aniline.[11a]

Although the appearance of two sharp singlets for the chloromethyl groups in the high-temperature spectrum of **4c** indicated that the 1,3 rearrangement of the sulfenyl group from one nitrogen to another could not be investigated by DNMR methods, we reasoned that it could be studied using conventional kinetics. Although some separation of constitutional isomers of **4c** could be accomplished by chromatography on silica gel, more convenient separation was achieved by crystallization of compound **4d**. Accordingly, this latter compound was chosen for the subsequent kinetic investigation.

The initially obtained product **4d** exhibited a broad melting range (165–175 °C) and doubling of most of the peaks in the 300-MHz NMR spectrum, reflecting the presence of the two constitutional isomers **5** and **6**. Upon subsequent recrystallization, the melting point rose and sharpened (188–189 °C), and the NMR spectra indicated

(11) (a) Raban, M.; Kenney, C. W. J., Jr.; Jones, F. B., Jr. *J. Am. Chem. Soc.* **1969**, *91*, 6677. (b) Raban, M.; Yamamoto, G. *J. Am. Chem. Soc.* **1977**, *99*, 4160.

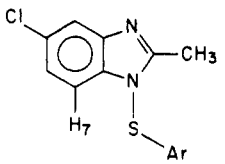
(12) Raban, M.; Jones, F. B., Jr. *J. Am. Chem. Soc.* **1971**, *93*, 2692.

Table II. Rate Constants for Isomerization of 4d at 65 °C[a]

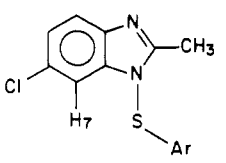
conc × 10^2, M		rate constants		
sulfenamide 4d	benzimidazole 2d	10^5k_1, s^{-1}	10^3k_2, s^{-1} M^{-1}	10^3k_c, s^{-1} M^{-1}
3.84	0.00	6.42	1.67	
3.84	0.00	5.90	1.53	
7.68	0.00	13.08	1.70	
7.68	0.00	12.95	1.68	
3.94	2.20	16.20		4.41
3.88	3.61	21.33		4.14

[a] $k_2 = (1.65 \pm 0.08) \times 10^{-3}$ M^{-1} s^{-1}, $k_c = (4.3 \pm 0.2) \times 10^{-3}$ M^{-1} s^{-1}.

that the resonances of one of the isomers declined dramatically. Although there were chemical shift differences between most of the corresponding protons in the two isomers, there was significant overlap in most instances. The best resolution observed was for protons that we have tentatively assigned to H_7. These protons appeared as a broad singlet at δ 7.78 for **5** and a doublet at δ 7.69 (^3J = 8.4 Hz) for **6**. Since these protons were well resolved and



6



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could be conveniently integrated, we chose them for the kinetic analysis. The rates of isomerization were measured by placing samples of measured concentrations in NMR tubes. The tubes were inserted into the heated probe at 65 °C, and spectra were taken (16 scans) at set intervals (15 min) after a short time for temperature equilibration. Each experiment was performed on at least two independent samples, and the results were averaged. The pseudo-first-order rate constants (k_1) were obtained by linear least-squares analysis using eq 1, where K is the

$$k_1 t = \left(\frac{-K}{K+1}\right) \ln\left(1 - \chi_B\left(\frac{1}{K+1}\right)\right) \quad (1)$$

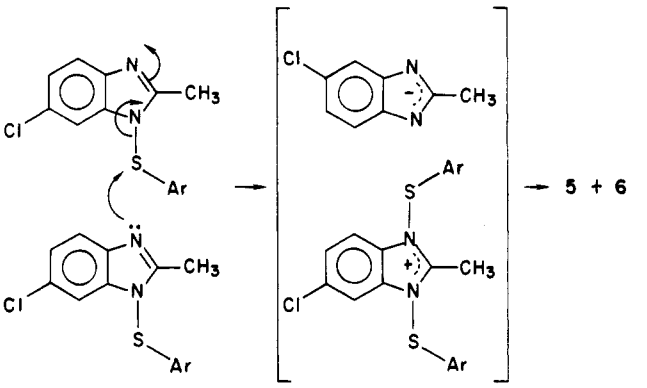
$$\text{rate} = k_1[S] = k_2[S]^2 + k_c[S][B] \quad (2)$$

equilibrium ratio of regioisomers and χ_B is the observed mole fraction of the minor isomer. The pseudo-first-order rate constants at two different concentrations and with added 2-methyl-5(6)-chlorobenzimidazole are gathered in Table II.

