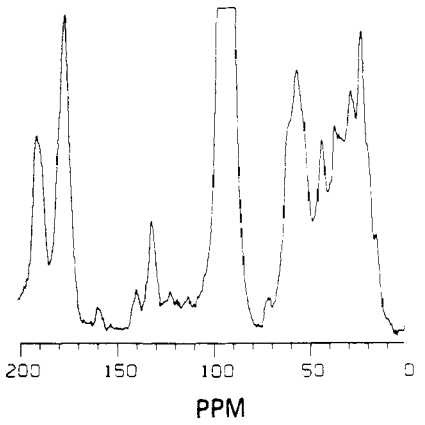

Figure 2. Natural abundance ^{13}C spectrum of isolated solid fd coat protein. Obtained from single-contact cross-polarization experiment with 1-ms mix time, 3-s recycle delay, 0.2-s acquisition time, and 12 000 transients. Signals from all carbons are present including the Delrin rotor at 90 ppm and its spinning side band at 195 ppm.

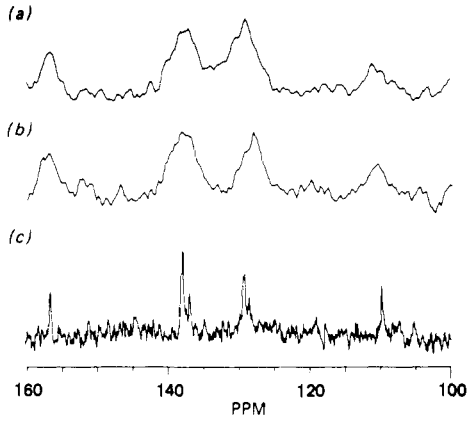

Figure 3. Nonprotonated aromatic carbon spectra of fd coat protein. (a) Isolated solid fd coat protein: cross polarized with 1-ms mix time, 3-s recycle delay, 0.1-s acquisition time, and a 90-μs delay without decoupling prior to data acquisition for 20 000 transients. (b) Solid fd virus: Same conditions as (a). (c) Detergent solubilized fd coat protein in water: sample is 6 mM in protein (10 mL) in 20-mm tube; weak noise-modulated proton decoupling is applied off-resonance and ^{13}C half echoes with 8-ms delay between pulses, 2-s recycle delay, and 0.4-s acquisition time for 64 000 transients were acquired.

a total of 10 nonprotonated aromatic resonances from 3 Phe, 2 Tyr, and 1 Trp.[12,13]

The spectrum in Figure 2 consists of signals from all the carbons of the isolated coat protein. The aliphatic carbons are in the region 10–70 ppm. All aromatic carbons are in the region 110–165 ppm with some separation of peaks apparent. The carbonyl carbons make up the band centered at 175 ppm. In this spectrum the only identifiable resonance is that of the two Tyr C_ζ at 160 ppm.

The nonprotonated aromatic carbon resonances of fd coat protein are shown in Figure 3. Spectrum a is from the same powder sample used in Figure 2, but was obtained with a 90-μs delay without proton decoupling prior to data acquisition to suppress the signals from carbons with bonded protons.[8] Spectrum b is of the intact virus which is 90% by weight coat protein; so the signals of the protein dominate. The protein solubilized in sodium dodecylsulfate detergent gives the ^{13}C spectrum c under conditions where only nonprotonated aromatic carbons appear.[14]

These three spectra can be compared directly. The most obvious difference is the narrower line widths of the detergent solubilized protein. The resonance at 160 ppm is from the two Tyr ζ carbons and in the best solution spectra two lines are completely resolved. The resonances at ~138 ppm are from the 3 Phe C_γ and the Trp ϵ_2 carbon; the contribution from the Trp carbon is probably reduced in the solid spectra owing to ^{14}N-induced splitting. Intensity at 130 ppm is due to the 2 Tyr C_γ and the Trp δ_2 carbon; these signals are completely overwhelmed by other ring carbons in the conventional proton-enhanced spectrum of Figure 2. Near 110 ppm in all three spectra is the resonance from the single γ carbon of Trp 26. Its assignment is unambiguous because there is only one Trp in the protein.[12,13] This is the only resonance that appears shifted in the solid compared with solution.

It is less time consuming to obtain a single carbon signal from a protein in the solid state than in solution. This is because of the greater ^{13}C magnetization resulting from cross-polarization than ^{13}C pulses and the recycling of data acquisition according to proton not carbon T_1. ^{13}C line widths are narrow enough in solid proteins to distinguish types of aromatic carbons. Resolution is sufficient for some experiments; for example, Tyr C_ζ pH titration over 12 ppm can be followed.

