SYNTHESIS AND REACTION OF 1-PHENYL-4-TRIMETHYLSTANNYL-1,2,3-TRIAZOLES

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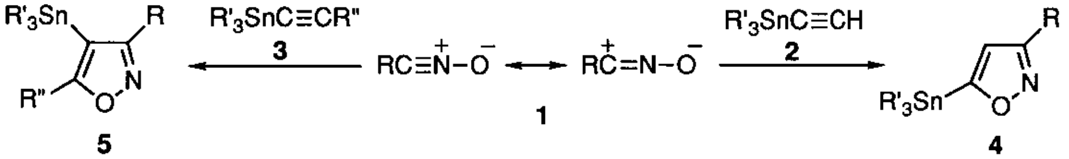
Abstract–1,3-Dipolar cycloaddition reaction of trimethylstannylacetylene with phenyl azide gave a regioselective product, 1-phenyl-4-trimethylstannyl-1,2,3-triazole. On the other hand, the reaction of trimethylstannyl-1-hexyne, -phenylacetylene, and -trimethylsilylacetylene with the azide yielded a mixture of the corresponding 4- and 5-trimethylstannyl-1-phenyl-1,2,3-triazoles.

Detrimethylstannylation, iodination, benzoylation, and palladium-catalyzed phenylation of 4-trimethylstannyl- and 4,5-bis(trimethylstannyl)-1-phenyl-1,2,3-triazoles were also described.

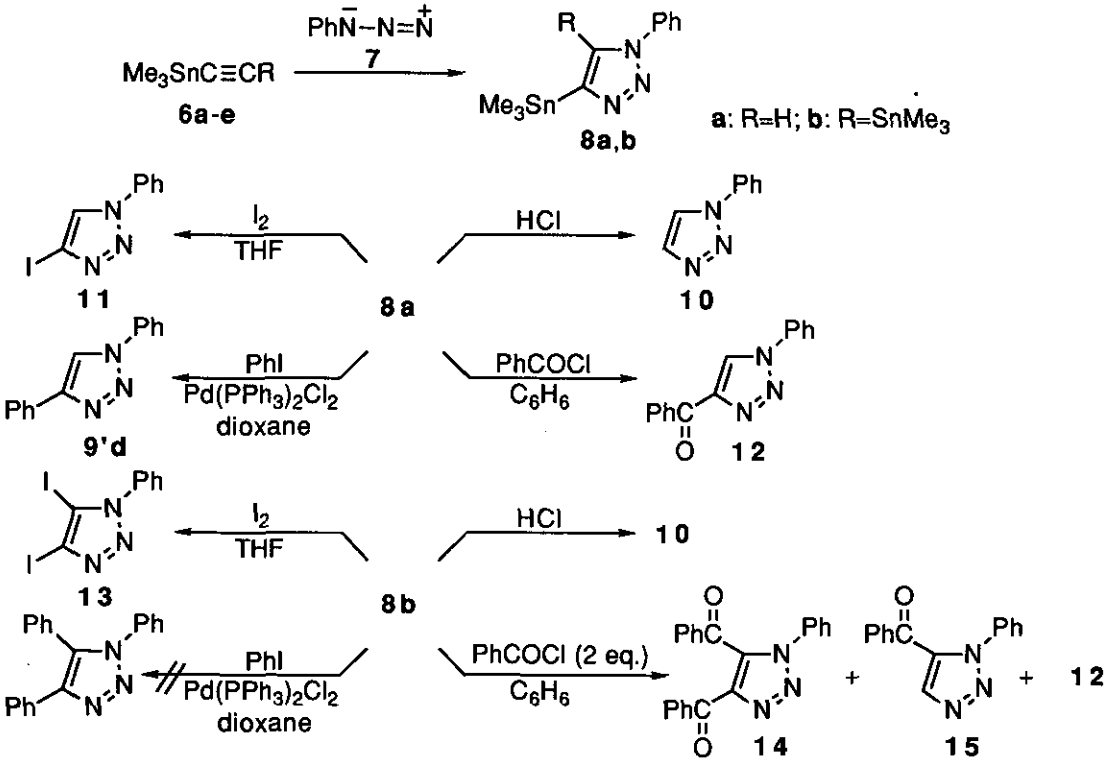
In the previous papers, we have reported the synthesis of trialkylstannylisoxazoles and pyrazoles by the 1,3-dipolar cycloaddition reaction of unsubstituted and substituted trialkylstannylacetylenes with nitrile oxides,[1-3] phenylsydnone,[4] and diazoalkanes.[4] Through the above study, it was found that the reaction of trialkylstannylacetylenes (**2**) with nitrile oxides (**1**) gave 5-trialkylstannylisoxazoles (**4**) exclusively. On the other hand, the same reaction of substituted trialkylstannylacetylenes (**3**) afforded 4-trialkylstannylisoxazoles (**5**) almost regioselectively.



