Unprecedented 1,4-Stannatropy : Effective Generation of Azomethine Ylides as Nitrile Ylide Equivalents from *N*-(Stannylmethyl)thioamides

Mitsuo Komatsu*, Yukihiro Kasano, Jin-ichi Yonemori, Yoji Oderaotoshi, Satoshi Minakata

Prof. Dr. Mitsuo Komatsu

Department of Applied Chemistry and Center for Atomic and Molecular Technologies
Graduate School of Engineering, Osaka University
Yamadaoka 2-1, Suita, Osaka, 565-0871, Japan

Research Center for Environmental Preservation, Osaka University

Yamadaoka 2-4, Suita, Osaka, 565-0871, Japan

Fax: +81-6-6879-7403

E-mail: komatsu@chem.eng.osaka-u.ac.jp

Yukihiro Kasano, Jin-ichi Yonemori, Dr. Yoji Oderaotoshi, Dr. Satoshi Minakata

Department of Applied Chemistry, Graduate School of Engineering, Osaka University

General Methods.: Melting points were determined on a Yanaco micro melting point apparatus and are uncorrected. IR spectra were obtained on a Jasco FT/IR-410 infrared spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL FT-NMR JNM EX 270 spectrometer (^{1}H NMR, 270 MHz; ^{13}C NMR, 68 MHz) using tetramethylsilane as an internal standard. Mass spectra and high-resolution mass spectral data were obtained on a JEOL DX-303 mass spectrometer. Products were purified by chromatography on silica gel 60 (Merck Co.), silica gel FL60D (Fuji Silysia

Chemical Co.), silica gel 60 [spherical, neutral] (Nacalai Tesque Inc.) or silica gel BW-300 (Fuji Silysia Chemical Co.). Preparative gel permeation liquid chromatography (GPLC) was performed on a JAI (Japan Analytical Industry) LC-908 instrument with JAIGEL 1H-2H columns and chloroform as an eluent. Analytical thin layer chromatography was performed using EM reagent 0.25 mm silica gel glass plates (silica gel 60 F254, 0.25 mm thickness) (Merck Co.). Visualization was accomplished with UV light and ethanolic phosphomolybdic acid followed by heating. All reactions were carried out under an atmosphere of nitrogen. Organic solvents were dried and distilled prior to use.

Experimental Procedure and Spectral Data

Preparation of *N*-(trimethylsilylmethyl)thiobenzamide (1b)

Lawesson reagent (0.210 g, 0.512 mmol) was added to a benzene solution (5 ml) of *N*-(trimethylsilylmethyl)benzamide[1] (**1a**) (0.184 g, 0.890 mmol), and the reaction mixture was refluxed for 6 h. The mixture was concentrated and purified by silica gel column chromatography (silica gel 60, Merck Co., eluent: hexane/ethyl acetate) to give thioamide **1b** (0.161 g, 0.854 mmol, 96%). Thioamide **1b** was confirmed by comparison of the spectral data with those reported in the reference.[2]

Preparation of *N*-(tributylstannylmethyl)thiobenzamide (1c)

n-Butyllithium (1.6 M hexane solution, 7.5 ml, 12 mmol) was added slowly to a THF solution (10 ml) of diisopropylamine (1.68 ml, 12 mmol) at -78 ºC, and the solution was stirred for 40 min at the same temperature. Benzamide (1.66 g, 13.7 mmol) was added to the reaction mixture, and was stirred for 3 h at -78 ºC.

Tributylstannylmethyl methanesulfonate[1] (4.8 g, 12 mmol) was added slowly to the reaction mixture, and was stirred overnight at room temperature. After the reaction was quenched with water (20 ml), the organic solvent was removed from the reaction mixture under reduced pressure. The residue and aqueous layer were extracted with hexane (10 ml x 3), and the combined organic layer was dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography (silica gel 60, Merck Co., eluent: hexane/ethyl acetate) to give *N*-(tributylstannylmethyl)benzamide (4.48 g, 10.6 mmol, 88%).

Lawesson reagent (2.43 g, 6 mmol) was added to a benzene solution (50 ml) of the benzamide (5.53 g, 13 mmol), and was heated at 60 ºC for 10 min. The mixture was concentrated and purified by silica gel column chromatography (silica gel 60 [spherical, neutral], Nacalai Tesque Inc., eluent: hexane/ethyl acetate) and gel permeation column chromatography (JAIGEL-2H, JAI Co. Ltd., eluent: chloroform) to give thioamide **1c** (0.926 g, 2.1 mmol, 16%).

