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RING-TRANSFORMATION EQUILIBRIUM WITH PARTICIPATION OF π-BONDED S^{IV} IN AN ISOTHIAZOLE SYSTEM. SYNTHESIS OF NON-RING-TRANSFORMED 5-(2-AMINOVINYL)ISOTHIAZOLE DERIVATIVE VIA 1,3-SILYL GROUP SHIFT

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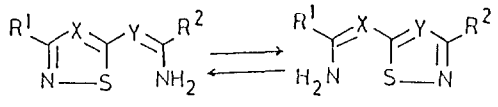
Abstract: Substituents at 5-position of 5-amino-3-methyl- and 3-p-chlorophenyl-5-methylisothiazoles (7 and 8) were silylated and then lithiated to couple with aromatic nitriles in order to afford the adducts (4 and 5) via 1,3-silyl group shift. Desilylation of 5 with TBAF gave solely non-ring-transformed product (3-α-form). By using the pure sample of 3-α-form, the reversible ring-transformation (bond switch) was observed under neutral conditions for the first time.

In the course of our investigations on bond switch at hypervalent sulfur atom, there were found a reversible ring-transformation (1-α ⇄ 1-β)[1] and an irreversible ring-transformation (2-α → 2-β),[2] depending on symmetrical and unsymmetrical nature of the interconverting sulfur containing heterocycles. Recently, we observed also such an equilibrium in 5-(2-aminovinyl) isothiazole system (3-α ⇄ 3-β) under basic conditions for synthesis.[3]

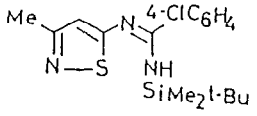
In this communication, we wish to describe a synthesis of N-silylated derivatives of 2, 3, and the related oxygen analogue, i.e., 4, 5, and 6, and of pure compounds of α-form of 3 by means of desilylation of 5 with tetra-n-butylammonium fluoride (TBAF).



1 : X = N, Y = N

2 : X = CH, Y = N

3 : X = CH, Y = CH



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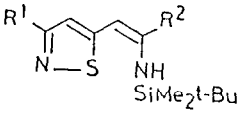
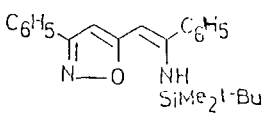


5

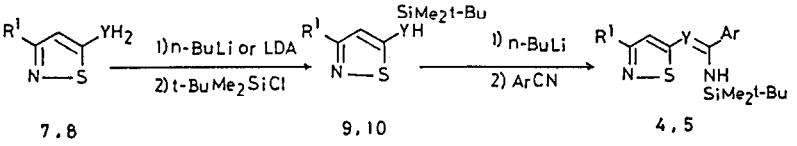
	R^1	R^2
5a	4-ClC_6H_4	4-ClC_6H_4
5b	4-ClC_6H_4	3,5-$Cl_2C_6H_3$
5c	4-ClC_6H_4	4-MeC_6H_4



6

1,3-Silyl Group Shift in Isothiazole Derivatives. 5-Amino-3-methylisothiazole (7) was prepared by the known procedure.[4] Reaction of N-lithio derivative of 7 with tert-butyldimethylsilyl chloride in THF gave a colorless crystalline product (9), mp 91-92 °C, in 54% yield.[5] The N-lithio derivative of 9 was treated with p-chlorobenzonitrile to afford 1 : 1 adduct (4) in 64% yield. ^{1}H NMR spectrum of 4 showed the following characteristic signals: δ ($CDCl_3$) 2.28 (s, 3H), 4.5 (brs, 1H), 6.22 (s, 1H), and 7.32 (brs, 4H), along with those for two methyl groups and for one tert-butyl group attached to silicon. On the basis of spectral data and elemental analyses, the structure of the adduct was assigned as 5-(N-silylaminomethylene)amino-3-methylisothiazole derivative (4).