Scheme 1

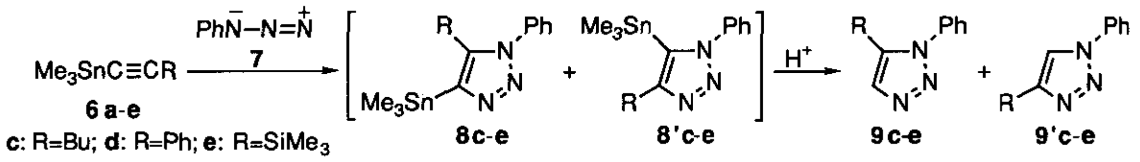
As continuation of the study, we report here the 1,3-dipolar cycloaddition reaction of trimethylstannylacetylenes (**6**) with phenyl azide (**7**). The reaction of trimethylstannylacetylene (**6a**) with **7** in benzene at 70°C gave a single product, 1-phenyl-4-trimethylstannyl-1,2,3-triazole (**8a**) in 69% yield. The cycloaddition reaction of bis(trimethylstannyl)acetylene (**6b**) with **7** gave 4,5-bis-(trimethylstannyl)-1-phenyl-1,2,3-triazole (**8b**) in 67% yield.

The detrimethylstannylation of **8a** and **8b** with hydrochloric acid gave 1-phenyl-1,2,3-triazole (**10**)[5] in 67 and 90% yields. Iodination with iodine of **8a** and **8b** gave the 4-iodo- (**11**) and 4,5-di-iodo-1,2,3-triazoles (**13**) in 93 and 71% yields, respectively. Benzoylation of **8a** with benzoyl chloride in benzene gave phenyl 1-phenyl-1,2,3-triazol-4-yl ketone (**12**) which was identical with an authentic specimen,[6] however, the reaction of **8b** with two equivalents of benzoyl chloride gave a mixture of dibenzoyl- (**14**) and monobenzoyltriazoles (**12** and **15**). Palladium-catalyzed phenylation of **8a** gave known 1,4-diphenyl-1,2,3-triazole (**9'd**)[7] in 68% yield, but the same reaction of **8b** gave no phenylated 1,2,3-triazoles, and the starting material was recovered.



Scheme 2

The reaction of trimethylstannyl-1-hexyne (**6c**) and phenyl(trimethylstannyl)acetylene (**6d**)with **7** gave a mixture of the 5- (**8c,d**) and 4-trimethystannyl-1-phenyl-1,2,3-triazoles (**8'c,d**) which were treated with conc. sulfuric acid in methanol to give 5-butyl-1-phenyl- (**9c**) and 1,5-diphenyl-1,2,3-triazoles (**9d**) mainly. On the contrary, the reaction of trimethylsilyl(trimethylstannyl)acetylene (**6e**) with **7** followed by detrimethylstannylation with hydrochloric acid of the cycloaddition products (**8e** and **8'e**) gave a 1:1 mixture of 5- (**9e**) and 4-trimethylsilyl-1,2,3-triazoles (**9'e**).



Scheme 3

As described as above (Scheme 1), in the 1,3-dipolar cycloaddition reaction with nitrile oxides, trialkylstannylacetylenes (**2**) gave 5-trialkylstannylisoxazoles (**4**) and substituted ones (**3**) gave 4-trialkylstannylisoxazoles (**5**). On the other hand, the cycloaddition reaction of trimethylstannylacetylene (**6a**) along with substituted trimethylstannylacetylenes (**6c,d**) except for **6e** yielded the 4-trimethylstannyl-1,2,3-triazoles (**8a,c,d**). The diverse regioselectivity is now under studying by molecular orbital theory.

EXPERIMENTAL

General Procedure of 1,3-Dipolar Cycloaddition Reaction of Trimethylstannylacetylenes (6) and Phenyl Azide (7)

A mixture of phenyl azide (**7**) (360 mg, 3 mmol) and a trimethylstannylacetylene (**6**) (4.5 mmol) in C_6H_6 (2 ml) was heated at 70°C for 24 h in a sealed tube. After cooling , the mixture was concentrated under reduced pressure to give the residue which was purified by recrystallization or destannylation under acidic conditions.

1-Phenyl-4-trimethylstannyl-1,2,3-triazole (8a)

Yield 69%. mp 84-86°C (pentane-hexane). ^{1}H-Nmr (CDCl$_3$, ppm): 0.43 (9H, s), 7.4-7.9 (5H, m), 7.93 (1H, s). *Anal.* Calcd for $C_{11}H_{15}N_3Sn$: C, 42.72; H, 4.85; N, 13.59. Found: C, 42.94; H, 4.95; N, 13.79.