Amide: colourless oil; ^{1}H NMR ($CDCl_3$) δ 7.65-7.75 (m, 2H), 7.30-7.50 (m, 3H), 6.50-6.45 (br, 1H), 3.02 (d, J = 5.3 Hz, $^2J_{H\text{-}Sn}$ = 28.0 Hz, 2H), 1.70-0.80 (m, 27H); ^{13}C NMR ($CDCl_3$) 167.6, 135.0, 131.0, 128.5, 126.6, 45.1, 29.1, 27.4, 13.7, 10.2; IR (neat) 1628 cm^{-1}; MS (CI) *m*/*z* 426 (M^++1, 11), 368 (100), 291 (3), 254 (2), 134 (5); HRMS (*m*/*z*, M^+) calcd. for $C_{20}H_{36}NOSn$: 426.1819, found: 426.1823.

Thioamide **1c**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 8.10-7.95 (br, 1H), 7.27-7.73 (m, 5H), 3.62 (d, J = 6.2 Hz, $^2J_{H\text{-}Sn}$ = 12.7 Hz, 2H), 1.70-0.80 (m, 27H).

Preparation of *N*-methyl-*N*-(tributylstannylmethyl)thiobenzamide (1d)

Lawesson reagent (0.93 g, 2.3 mmol) was added to a benzene solution (15 ml)

of *N*-methyl-*N*-(tributylstannylmethyl)benzamide[3] (2.00 g, 4.6 mmol), and was heated at 60 ºC for 4 h. The mixture was concentrated and purified by silica gel column chromatography (silica gel 60 [spherical, neutral], Nacalai Tesque, eluent: hexane/ethyl acetate) and gel permeation column chromatography (JAIGEL-2H, JAI Co. Ltd., eluent: chloroform) to give thioamide **1d** (1.04 g, 2.3 mmol, 50%).

Thioamide **1d**: yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.32-7.25 (m, 5H), 3.82 (s, $^{2}J_{H\text{-}Sn}$ = 13.5 Hz, 2H), 3,17 (s, 3H), 1.70-0.80 (m, 27H); ^{13}C NMR ($CDCl_3$) 193.2, 143.1, 128.1, 128.0, 126.0, 46.0, 44.2, 29.0, 27.4, 13.7, 11.3.

Preparation of *N*-(tributylstannylmethyl)thioisobutyramide (1e)

Thioamide **1e** was synthesized by the same procedure as that for thioamide **1c** [*N*-(tributylstannylmethyl)isobutyramide: 53% yield, thioamide **1e**: 20% yield].

Amide: colourless oil; ^{1}H NMR ($CDCl_3$) δ 5.70-5.60 (br, 1H), 2.80 (d, J = 5.0 Hz, $^{2}J_{H\text{-}Sn}$ = 14.5 Hz, 2H), 2.53 (sep, J = 6.9 Hz, 1H), 1.58-1.23 (m, 18H), 1.13 (d, J = 6.9 Hz, 6H), 0.89 (t, J = 7.0 Hz, 9H); ^{13}C NMR ($CDCl_3$) 176.6, 35.5, 29.0, 27.3, 24.1, 19.7, 13.6, 10.0; IR (neat) 1630 cm^{-1}.

Thioamide **1e**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.65-7.55 (br, 1H), 3.40 (d, J = 6.2 Hz, $^{2}J_{H\text{-}Sn}$ = 13.4 Hz, 2H), 2.78 (sep, J = 7.0 Hz, 1H), 0.80-1.60 (m, 18H), 1.13 (d, J = 7.0 Hz, 6H), 0.89 (t, J = 7.0 Hz, 9H); ^{13}C NMR ($CDCl_3$) 205.2, 43.9, 33.9, 29.2, 27.5, 22.8, 13.8, 11.2.

Preparation of *N*-(tributylstannylmethyl)thioformamide (1f)

n-Butyllithium (1.6M hexane solution, 7.5 ml, 12 mmol) was slowly added to a THF solution (30 ml) of formamide (0.44 ml, 11 mmol) at -78 ºC, and was stirred for 1

h at -78 ºC. A DMF solution (30 ml) of tributylstannylmethyl methanesulfonate (4.0 g, 10 mmol) was added to the THF solution, and the mixuture was warmed to room temperature and stirred for 12 h. After the reaction was quenched with water (50 ml), the mixture was extracted with hexane (50 ml x 4), and the combined organic layer was dried over anhydrous potassium carbonate and concentrated. The residue was purified by silica gel column chromatography (silica gel 60, Merck Co., eluent: hexane/ethyl acetate) to give *N*-(tributylstannylmethyl)formamide (1.96 g, 5.6 mmol, 56%).