As the data in Table II indicate, the pseudo-first-order rate constant was proportional to concentration of the sulfenamide, [S], and we calculated the second-order rate constant by dividing the pseudo-first-order rate constant by the substrate concentration: $k_2 = (1.65 \pm 0.08) \times 10^{-3}$ M^{-1} s^{-1}. The addition of benzimidazole **2d** also dramatically accelerates the reaction, and we could calculate the rate for catalysis by added methylchlorobenzimidazole using eq 2: $k_c = (4.3 \pm 0.2) \times 10^{-3}$ M^{-1} s^{-1}.

Initially we envisioned three types of mechanisms possible for this rearrangement: (a) 1,3-sigmatropic rearrangement, (b) dissociation–recombination, and (c) bimolecular exchange. While suprafacial 1,3 sigmatropic rearrangements of hydrogen are forbidden according to the Woodward–Hoffmann rules, the rearrangement of other atoms is allowed if the rearranging atom undergoes inversion of configuration. Such a mechanism would be characterized by first-order kinetics and hence can be

Scheme II. Bimolecular Mechanism for 1,3 Rearrangement



excluded in the present case. While a heterolytic dissociation–recombination mechanism is improbable, a homolytic mechanism involving dissociation of **4** into 2,4-dinitrophenylthiyl and benzimidazolyl radicals seemed a very viable possibility. Indeed, this seems the likely mechanism for the rearrangement of 3-(arylthio)-indolenines into *N*-(arylthio)indoles reported by Dmitrienko et al.[6] This latter rearrangement takes place in low yield, and the product is accompanied by large amounts of diaryl disulfide and indole, suggestive of the formation of free radicals. This mechanism, also, would require first-order kinetics and can be excluded here.

A bimolecular mechanism that involves nucleophilic attack by the pyridine-type nitrogen of one sulfenamide molecule on the sulfenyl sulfur of another seems the most reasonable possibility (Scheme II). Both the imidazolyl cation and anion are resonance stabilized, and while we cannot exclude the possibility of such a mechanism in the indole series, we can certainly understand why it would be far more accessible in the benzimidazole series.

The observation of catalysis by 5-chloro-2-methylbenzimidazole (**4d**) is also consistent with this mechanism. It is not surprising that the second-order rate constant for catalysis by k_c is larger than k_2 since we would expect the unsubstituted benzimidazole to be a better nucleophile than the *N*-sulfenyl derivative. Also consistent with this mechanism was our observation that the rate of isomerization was much greater in polar solvents; when the sulfenamide was dissolved in acetone-d_6, equilibrium occurred too rapidly for the rate to be measured at room temperature.

Our observation, that the rearrangement of (arylthio)-benzimidazoles takes place at a lower temperature than that reported for the rearrangement of indolenine sulfides to *N*-sulfenyl indoles, is consistent with the proposed mechanism and the structural differences between the two systems. The resonance stabilization of anion and cation associated with the imidazole system makes the bimolecular mechanism more accessible here than in the indolenine–indole rearrangement. In the latter case, rearrangement takes place at a higher temperature and apparently via a different mechanism, viz. radical dissociation. It is reasonable to suppose that radical dissociation could take place in the benzimidazoles as well as at elevated temperatures. Our results support the contention of Dmitrienko et al.[6] that initial attack of sulfenyl chloride on indoles takes place at a carbon rather than nitrogen. Certainly the rearrangements reported here and by Dmitrienko et al. require far more stringent conditions than in the reactions of indole salts and sulfenyl chloride described earlier.[5] One possible explanation for the sulfenylation at carbon, even under conditions where acyla-

tion and alkylation take place at nitrogen, involves the hard and soft acid and base (HSAB) concept. The propensity for attack at carbon is related to the softness of the electrophile. Thus, alkylation takes place more readily at carbon than does acylation. If we judge sulfenyl halides to be even softer reagents than alkyl halides, we may expect even greater propensity for reaction at carbon in the sulfenylation of indoles.