Treatment of 3-p-chlorophenyl-5-methylisothiazoles (8) with LDA, followed by silylation, furnished 5-silylmethylisothiazole (10) in good yield. The lithio derivative of 10 was reacted with the corresponding aromatic nitriles to give the N-silylated product (5) in moderate yields via 1,3-silyl group shift.[6] The structural assignment of these products (5) is based upon the spectral features and elemental analyses. In the ^{1}H NMR spectrum of 5a, the vinyl proton is seen as a singlet with a chemical shift of δ 5.86 and the heterocyclic one as a singlet at δ 7.32 together with other characteristic signals in $CDCl_3$ solution (Table I). By the same methodology, the oxygen analogue (6) was also prepared in moderate yield.



7,8 9,10 4,5

	R^1	Y	Ar
4	Me	N	4-ClC_6H_4
5a	4-ClC_6H_4	CH	4-ClC_6H_4
5b	4-ClC_6H_4	CH	3,5-$Cl_2C_6H_3$
5c	4-ClC_6H_4	CH	4-MeC_6H_4

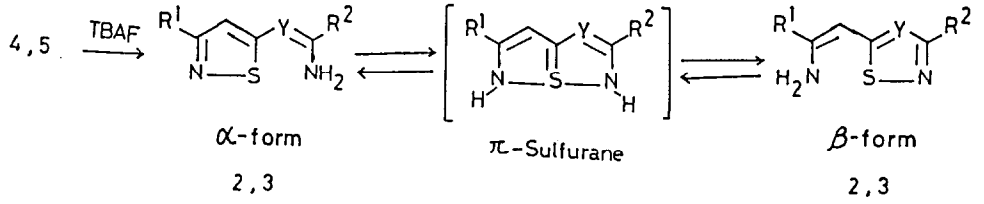
Desilylation of 4 and 5; Synthesis of Pure α-Form. Desilylation of 4 (Y = N) with TBAF at -78 °C in THF gave rise to 5-(2-amino-2-methylvinyl)-3-p-chlorophenyl-1,2,4-thiadiazole (2-β) as a sole product instead of the expected isothiazole derivative (2-α). The spectral data completely coincided with those of the adduct of lithio derivative of 7 with p-chlorobenzonitrile where occurrence of ring-transformation was fully demonstrated recently by us.[2] On the other hand, desilylation of 5 (Y = CH) under the same conditions gave the non-ring-transformed-α-form of 5-(2-aminovinyl)isothiazoles (3-α) in good yields in a pure state after recrystallization from ether-hexane. Structural assignment to 3-α is founded upon ^{1}H NMR spectrum. α-Form of 3a, 3b, and 3c showed a set of singlets for vinyl and heterocyclic hydrogens at δ 5.88, 7.33; 5.87, 7.84; and 5.93, 7.34, respectively. Peaks to show the existence of β-form could not be detected for 3b and 3c.

Furthermore, reversible ring-transformation (bond switch) in this system was confirmed by heating the pure sample of 3b-α and 3c-α at 50 °C for 30 h in