Lawesson reagent (1.1 g, 2.8 mmol) was added to a THF solution (60 ml) of the formamide (1.96 g, 5.6 mmol), and was stirred at room temperature for 10 min. The solution was concentrated and purified by silica gel column chromatography (silica gel 60 [spherical, neutral, Nacalai Tesque Inc.] dried in an oven at 200 ºC under reduced pressure, eluent: hexane/ethyl acetate) to give thioamide **1f** (1.53 g, 4.2 mmol, 75%).

Amide: colourless oil; ^{1}H NMR ($CDCl_3$) δ 8.11 (s, 1H), 5.58 (brs, 1H), 2.87 (d, J = 5.5 Hz, $^{2}J_{H\text{-}Sn}$ = 14.0 Hz, 2H), 1.60-0.80 (m, 27H); ^{13}C NMR ($CDCl_3$) 160.9, 29.0, 27.4, 22.6, 13.7, 10.0.

Thioamide **1f**: pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 9.18 (s, 1H), 7.71 (brs, 1H), 3.48 (dd, J = 6.2, and 0.8 Hz, $^{2}J_{H\text{-}Sn}$ = 13.4 Hz, 2H), 1.60-0.80 (m, 27H); ^{13}C NMR ($CDCl_3$) 183.5, 31.8, 29.0, 27.4, 13.7, 11.0.

Preparation of *N*-methyl-*N*-(tributylstannylmethyl)thioformamide (1g)

Thioamide **1g** was synthesized by the same procedure as that for thioamide **1f** [*N*-methyl-*N*-(tributylstannylmethyl)formamide: 63% yield, thioamide **1g**: 52% yield].

Amide: colourless oil; ^{1}H NMR ($CDCl_3$) δ 7.93 (s, 1H), 2.94 (s, 3H), 2.86 (s, $^{2}J_{H\text{-}Sn}$ = 14.2 Hz, 2H), 1.55-0.80 (m, 27H); ^{13}C NMR ($CDCl_3$) 160.9, 37.9, 30.5, 29.0, 27.3, 13.6,

10.4.

Thioamide **1g**: colourless oil; ^{1}H NMR ($CDCl_3$) δ 8.90 (s, 1H), 3.54 (s, $^{2}J_{H\text{-}Sn}$ = 13.8 Hz, 2H), 3.29 (s, 3H), 1.70-0.80 (m, 27H); ^{13}C NMR ($CDCl_3$) 180.8, 37.9, 30.5, 29.0, 27.3, 13.6, 10.4.

General procedure for cycloaddition of α-metalloamides or α-metallothioamides with dipolarophiles

A benzene solution (0.5 ml) of a dipolarophile (0.18 mmol) was added to a α-metallothioamide (0.06 mmol) and mesitylene (2.6 mg, 0.022 mmol), an internal standard, in a reaction tube, which was then sealed. The solution was heated to reaction temperature until the reaction was finished, and the mixture was purified by silica gel column chromatography (Fuji Silysia, FL-60D [spherical], eluent: hexane/ethyl acetate) to give the corresponding cycloadduct.

Cycloadducts **3a**[2], **3c**[4], **4a**[2], **4b**[5], **4g**[6], **5a**[2], **5b**[5], and **5c**[7] were confirmed by comparison of their NMR and mass spectral data with those reported in the references.

6,8-Dioxo-2-phenyl-3,7-diazabicyclo[3.3.0]octa-2-ene (3b): colourless solid; mp 116-119 ºC; ^{1}H NMR ($CDCl_3$) δ 8.25 (dd, *J* = 7.8 and 1.6 Hz, 2H), 7.57-7.30 (m, 8H), 4.81 (dt, *J* = 8.8 and 2.2 Hz, 1H), 4.66 (dd, *J* = 6.3 and 2.2 Hz, 2H), 3.93 (dt, *J* = 8.8 and 6.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) 176.9, 172.2, 166.5, 131.8, 131.4, 129.2, 129.0, 128.7, 128.4, 126.3, 63.6, 56.0, 44.6; IR (neat) 1710, 1497, 1384, 1196 cm^{-1}; MS (EI) *m*/*z* 290 (M^+, 22), 143 (11), 117 (100), 68 (22).

***trans*-3,4-Bis(methoxycarbonyl)-1-pyrroline (3d):** colourless oil; ^{1}H NMR ($CDCl_3$) δ

7.33 (d, J = 3.2 Hz, 1H), 4.00-3.60 (m, 4H), 3.74 (s, 3H), 3.67 (s, 3H).