Experimental Section

^{13}C NMR spectra were measured on a JEOL JNM-FX60 spectrometer at 15 MHz. They were recorded with 8192 data points and 5000–15000 scans (zero filling) at ambient temperature. A Varian T-60 CW spectrometer was used to measure the 60-MHz ^1H NMR spectra. Proton chemical shifts of benzimidazoles 1 and 2 are reported in δ units and were measured at 60 MHz on solutions in $CDCl_3$. All high-field, variable-temperature 300-MHz ^1H NMR spectra were recorded with 16K data points on a Nicolet NTC 1180 FT spectrometer. Proton chemical shifts of benzimidazole sulfenamides 3 and 4 are reported in δ units and were measured at 300 MHz on solutions in toluene-d_8 except as indicated. The coalescence studies were done in sealed tubes with 0.6–1.0% solutions in toluene-d_8. Kinetics of rearrangement were measured in $CDCl_3$. Chemical shifts in all spectra are relative to internal Me_4Si.

All melting points are uncorrected and were taken on a Thomas-Hoover melting point apparatus.

o-Phenylenediamine, glacial acetic acid, monochloroacetic acid, propanoic acid, 2-phenylpropanoic acid, and phenylacetic acid were all commercially available and not purified before use. 2,4-Dinitrobenzenesulfenyl chloride was prepared as previously reported. Reagent grade tetrahydrofuran was dried over lithium aluminum hydride and distilled before use.

Substituted benzimidazoles were prepared by using either procedure A (excess carboxylic acid) or procedure B (HCl catalysis). The molecular formulas of all new compounds were confirmed by elemental analysis or high-resolution mass spectrometry (exact mass determination).

Benzimidazoles. Procedure A. 2-Ethylbenzimidazole (1a): crude yield 45%; mp 166–168 °C (lit. mp 172[13]–173 °C[14]); ^1H NMR δ 1.78 (CH_3, t, 3 H), 3.05 (2 H, q, CH_2), 7.25 (2 H, m), 7.62 (2 H, m), 11.10 (1 H, br s, NH); ^{13}C NMR δ 11.70, 22.10, 114.23, 122.09, 138.53, 157.12.

5-Chloro-2-ethylbenzimidazole (2a). Propanoic acid (5.33 g, 0.07 mol) and 4-chloro-*o*-phenylenediamine (5.7 g, 0.07 mol) were placed in a 100-mL round-bottom flask, fitted with a condenser and magnetic stirrer, and then allowed to reflux with stirring for 6 h. The acidic reaction mixture was cooled to room temperature and then made just basic to litmus with 10% sodium hydroxide. A white crystalline solid was obtained and recrystallized from benzene and cyclohexane: yield 77%; mp 164–166 °C (lit.[15] mp 170–171 °C); ^1H NMR δ 1.40 (3 H, CH_3), 2.92 (2 H, q, CH_2), 7.10 (1 H, m), 7.39–7.47 (2 H, m), 11.87 (1 H, s, NH); ^{13}C NMR ($CDCl_3$) δ 11.8, 21.8, 114.0, 115.0, 120.9, 125.2, 137.1, 139.9, 157.6.