Table I. Yields and ^{1}H NMR Spectral Data of New Compounds

Compd	Yield (%)	mp (°C) (solvent)	^{1}H NMR (δ, $CDCl_3$)
4	64	124-126 (ether-hexane)	0.28(s,6H),0.98(s,9H),2.28(s,3H),4.33-4.62 (br s,1H),6.22(s,1H), and 7.32(s,4H).
5a	61	128-130 (ether-hexane)	-0.05(s,6H),1.04(s,9H),3.78(brs,1H),5.86(s,1H), 7.32(s,1H),7.38(s,4H),and 7.41,7.87(ABq,J=8Hz,4H).
5b	50	170-173 (ether-pentane)	-0.01(s,6H),1.00(s,9H),3.7(brs,1H),5.90(s,1H), 7.38(s,3H), and 7.42,7.87(ABq,J=9Hz,4H).
5c	45	114-116 (pentane)	-0.08(s,6H),1.12(s,9H),2.38(s,3H),3.7-3.9(brs,1H), 5.82(s,1H),7.30(s,1H),7.17,7.35(ABq,J=8.6Hz,4H), and 7.41,7.86(ABq,J=8.7Hz,4H).
6	66	117-119 (pentane)	-0.01(s,6H),1.12(s,9H),5.43(s,1H),6.11(brs,1H), 6.28(s,1H),7.32-7.82(m,8H),and 7.82-8.15(m,2H).
9	54	91-92 (hexane)	0.27(s,6H),0.97(s,9H),2.32(s,3H),4.0-4.4(brs,1H), 6.21(s,1H).
10	98	81-83 (hexane)	0.05(s,6H),0.93(s,9H),2.43(s,2H),7.12(s,1H), and 7.36,7.83(ABq,J=8Hz,4H).
3a ($\alpha = \beta$)	57	136-141 (ether-hexane)	4.31(brs,2H),5.88(s,1H),7.33(s,1H),7.38,7.48 (ABq,J=9.0HZ,4H), and 7.38,7.86(ABq,J=8.6 Hz,4H).
3b-α	70	168-174 (ether-hexane)	5.87(s, 1H),6.02(brs,2H),7.48,8.06(ABq,J=8Hz,4H), 7.58(t,J=1.8Hz,1H),7.68(d,J=1.8Hz,2H), and 7.84(s,1H). (DMSO-d_6)
3c-α	57	168-170 (ether-hexane)	2.39(s,3H),4.32(brs,2H),5.93(s,1H),7.34(s,1H), 7.30,7.47(ABq,J=8.4Hz,4H), and 7.41,7.89(ABq,J=8.8Hz,4H).
3b-β	—	——	5.74(s,1H),6.02(brs,2H),7.46,7.68(ABq,J=9.0Hz,4H), 7.53(t,J=1.8Hz,1H),7.91[7](s,1H), and 8.07(d,J=1.8Hz,2H). (DMSO-d_6)
3c-β	—	——	2.39(s,3H),4.32(brs,2H),5.91[7](s,1H),7.1-7.6(m,7H), and 7.84(ABq,J=8.1Hz,2H).

C_6D_6 solution. A set of singlets for vinyl and heterocyclic hydrogens appeared for 3b-β and 3c-β at δ 5.74, 7.91 and 5.91 and one burried in aromatic hydrogens, respectively.[7] Equilibrium ratio (β/α) was close to unity. On the other hand, neither such equilibration nor ring-trasformation was observed for the unsymmetrical oxygen analogue (11).[8] Hence, such a ring-transformation can be understood in terms of bond switch at π-hypervalent sulfur due to unique stability of π-sulfurane intermediate. The kinetic investigation is now in progress in details.[9]

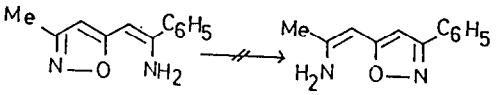


2 : Y = N ; R^1=Me , R^2 = 4-ClC_6H_4

3 : Y = CH; a, R^1 = R^2 = 4-ClC_6H_4

b, R^1 = 4-ClC_6H_4, R^2 = 3,5-$Cl_2C_6H_3$

c, R^1 = 4-ClC_6H_4, R^2 = 4-MeC_6H_4



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References and Notes

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2) (a) K. Akiba, A. Noda, and K. Ohkata, Phosphorus & Sulfur, 16, 111 (1983). (b) P. J. Pogorzelec and D. H. Reid, J. Chem. Soc., Chem. Commun., 1983, 289.

3) K. Akiba, K. Kashiwagi, Y. Ohyama, and K. Ohkata; to be submitted for publication as a full paper.

4) A. Adams and R. Slack, J. Chem. Soc., 3061 (1959).

5) Analytical and spectral data for all new compounds were fully compatible with the given assignments.

6) The details of the geometric considerations (E, Z) will be presented in a full paper. Such a 1,3-silyl group shift was observed in pyridine derivatives; T. Konakahara and K. Sato, Bull. Chem. Soc. Jpn., 56, 1241 (1983).

7) Determined by subtraction of peaks for the α-form from those in equilibrium with the β-form.

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