3,4-Dicyano-1-methyl-2-phenyl-2-pyrroline (4c): colourless solid; ^{1}H NMR ($CDCl_3$) δ 7.55-7.35 (m, 5H), 4.08 (dd, J = 11.1 and 7.3 Hz, 1H), 3.91 (t, J = 11.1 Hz, 1H), 3.83 (dd, J = 11.1 and 7.3 Hz, 1H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$) 167.2, 131.1, 129.0, 128.1, 127.6, 118.5, 117.4, 74.1, 57.7, 36.1 31.5; IR (neat) 1710, 1497, 1384, 1196 cm^{-1}; MS (EI) m/z 209 (M^+, 95), 182 (100), 140 (23), 118 (60), 70 (19); HRMS (m/z, M^+) calcd. for $C_{13}H_{11}N_3$: 209.0953, found: 209.0943.

3-Methoxycarbonyl-1-methyl-2-phenyl-2-pyrroline (4d): colourless solid; ^{1}H NMR ($CDCl_3$) δ 7.45-7.20 (m, 5H), 3.49 (s, 3H), 3.49 (t, J = 10.5 Hz, 2H), 2.88 (t, J = 10.5 Hz, 2H), 2.06 (s, 3H); ^{13}C NMR ($CDCl_3$) 166.7, 132.3, 130.6, 128.6, 128.4, 127.9, 127.8, 54.1, 50.2, 35.8, 28.1.

3,4-Dicyano-2-isopropyl-2-pyrroline (4e): colourless solid; ^{1}H NMR (C_6D_6) δ 3.10-3.00 (br, 1H), 3.05 (dd, J = 11.4 and 6.4 Hz, 1H), 2.87 (ddd, J = 10.4, 6.4, and 1.4 Hz, 1H), 2.57 (ddd, J = 11.4, 10.4, and 1.4 Hz, 1H), 2.42 (sep, J = 7.0 Hz, 1H), 0.74 (d, J = 7.0 Hz, 3H), 0.78 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) 173.9, 118.7, 116.9, 71.4, 50.2, 32.5, 27.9, 20.3, 20.2; MS (EI) m/z 161 (M^+, 48), 146 (25), 144 (22), 83 (100), 41 (36); HRMS (m/z, M^+) calcd. for $C_9H_{11}N_3$: 161.0953, found: 161.0953.

3,4-Dicyano-2-pyrroline (4f): dark brown solid; ^{1}H NMR (C_6D_6) δ 5.75 (d, J = 3.2 Hz, 1H), 2.83 (ddd, J = 11.6, 6.5, and 1.4 Hz, 1H), 2.66 (ddd, J = 10.6, 6.5, and 1.4 Hz, 1H), 2.53 (brdt, J = 3.2 and 1.4 Hz, 1H), 2.35 (dd, J = 11.6 and 10.6 Hz, 1H).

3,4-Dicyano-1-methyl-2-pyrroline (4h): light brown solid; ^{1}H NMR (C_6D_6) δ 5.48 (s, 1H), 2.98 (dd, *J* = 11.6 and 6.7 Hz, 1H), 2.55 (dd, *J* = 10.8 and 6.7 Hz, 1H), 2.18 (dd, *J* = 11.6 and 10.8 Hz, 1H), 1.63 (s, 3H); ^{13}C NMR ($CDCl_3$) 155.4, 118.1, 116.5, 73.9, 56.8, 36.8, 32.7.

1 D. E. Seitz, J. J. Carroll, C. P. M. Cartaya, S.-H. Lee and A. Zapata, *Synth. Comm.*, 1983, **13**, 129.

2 O. Tsuge, S. Kanemasa and K. Matsuda, *J. Org. Chem.*, 1986, **51**, 1997.

3 A. F. Burchat, J. M. Chong and N. Nielsen, *J. Org. Chem.*, 1996, **61**, 7627.

4 O. Tsuge, S. Kanemasa, T. Yamada and K. Matsuda, *J. Org. Chem.*, 1987, **52**, 2523.

5 A. Padwa, G. Haffmanns and M. Tomas, *J. Org. Chem.*, 1984, **49**, 3314.

6 R. Smith and T. Livinghouse, *J. Org. Chem.*, 1983, **48**, 1554

7 J. Woo, S. T. Sigurdsson and P. B. Hopkins, *J. Am. Chem. Soc.*, 1993, **115**, 3407.