Procedure B. 2-(Chloromethyl)benzimidazole (1c). Monochloroacetic acid (7.5 g, 0.08 mol) and *o*-phenylenediamine (7.57 g, 0.07 mol) were refluxed in 60 mL of 5 N HCl for 7.5 h with stirring. After the reaction mixture was cooled to ca. 5 °C, it was neutralized with aqueous ammonium hydroxide. The precipitated product was collected by vacuum filtration (9.5 g, yield 81%) and recrystallized from benzene/hexane: mp 152.5–155 °C (lit. mp 162,[16] 165 °C[17]); ^1H NMR δ 4.81 (2 H, s, CH_2), 7.20 (2 H, m), 7.56 (2 H, m), 9.14 (2 H, s, NH); ^{13}C NMR (acetone-d_6) δ 41.4, 116.3, 123.4, 140.1, 150.6.

2-Benzylbenzimidazole (1b) was obtained in 76% yield: mp 183–185 °C (lit. 187,[18] 183–184,[19] 191 °C[19]); ^1H NMR δ 4.18 (CH_2, 2 H), 7.13 (2 H, m), 7.27 (phenyl); 7.53 (2 H, m), ^{13}C NMR 36.43, 1149.23, 121.76, 126.51, 128.26 (2), 136.26, 138.08, 153.47.

5-Chloro-2-(chloromethyl)benzimidazole (2c) was recrystallized from benzene and hexanes: 74% crude yield; mp 138.5–141 °C (lit. mp 140,[16] 136–138 °C[20]); ^1H NMR δ 4.92 (2 H, s, CH_2), 7.06 (1 H, m), 7.30 (1 H, m), 7.63 (1 H, m); ^{13}C NMR Me_2SO-d_6) δ 38.00, 115.07, 116.43, 122.60, 126.76, 137.16, 139.56, 151.13.

5-Chloro-2-methylbenzimidazole (2d) was obtained in 27% crude yield and recrystallized from ethanol and water: mp 203.5–205 °C (lit. mp 199,[21] 203,[22] 198–200 °C[23]); ^1H NMR δ 2.45 (CH_3, s, 3 H), 7.06 (1 H, m), 7.43 (1 H, m), 7.50 (1 H, m); ^{13}C NMR (Me_2SO-d_6) δ 14.5, 114.1, 115.0, 121.1, 125.4, 137.4, 140.1, 152.8.

5-Chloro-2-benzylbenzimidazole (2b), 98% yield, was recrystallized from water/ethanol: mp 169.5–171.5 °C (lit.[24] mp 172–174.5 °C); ^1H NMR δ 4.20 (2 H, s, CH_2), 7.20 (1 H, m), 7.33–7.46 (5 H, m), 7.55 (1 H, m) 7.63 (1 H, m).

2-(1-Phenylethyl)benzimidazole (1d) was obtained in 48% yield: mp 202–204 °C; ^1H NMR 1.82 (3 H, d, CH_3), 4.43 (1 H, q, CH), 7.12–7.67 (phenyl); ^{13}C NMR δ 19.51, 40.30, 114.56, 122.30, 126.97, 127.36, 128.72, 158.28.

Benzimidazole Sulfenamides 3 and 4. *N*-[(2,4-Dinitrophenyl)thio]-2-(1-phenylethyl)benzimidazole (3d). A solution of 2,4-dinitrobenzenesulfenyl chloride (1.056 g, 0.0045 mol) in 80 mL of dry tetrahydrofuran (THF) was added dropwise to a stirred solution of 1.0 g (0.0045 mol) of 2-(1-phenylethyl)benzimidazole and 0.5 g (0.0050 mol) of triethylamine in 120 of dry THF. The solution became orange-yellow after 20 min and the reaction mixture was heated to reflux for ca. 4 h and allowed to stir at room temperature ca. 16 h. After filtration of the white ammonium salt, the solvent was removed in vacuo, yielding an orange-yellow solid 1.8 g, 95%, which was recrystallized twice from benzene/hexane: mp 211–212.5 °C; ^1H NMR δ 1.78 (3 H, q, CH_3), 4.02 (q, CH), 4.37 (q, CH), 5.17 (d), 5.63 (d), 6.3–7.4 (m), 7.98 (d), 8.4 (d).