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References and Notes

(1) Opella, S. J. *Science* **1977**, *198*, 158–165.
(2) Allerhand, A. *Acc. Chem. Res.* **1979**, *11*, 469–474.
(3) Haeberlen, U. "High Resolution NMR in Solids"; Academic Press: New York, 1976.
(4) Haeberlen, U.; Waugh, J. S. *Phys. Rev.* **1969**, 185, 420–429.
(5) Pines, A.; Gibby, M. G.; Waugh, J. S. *J. Chem. Phys.* **1973**, *59*, 569–590.
(6) Schaefer, J.; Stejskal, E. O. *J. Am. Chem. Soc.* **1976**, *98*, 1031–1032.
(7) Oldfield, E.; Norton, R. S.; Allerhand, A. *J. Biol. Chem.* **1975**, *250*, 6381–6402.
(8) Opella, S. J.; Frey, M. H. *J Am Chem. Soc*, preceding paper in this issue.
(9) Lippmaa, E.; Alla, M.; Kundla, E. 18th Experimental NMR Conference, Asilomar, Calif., 1977.
(10) Opella, S. J.; Frey, M. H.; DiVerdi, J. A., unpublished work.
(11) Cross, T. A.; Opella, S. J. *J. Supramol. Struct.*, in press
(12) Asbeck, F.; Beyreuther, K.; Köhler, H.; von Wettstein, G.; Braunitzer, G. *Hoppe-Seyler's Z. Physiol. Chem.* **1969**, *350*, 1047–1066.
(13) Nakashima, Y.; Konigsberg, W. *J. Mol. Biol.* **1974**, *88*, 598–600.
(14) Opella, S. J.; Cross, T. A., unpublished work.

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Bond Switch with Participation of π-Bonded S^{IV} in a Thiadiazole Ring System[1]

Sir:

It has been reported that π-hypervalent sulfur plays an important role in effecting cycloaddition of iminothiazolines to activated acetylenes,[2] nitriles,[3] isothiocyanates,[4] and also in similar reactions involving 1,2-dithiole-3-thiones.[5] We recently reported a unique example of rapid equilibrium due to acid-catalyzed bond switch at π-hypervalent sulfur.[6] We now describe a ring-transformation equilibrium of the 1,2,4-thiadizole ring in neutral solution which can be understood as due to bond switch at π-hypervalent sulfur.

When 5-amino-3-methyl-1,2,4-thiadiazole (**1**) is heated with a nitrile in the presence of aluminum trichloride (molar ratio 1.0:1.0–2.0:1.0–1.5) at 80–110 °C for 0.5–1.5 h, the 1:1 adduct (**2**) was obtained in a moderate yield after usual workup[7] fol-

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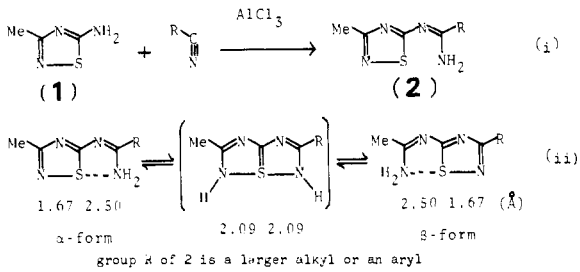
Table I. Some 1,2,4-Thiadiazoles (2) and Their Two Forms at Equilibrium[a]

2	R	Me[a] α form	Me[a] β form	R[a] α form	R[a] β form	β/α at equilibrium	mp, °C	yield, %
a	Me	2.51		2.22		1.00	109.5-111.5	34
b	CH_2Cl	2.55	2.22	4.30	4.61	2.14	103.5-104.2	45
c	CH_2Me	2.52	2.21	1.28(t)	1.34 (t)[b]	1.68	visc oil	59
d	$CHMe_2$	2.52	2.21	1.27(d)	1.34 (d)[c]	2.53	93.1-94.0	49
e	CMe_3	2.50	2.21	1.32	1.40	8.57	91.5-92.2	42
f	p-MeC_6H_4	2.55	2.23			5.99	146.0-147.5	41
g	C_6H_5	2.57	2.23			14.5	148.0-148.7	50
h	p-ClC_6H_4	2.58	2.26			~50	121.0-122.0	55

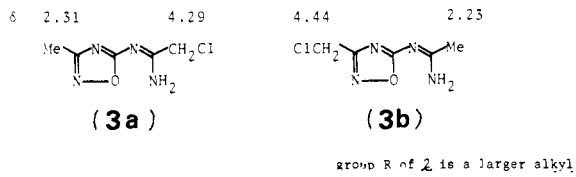
[a] ^1H NMR data: δ values in $CDCl_3$ at 34 °C, Me_4Si as internal standard. [b] CH_2Me, J = 7.2 Hz. [c] $CHMe_2$, J = 6.6 Hz.

lowed by purification by dry column chromatography (Merck, Al_2O_3, $CHCl_3$) and recrystallization of the eluted adduct from benzene-hexane (eq i).