1-Phenyl-4,5-bis(trimethylstannyl)-1,2,3-triazole (8b)

Yield 67%. mp 149-150°C (C_6H_6-hexane). ^{1}H-Nmr (CDCl$_3$, ppm): 0.12 (9H, s), 0.42 (9H, s), 7.4-7.6 (5H, m). *Anal. Calcd for* $C_{14}H_{23}N_3Sn_2$*: C, 35.52; H, 4.86; N, 8.88. Found: C, 35.69; H, 4.89;* N, 8.95.

Detrimethylstannylation of Trimethylstannyl-1,2,3-triazoles with HCl

A trimethylstannyl-1,2,3-triazole (0.6 mmol) and 3N HCl (10 ml) in MeOH (10 ml) was stirred at room temperature for 2 h. After dilution with H_2O, the mixture was extracted with Et_2O. The ethereal extract was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column using hexane-AcOEt (20:1) as an eluent and then recrystallized.

1-Phenyl-1,2,3-triazole (10) from 8a

Yield 67%. mp 55°C (pentane-hexane). lit.,[5] mp 56°C. ^{1}H-Nmr ($CDCl_3$, ppm): 7.3-7.9 (6H, m), 7.95 (1H, d, *J*=2 Hz).

1-Phenyl-1,2,3-triazole (10) from 8b

Yield 90%. mp 55°C (pentane-hexane).

1-Phenyl-5-trimethylsilyl-1,2,3-triazole (9e)

Yield 35%. mp 86-87°C (hexane). ^{1}H-Nmr ($CDCl_3$, ppm): 0.18 (9H, s), 7.5-7.6 (5H, m), 7.83 (1H, s). *Anal.* Calcd for $C_{11}H_{15}N_3Si$: C, 60.83; H, 6.91; N, 19.35. Found: C, 60.85; H, 6.99; N, 19.42.

1-Phenyl-4-trimethylsilyl-1,2,3-triazole (9'e)

Yield 35%. mp 89-90°C (hexane). ^{1}H-Nmr ($CDCl_3$, ppm): 0.36 (9H, s), 7.4-7.8 (5H, m), 7.93 (1H, s). *Anal.* Calcd for $C_{11}H_{15}N_3Si$: C, 60.83; H, 6.91; N, 19.35. Found: C, 61.11; H, 7.04; N, 19.36.

Detrimethylstannylation of Trimethylstannyl-1,2,3-triazoles with H_2SO_4

A trimethylstannyl-1,2,3-triazole (2 mmol) and conc. H_2SO_4 (400 mg) was stirred at room temperature for 2 h. After addition of ice, the mixture was extracted with Et_2O. The ethereal extract was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on a silica gel column using hexane-AcOEt (10:1) as an eluent or distilled under reduced pressure.

5-Butyl-1-phenyl-1,2,3-triazole (9c)

Yield 22%. bp 115-125°C/2 mmHg. ^{1}H-Nmr ($CDCl_3$, ppm): 0.7-1.8 (7H, m), 2.5-2.8 (2H, m), 7.3-7.7 (5H, m). *Anal.* Calcd for $C_{12}H_{15}N_3$: C, 71.64; H, 7.46; N, 20.90. Found: C, 71.70; H, 7.50; N, 20.90.

4-Butyl-1-phenyl-1,2,3-triazole (9'c)

Yield trace. Viscous liquid. ^{1}H-Nmr ($CDCl_3$, ppm): 0.6-1.9 (7H, m), 2.7-3.0 (2H, m), 7.4-7.8 (5H, m). High Resolution ms Calcd for $C_{12}H_{15}N_3$: 201.1266. Found: 201.1262.

1,5-Diphenyl-1,2,3-triazole (9d)

Yield 39%. mp 112-114°C (Et_2O-hexane). lit.,[7] mp 113°C. ^{1}H-Nmr ($CDCl_3$, ppm): 7.2-7.5 (10H, m), 7.83 (1H, s). High Resolution ms Calcd for $C_{16}H_{16}N_3Sn$: 370.0366. Found: 370.0342.

1,4-Diphenyl-1,2,3-triazole (9'd)

Yield trace. mp 182-185°C (CH_2Cl_2-hexane). lit.,[6] mp 184-185°C. ^{1}H-Nmr ($CDCl_3$, ppm): 7.3-8.0 (10H, m), 8.20 (1H, s).