***N*-[(2,4-Dinitrophenyl)thio]-2-ethylbenzimidazole (3a)** was obtained in 81% yield and recrystallized from benzene/hexane: mp 189–191 °C; ^{13}C NMR (Me_2SO-d_6) δ 11.9, 21.0, 110.3, 120.5, 121.6, 122.4 (2), 124.9, 128.9, 136.3, 142.5, 143.2, 146.1, 147.8, 159.7; ^1H NMR δ 1.34 (3 H, t, CH_3), 2.4–2.7 (2 H, m, CH_2), 5.59 (1 H, d), 6.75 (1 H, q), 7.0–7.2 (m), 7.88 (1 H, d), 8.29 (1 H, d).

***N*-[(2,4-Dinitrophenyl)thio]-2-benzylbenzimidazole (3b)** was obtained in 57% yield: mp 185–187 °C; ^{13}C NMR δ 34.6, 110.3, 120.7 (2), 124.4, 125.1, 126.8 (2), 128.5, 129.2, 129.6, 135.1, 136.8, 142.0, 143.0, 145.0, 146.5, 157.0; ^1H NMR δ 3.88 (2 H, q, CH_2), 5.47 (1 H, d), 6.6–7.2 (m), 7.87 (1 H, d), 8.42 (1 H, d).

***N*-[(2,4-Dinitrophenyl)thio]-2-ethyl-5(6)-chlorobenzimidazole (4a)** was obtained in 74% crude yield and recrystallized from benzene/hexane: mp 145–150 °C; ^1H NMR δ 1.37 (3 H, m, CH_3), 2.5 (2 H, m, CH_2), 5.58 (2 H, d), 6.7–7.3 (m), 7.62 (1 H, d), 7.89 (1 H, d), 8.27 (1 H, d); ^{13}C NMR (Me_2SO-d_6) δ 11.6, 20.9, 110.6, 111.0, 120.3, 121.2, 121.6, 124.6, 125.0, 128.8, 130.1, 130.3, 134.9, 137.1, 141.7, 142.6, 144.6, 146.1, 146.8, 160.4, 161.1.

***N*-[(2,4-Dinitrophenyl)thio]-2-(chloromethyl)benzimidazole (3c)** was obtained in 74% crude yield: mp 158–160 °C; ^1H NMR δ 4.35 (2 H, q, CH_2), 5.87 (1 H, d), 6.8–7.3 (m), 7.89 (1 H, d), 8.30 (1 H, d); ^{13}C NMR δ 36.0, 110.7, 121.4, (2), 124.9, 125.8 (2), 128.3, 136.6, 142.8 (2), 146.2 (2), 152.8.

***N*-[(2,4-Dinitrophenyl)thio]-2-benzyl-5(6)-chlorobenzimidazole (4b)** was obtained in 81% crude yield and recrystallized from benzene/hexane: mp 160–173 °C; ^1H NMR δ 3.67 (2 H, q, CH_2), 4.04 (q), 5.15 (q), 6.5–7.4 (m), 7.62 (1 H, d), 7.94 (1 H, d), 8.33 (1 H, d).

***N*-[(2,4-Dinitrophenyl)thio]-2-(chloromethyl)-5(6)-chlorobenzimidazole (4c)** was obtained in 96% crude yield: mp 150–158 °C; ^1H NMR δ 4.1–4.3 (m, CH_2), 5.71 (d), 6.7–7.1 (m), 7.56 (1 H, d), 7.87 (1 H, d), 8.24 (1 H, q); ^{13}C NMR (Me_2SO-d_6) δ 35.9, 111.1, 111.6, 121.5, 122.5, 125.7, 126.5, 129.0, 131.0, 132.2,