The ^1H NMR spectrum of 5-(1-aminoethylimino)-3-methyl-1,2,4-thiadizole (**2a**) shows two singlets at δ 2.51 (3-Me) and 2.22 (Me of the amidino group). However, to our surprise, the spectrum of the chloromethyl compound (**2b**), shows two pairs of singlets (Table I): one pair at δ 2.55 and 4.30 (α form) and the other at 2.22 and 4.61 (β form), the ratio (β/α) being 2.14 ($CDCl_3$, at 34 °C). A series of compounds (**2**) show the same phenomenon (Table I). This fact can be rationalized only by assuming the occurrence of ring transformation according to eq ii, the bond switch being facilitated by participation of π-hypervalent sulfur.

In order to confirm this rationalization, the corresponding oxygen analogues (**3a** and **3b**) were prepared from 5-amino-



1,2,4-oxadiazoles[8] according to eq i. **3a** (mp 126-128 °C) and **3b** (mp 155.0-155.7 °C) show single methyl and chloromethyl signals as shown below, thus confirming the rationalization.

The β form is more favored when the group R of **2** is a larger alkyl group or a phenyl group with an electron-withdrawing substituent. This fact is consistent with the increase in steric hindrance encountered by the group R when it is attached to the amidino group than when it is on the thiadiazole ring and also with the conjugation of the benzene ring with the heterocycle. In **2b**, the electron-withdrawing effect of the chlorine atom may be operative, because the van der Waals radius of a chlorine atom is smaller than that of a methyl group (cf. **2c**).[9]

The equilibrium was measured for **2b** at 34 °C in several solvents and it is shown that the β form is more favored in solvents with lone-pair electrons; β/α ratios in different solvents are 2.23 (PhH), 2.08 (PhCl), 4.47 (Me_2CO-d_6), 5.74 (Me_2SO-d_6), and 6.53 (MeOH-d_4). The temperature dependence of the equilibrium was measured for the *tert*-butyl compound **2e** in chlorobenzene; β/α ratios at different temperatures are 7.66 (54), 6.78 (69), 6.14 (85), and 5.49 (116). The α form is more favored at higher temperatures and the resulting thermodynamic parameters are ΔH −1.21 kcal/mol and ΔS 0.25 eu.

These facts indicate that the sulfur atom moves back and forth ~0.8 Å along the N—S- - -N line during the ring transformation, the rate of which is slow enough to be detected by NMR (34-120 °C) and is fast enough for normal handling of the sample solution.[10]

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References and Notes

(1) Part 9 of Chemistry of Hypervalent Sulfur. For part 8, see ref 6.
(2) K. Akiba, M. Ochiumi, T. Tsuchiya, and N. Inamoto, *Tetrahedron Lett.*, 459 (1975); K. Akiba, T. Tsuchiya, and N. Inamoto, *ibid.*, 1877 (1976); M. Baudy and A. Robert, *J. Chem. Soc., Chem. Commun.*, 912 (1976).
(3) J. E. Oliver and A. B. DeMilo, *J. Org. Chem.*, **39**, 2225 (1974); K. Akiba, T. Tsuchiya, M. Ochiumi, and N. Inamoto, *Tetrahedron Lett.*, 455 (1975).
(4) G. L'abbé, A. Timmerman, C. Martens, and S. Toppet, *J. Org. Chem.*, **43**, 4951 (1978).
(5) J. L. Deroque, M. Perrier, and J. Vialle, *Bull. Soc. Chim. Fr.*, 2062 (1968); H. Behringer, D. Bender, J. Falkenberg, and R. Wiedenman, *Chem. Ber.*, 101, 1428 (1968).
(6) K. Akiba, S. Arai, T. Tsuchiya, and F. Iwasaki, *Angew. Chem., Int. Ed. Engl.*, **18**, 166 (1979).
(7) P. Oxley, M. W. Partridge, and W. F. Short, *J. Chem. Soc.*, 1110 (1947). The temperature and heating time were different for each compound. Heating was stopped when a clear pale yellow viscous oil was obtained. Overheating should be avoided.
(8) K. R. Huffman and F. C. Schaffner, *J. Org. Chem.*, **28**, 1816 (1963).
(9) L. Pauling, "The Nature of The Chemical Bond", 3rd ed., Cornell University Press, 1960, Chapter 7.
(10) Exact structure determination of **2** by the X-ray method has not been carried out yet, but the N—S- - -N distance was taken from that of an analogous compound in ref 6.
(11) All compounds except **2c**, which gave approximate but acceptable data, gave satisfactory elemental analysis.

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Structure of (3-Chloro-2-hydroxy-5-nitrophenyl)-(2′-chlorophenyl)iodonium Hydroxide Inner Salt

Sir:

The reaction of phenols with phenyliodine diacetates, in general, leads to the formation of mixtures of products including acetoxyphenols and benzoquinones.[1] A notable exception was the report by Fox and Pausacker[2] that on treatment of 4-nitrophenol with phenyliodine diacetate they obtained in 85% yield a yellow crystalline compound, to which they assigned structure **1**. On heating **1**, the *o*-iododiphenyl ether **2** was obtained. In a synthesis of specific chlorinated dibenzofurans,[3] we have used the oxidation of chlorinated 4-nitrophenols with chlorinated phenyliodine diacetates to yield