BOND SWITCH WITH PARTICIPATION OF π-BONDED S^{IV} FROM ISOTHIAZOLE TO THIADIAZOLE RING SYSTEM[1]

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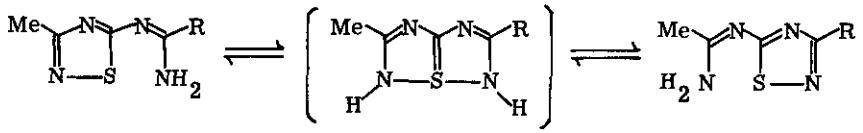
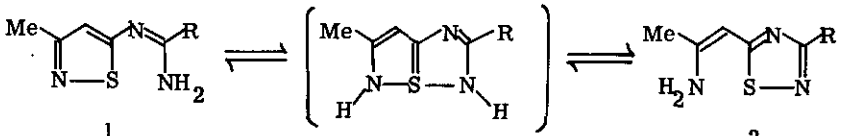
Abstract 5-Amino-3-methylisothiazole (3) gave 1:1 adduct with aromatic nitriles and ethyl acetimidate and the structure of the adduct was shown to be *3-substituted 5-(2-amino-2-methylvinyl)-1, 2, 4-thiadiazole* (2), where ring transformation took place from isothiazole to 1, 2, 4-thiadiazole.

We have recently reported on the presence of ring-transformation equilibrium (1) effected by bond switch with participation of π-bonded S^{IV} in a thiadiazole ring system, where thiathiophthene-analogous system is invoked as an intermediate.[2] In connection with this, it is of interest to examine whether similar equilibrium can exist in an isothiazole-thiadiazole ring system as shown in (2).



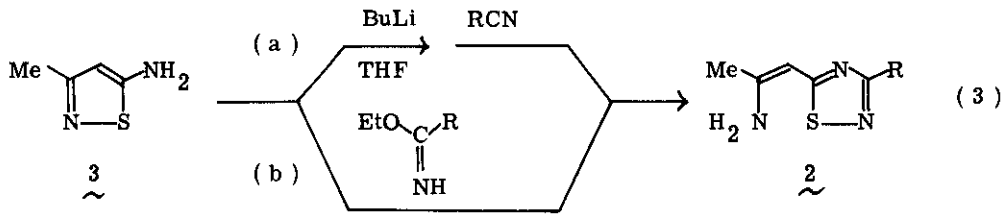
(1)



(2)

1 2

We tried to prepare 1 according to (3) and actually obtained a formal 1:1 adduct of 5-amino-3-methylisothiazole[3] [3 : ^{1}H-NMR (δ in $CDCl_3$), 2.30 (s, 3H), 4.30-5.30 (br.s, 2H), 6.10 (s, 1H)] and a nitrile (RCN), but the true structure was shown to be 2 as described below.



With aromatic nitriles, lithio derivative of 3 gave the adduct in moderate yields, but with aliphatic nitriles, no adduct was obtained by the same procedure and 3 was heated with acetimidate in ethanol or without solvent. Typical examples are shown below.

(a) : Buthyllithium in hexane (6.74 mL, 9.65 mM) was added to 5-amino-3-methylisothiazole (1.00 g, 8.77 mM) in tetrahydrofuran (53 mL) at -78 °C with stirring under nitrogen. After the solution being stirred for 30 min, benzonitrile (1.08 g, 10.52 mM) in the same solvent (9 mL) was added to the solution with a syringe and the mixture was stirred overnight without cooling. After addition of water (90 mL), the mixture was extracted with ether (70 mL × 3) and the solution was dried with magnesium sulfate. After evaporation of the solvent, the residue was recrystallized from hexane-benzene (5:1) to give pale orange crystals of 2a (0.896 g, 4.15 mM, mp 121.5-122.5 °C, 47%).

(b) : 5-Amino-3-methylisothiazole (1.20 g, 10.5 mM) and ethyl acetimidate (2.31 g, 26.5 mM) were dissolved in ethanol (15 mL) and refluxed for 3 h. After evaporation of the solvent, the residue was eluted through an alumina column (28 mm×30 cm) with benzene quickly, due to slow decomposition of the product on alumina. The residue after evaporation of the solvent was recrystallized from benzene to give 2e, mp 97-98 °C, 0.605 g, 38%.