(13) Hölljes, G. J.; Wagner, G. C. *J. Org. Chem.* **1944**, *9*, 31.
(14) Phillips, M. A. *J. Chem. Soc.* **1928**, 2393.
(15) Abbott, L. D., Jr.; Gindin, R. A. *Proc. Soc. Exp. Biol. Med.* **1957**, *96*, 846.
(16) King, F. E.; Acheson, R. M.; Spensley, P. C. *J. Chem. Soc.* **1949**, 1401.
(17) Bloom, A.; Day, A. R. *J. Org. Chem.* **1939**, *4*, 14.
(18) Walther, R.; von Pulawski, T. *J. Prakt. Chem.* **1899**, *59*, 249.
(19) King, F. E.; Acheson, R. M. *J. Chem. Soc.* **1949**, *1396*.
(20) Knoblock, W. *Chem. Ber.* **1958**, *91*, 2557.
(21) Ullman, F.; Mauthner, F. *Chem. Ber.* **1903**, *36*, 4026.
(22) Fischer, O. *Chem. Ber.* **1905**, *38*, 320.
(23) Roy, J.; Bhaduri, A. P. *Indian J. Chem., Sect. B* **1979**, *17B*, 164.
(24) Osone, M.; Tanimoto, S.; Oda, R. *Yuki Gosei Kagaku Kyokaishi* **1966**, *24*, 562; *Chem. Abstr.* **1966**, *65*, 10577g.

135.3, 141.5, 142.7, 143.6, 145.7, 146.5, 153.6, 154.3.

Synthesis and Separation of 5(6)-Chloro-*N*-[(2,4-dinitrophenyl)thio]-2-methylbenzimidazole (4d). A solution of the arenesulfenyl chloride (1.230 g, 5.2 mmol) in dry THF was added dropwise to a stirred THF solution of 5-chloro-2-methylbenzimidazole (0.838 g, 5.0 mmol), and the mixture was allowed to stir for 4 h at room temperature. After filtration, the crude product, 1.797 g, was obtained by removal of solvent in vacuo. The first recrystallization from benzene and hexanes yielded 0.411 g (22.6%), mp 182–184.5 °C. The once-crystallized sulfenamide was again dissolved in a minimum of boiling benzene and filtered hot. To the hot benzene solution were added boiling hexanes until the solution became cloudy. The sulfenamide solution was allowed to cool slowly and then to sit at room temperature overnight. The pale yellow crystals were vacuum filtered and dried in a vacuum oven. High-field ^{1}H NMR indicated that one isomer is enriched 10:1: mp 188–189 °C; ^{1}H NMR (one isomer, $CDCl_3$) δ 2.64 (CH_3), 6.38 (d), 7.25–7.37 (m), 7.63 (d), 7.79 (s), 8.26 (q), 9.23 (d).

Registry No. **1a**, 1848-84-6; **1b**, 621-72-7; **1c**, 4857-04-9; **1d**, 91709-01-2; **2a**, 34569-15-8; **2b**, 7118-63-0; **2c**, 20443-38-3; **2d**, 2818-69-1; **3a**, 91709-02-3; **3b**, 91709-03-4; **3c**, 91709-04-5; **3d**, 91709-05-6; **4a**, 91709-06-7; **4b**, 91709-07-8; **4c** (5-chloro), 91709-08-9; **4c** (6-chloro), 95891-99-9; **4d** (5-chloro), 95864-47-4; **4d** (6-chloro), 95864-48-5; CH_3COOH, 64-19-7; $ClCH_2COOH$, 79-11-8; CH_3CH_2COOH, 79-09-4; $PhCH(CH_3)COOH$, 492-37-5; $PhCH_2COOH$, 103-82-2; *o*-phenylenediamine, 95-54-5; 4-chloro-*o*-phenylenediamine, 95-83-0; 2,4-dinitrobenzenesulfenyl chloride, 528-76-7.