Iodination of Trimethylstannyl-1,2,3-triazoles (8a and 8b)

Iodine (280 mg, 1.1 mmol) in THF (20 ml) was added dropwise to **8a** or **8b** (1 mmol) in THF (10 ml) with stirring at room temperature, and the mixture was stirred for 1.5 h. After dilution with H_2O, the mixture was extracted with Et_2O. The ethereal extract was washed with aq. $Na_2S_2O_3$, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a silica gel column with CH_2Cl_2 as an eluent.

4-Iodo-1-phenyl-1,2,3-triazole (11)

Yield 93%. mp 149-150°C (C_6H_6-hexane). ^{1}H-Nmr ($CDCl_3$, ppm): 7.4-7.8 (5H, m), 8.03 (1H, s). *Anal.* Calcd for $C_8H_6N_3I$: C, 35.56; H, 2.22; N, 15.56; I, 46.67. Found: C, 35.62; H, 2.37; N, 15.73; I, 46.85.

4,5-Diiodo-1-phenyl-1,2,3-triazole (13)

Yield 71%. mp 168°C (C_6H_6-hexane). ^{1}H-Nmr ($CDCl_3$, ppm): 7.5-7.6 (5H, br). *Anal.* Calcd for $C_8H_5N_3I_2$: C, 24.30; H,1.27; N, 10.63; I, 63.80. Found: C, 24.07; H, 1.41; N, 10.75; I, 63.85.

1,4-Diphenyl-1,2,3-triazole (9'd) by Palladium-Catalyzed Phenylation of 8a

A mixture of **3a** (155 mg, 0.5 mmol), iodobenzene (150 mg, 0.75 mmol) and $Pd(PPh_3)_2Cl_2$ (11 mg, 0.015 mmol) in dioxane (5 ml) was refluxed for 3.5 h. The mixture was extracted with Et_2O. The ethereal extract was dried over $MgSO_4$, and the extract was concentrated under reduced pressure. The residue was chromatographed on a silica gel column with CH_2Cl_2 as an eluent to give colorless prisms which were recrystallized from CH_2Cl_2-hexane. Yield 100 mg (68%). mp 182-185°C. lit.,[7] mp 184-185°C.

Phenyl 1-Phenyl-1,2,3-triazol-4-yl Ketone (12)

A mixture of **8a** (310 mg, 1 mmol) and benzoyl chloride (170 mg, 1.2 mmol) in C_6H_6 (5 ml) was refluxed for 19 h. The mixture was extracted with Et_2O, and the extract was dried over $MgSO_4$. The residue obtained from the ethereal extract was chromatographed on a silica gel column with C_6H_6-hexane (4:1) as an eluent to give colorless prisms which were recrystallized from C_6H_6-

hexane. Yield 100 mg (40%). mp 120-121°C. lit.,[6] mp 123°C. Ir ($CHCl_3$, cm^{-1}): 1655. ^{1}H-Nmr ($CDCl_3$, ppm): 7.4-7.9 (8H, m), 8.4-8.6 (2H, m), 8.67 (1H, s).

Benzoylation of 3b with Benzoyl Chloride

A mixture of **8b** (240 mg, 0.5 mmol) and benzoyl chloride (160 mg, 1.1 mmol) in C_6H_6 (5 ml) was refluxed for 34 h. The mixture was extracted with Et_2O, and the extract was dried over $MgSO_4$. The residue obtained from the ethereal extract was chromatographed on a silica gel column with hexane-AcOEt (4:1) as an eluent. First eluate gave colorless prisms (4,5-dibenzoyl-1-phenyl-1,2,3-triazole: **14**) which was recrystallized from Et_2O. Yield 20 mg (11%). mp 167-169°C. Ir ($CHCl_3$, cm^{-1}): 1680, 1655. ^{1}H-Nmr ($CDCl_3$, ppm): 7.3-8.0 (13H, m), 8.4-8.6 (2H, m). *Anal.* Calcd for $C_{22}H_{15}N_3O_2$: C, 74.79; H, 4.25; N, 11.90. Found: C, 74.56; H, 4.54; N, 11.98.

Second eluate gave colorless needles (phenyl 1-phenyl-1,2,3-triazol-4-yl ketone: **12**) which was recrystallized from Et_2O-hexane. Yield 20 mg (16%). mp 120-121°C. lit.,[6] mp 123°C.

Third eluate gave colorless prisms (phenyl 1-phenyl-1,2,3-triazol-5-yl ketone: **15**) which was recrystallized from hexane. Yield 80 mg (64%). mp 95-97°C. Ir ($CHCl_3$, cm^{-1}): 1670. ^{1}H-Nmr ($CDCl_3$, ppm): 7.4-7.7 (8H, m), 7.9-8.0 (2H, m), 8.07(1H, s). *Anal.* Calcd for $C_{15}H_{11}N_3O$: C, 72.29; H, 4.42; N, 16.87. Found: C, 72.25; H, 4.54; N, 16.83.

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