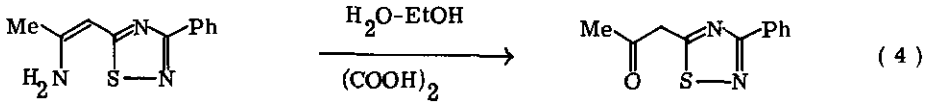
Yields and physical data of the adduct (2), 3-substituted 5-(2-amino-2-methylvinyl)-1, 2, 4-thiadiazole, are shown in the Table.[4] The remarkable high field shift of the methyl and the ring proton of 3 from δ ($CDCl_3$) 2.30 and 6.10 to 2.02 and 5.38, respectively, clearly shows the conversion of the isothiazole ring to the aminovinyl group. Moreover, the distinct difference of chemical shift of ortho and meta-para protons of the aromatic ring (R) clearly indicates that the

aromatic ring is conjugated with some heterocycle,[5] i.e., thiadiazole in this case, and the chemical shift of the second methyl group (R) of 2e lies at the expected chemical shift of the methyl group at position 3 of 1, 2, 4-thiadiazole.[2]

Table Yields and Physical Data of 3-Substituted 5-(2-amino-2-methylvinyl)-1, 2, 4-thiadiazole (2)

Compd. (R)	m.p. (°C)	yield (%)	^{1}H NMR in $CDCl_3$ Me-	-CH=	$-NH_2$	R		IR nujol
2a	121.5	47	2.02	5.38	6.40	7.30-7.60(m, 3H)		3350
(C_6H_5)	122.5		(s)	(s)	6.90	8.00-8.40(m, 2H)		1330
2b	121	33	2.00	5.38	6.50	6.95(d, 2H)	3.82	3340
($MeOC_6H_4$)	122		(s)	(s)	6.70	8.18(d, 2H) J=8HZ	(s)	1330
2c	93	40	2.02	5.40	6.40	7.25(d, 2H)	2.40	3350
(MeC_6H_4)	95		(s)	(s)	6.90	8.10(d, 2H) J=8Hz	(s)	1330
2d	132	40	2.02	5.38	6.50	7.40(d, 2H)		3380
(ClC_6H_4)	133		(s)	(s)	7.00	8.20(d, 2H) J=8Hz		1330
2e	97	38	2.00	5.30	6.10	2.58		
(Me)	98		(s)	(s)	7.00	(s)		

In order to confirm the rationalization, the adduct (2a : 200 mg) was hydrolyzed in water (3 ml)-ethanol (3 ml) in the presence of oxalic acid (50 mg) and the product was determined to be 5-acetonyl-3-phenyl-1, 2, 4-thiadiazole (4a : mp 112-114 °C, 40%), thus illustrating the presence of the enamino group in the adduct (2).[6] ^{1}H-NMR ($CDCl_3$) of 4a showed the corresponding peaks of the methyl and methylene groups at 2.40 and 4.40 and those of the phenyl which are almost exactly the same as those of 2a.[2,5]



2a 4a (4)

Therefore, it was concluded that ring-transformation took place from isothiazole to thiadiazole in the present system and the equilibrium between the two rings with participation of π-bonded S^{IV} could not be detected in $CDCl_3$, CCl_4, MeOH-d_4, and MeCN-d_3 by ^{1}H-NMR at ambient temperature. This fact may be attributed to greater stability of the thiadiazole ring compared with the isothiazole ring.

References and Notes

1. Part 11 of Chemistry of Hypervalent Sulfur, For Part 10, see : Y. Yamamoto and K. Akiba, Heterocycles, 13, 297 (1979).
2. K. Akiba, T. Kobayashi, and S. Arai, J. Am. Chem. Soc., 101, 5857 (1979).
3. A. Adams and R. Slack, J. Chem. Soc., 1959, 3061.
4. All 2 gave correct elemental analyses.
5. L. A. Lee and J. W. Wheeler, J. Org. Chem., 37, 348 (1972) ; R. N. Butler, Can. J. Chem., 51, 2315 (1972).
6. 4a gave correct elemental analyses. By the same procedure, 2b-2d gave the corresponding 4b-4d in 20-40% yield, but some more purification is necessary to obtain correct elemental analyses.

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