Kinetic Isotope Effects and Pressure Effects in Several Hydrogen-Transfer Reactions of Tetralin and Related Compounds

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The H/D kinetic isotope effects and activation volumes have been measured for several hydrogen-transfer reactions using tetralin, dihydronaphthalenes, cyclohexa-1,4-diene, and cyclohexanol as donors. The isotope effects were found to exhibit different patterns for reactions of different mechanisms. They indicate whether hydrogen is in transit in the activated complex and show the number of atoms in transit (one or two). The KIE for the reaction of tetralin with quinones is consistent with concerted transfer of two hydrogens whereas the other reactions were found to be stepwise. The activation volumes lie within the range −23 to −33 mL/mol and do not seem to differentiate among bimolecular mechanisms. The relevance to previous studies of the KIE and ΔV^* for coal hydrogenation reactions is discussed.

The mechanisms of reactions by which tetralin, dihydronaphthalenes, and cyclohexadienes transfer hydrogen to various reagents have been studied for more than 20 years, and yet there are many inconsistencies and puzzling results which remain to be clarified. Much of the work has been stimulated by the recent revival of interest in coal liquefaction which is often accomplished by indirect hydrogenation using tetralin or related donor solvents. Probably the most extensive survey of acceptors was conducted by Benjamin, Raaen, Maupin, Brown, and Collins,[1] who tested 53 potential acceptor compounds with tetralin as a donor. Dihydronaphthalenes, cyclohexadienes, and alcohols have also been used as reductive agents.[2-11] Free radical reactions, ionic reactions, and pericyclic reactions seem to be exemplified by one or another of the reagent combinations which have been studied to date.

Recently we have reported kinetic isotope effects for the reaction of subbituminous coal with several deuterated derivatives of tetralin and 1,2-dihydronaphthalene.[12] The pattern of effects was so different for these two hydrogen donors as to suggest that they react by different mechanisms. This result prompted us to test several model hydrogen-transfer reactions in order to determine whether the isotope effects can be reconciled with other evidence pertaining to mechanism.

A mechanistic path (Scheme I) which many have thought to be exhibited by the reaction of coal with tetralin is bond homolysis followed by hydrogen abstraction from a donor (DH_2).

Scheme I

$$R_2 \xrightarrow{\text{slow}} 2R\cdot$$

$$2R\cdot + DH_2 \xrightarrow{\text{fast}} 2RH + D$$

An example of this type which has been thoroughly studied is the conversion of bibenzyl to toluene. The measured activation energy and entropy are appropriate to the mechanism,[13,14] and even more revealing is the activation volume,[14] +31 mL/mol, which indicates bond

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(1) Benjamin, B. M.; Raaen, V. F.; Maupin, P. H.; Brown, L. L.; Collins, C. J. *Fuel* **1978**, *57*, 269.
(2) Braude, E. A.; Jackman, L. M.; Linstead, R. P. *J. Chem. Soc.* **1954**, 3564.
(3) Muller, P. *Helv. Chim. Acta* **1973**, *56*, 1243.
(4) Muller, P.; Joly, D. *Tetrahedron Lett.* **1980**, 3033.
(5) Fleming, J.; Wildsmith, E. *J. Chem. Soc.* D **1970**, 223.
(6) Heesing, A.; Mullers, W. *Chem. Ber.* **1980**, *113*, 24.
(7) Stoos, F.; Rocek, J. *J. Am. Chem. Soc.* **1972**, *94*, 2719.
(8) Virk, P. S. *Fuel* **1979**, *58*, 149.
(9) Virk, P. S.; Bass, D. H.; Eppig, C. P.; Ekpenyong, D. J. *Prepr.—Am. Chem. Soc., Div. Pet.* **1979**, *24* (2), 144.
(10) Garry, M. J.; Virk, P. S. *Prepr.—Am. Chem. Soc., Div., Pet. Chem.* **1980**, *25* (4), 132.
(11) King, J.; Stock, L. M. *Fuel* **1981**, *60*, 748.
(12) Brower, K. R.; Pajak, J. *J. Org. Chem.* **1984**, *49*, 3970.
(13) McMillen, D. F.; Ogier, W. C.; Ross, D. S. *J. Org. Chem.* **1981**, *46*, 3322.
(14) Brower, K. R. *J. Org. Chem.* **1980**, *45*, 1004.

0022-3263/85/1950-2210$01.50/0