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Tellurium-metal exchange reaction of *n*-butyl 2-pyridinyl telluride derivatives with *n*-butyllithium or dilithium dimethylcyanocuprate proceeded smoothly to give the corresponding 2-pyridinylmetal derivatives, which are important intermediates for functionalization of pyridines.

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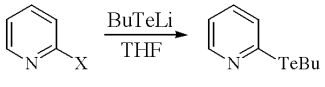
Organometal compounds such as organolithiums or organocuprates play important roles in organic synthesis [1] and therefore, the development of efficient methods for the preparations of organometal compounds is of importance. In recent years, organotellurium compounds as precursors of organometal compounds have been studied actively [2]. By treatment of diorganyl tellurides with alkyllithiums or alkylcuprates, a tellurium-metal exchange reaction occurs, generating organolithiums (alkyl-, allyl-, aryl-, benzyl-, ethynyl- and vinyllithium) or organocuprates, respectively. Acyl- and aroyllithiums are also generated by the corresponding telluroesters.

The chemistry of pyridine derivatives has been studied extensively because pyridine derivatives are important for pharmaceuticals, chemicals and so on. Aryl and heteroarylmetal compounds can be usually prepared by halogen-metal exchange reaction or hydrogen-metal exchange reaction. Especially, halogen-metal exchange reaction of arylhalides has been developed as one of the major tools of organic synthesis [3]. In 1987, Hiiro reported a new method, which provides phenyllithium compounds from corresponding tellurides *via* a tellurium-lithium exchange reaction [4]. In connection with our recent studies on pyridinylmetal derivatives [5], we have investigated the preparations and reactions of *n*-butyl 2-pyridinyl telluride derivatives [6].

Initially, *n*-butyl 2-pyridinyl telluride **2** was prepared by the nucleophilic substitution of a 2-halopyridine and with lithium *n*-butanetellurolate (Scheme 1, Table 1). Compound **2** was generated from each 2-halopyridine. However, *n*-butyl 3-pyridinyl telluride was scarcely generated from 3-bromopyridine, and nucleophilic substitution at the 3-position of the pyridine ring is known to be generally inactive. Nucleophilic substitution of halopyridines with lithium *n*-butanetellurolate was only found to proceed smoothly at the 2-position of the pyridine ring.

The tellurium-metal exchange reaction of compound **2** was then investigated using *n*-butyllithium and dilithium dimethylcyanocuprate. The results are summarized in

Scheme 1



1a-c **2**

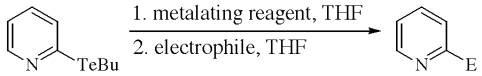
Table 1

Preparation of *n*-Butyl 2-pyridinyl Telluride **2**

Compound	Substituent X	Reaction temp.	Reaction time/h	Yield (%)
1a	Cl	Room temp.	20	29
1a	Cl	Room temp.	72	33
1a	Cl	60 °C	24	41
1a	Cl	Reflux	92	61
1b	Br	Room temp.	20	55
1b	Br	Reflux	92	70
1c	I	Room temp.	20	56
1c	I	Room temp.	92	62

Scheme 2 and Table 2. When compound **2** was treated with dilithium dimethylcyanocuprate in tetrahydrofuran at -20 °C and then 2-cyclohexen-1-one, the 1,4-addition as a characteristic reaction of cuprates proceeded to give 3-(2-pyridinyl)cyclohexanone **3d** (41%). From these results, the tellurium-metal exchange reaction is considered to proceed to form the 2-pyridinylmetal intermediate.

Scheme 2



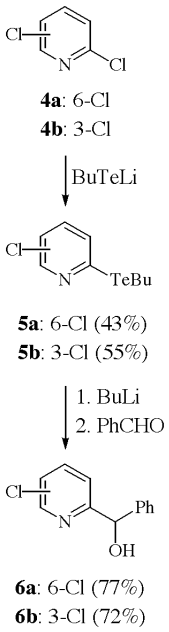
2 **3a-d**

We next examined this methodology using dihalopyridines. First, preparation and reaction of *n*-butyl 6-chloro-2-pyridinyl telluride **5a** was investigated (Scheme 3). Though 2,6-dichloropyridine **4a** possesses two chlorine atoms, compound **5a** was prepared as an important precursor for monofunctionalization of pyridines at the 2-position. Compound **5a** was treated with *n*-butyllithium in tetrahydrofuran at -78 °C and then benzaldehyde, to give compound **6a**. Similarly, *n*-butyl 3-chloro-2-pyridinyl telluride **5b** was also investigated (Scheme 3). The nucleophilic substitution reaction of lithium *n*-butanetellurolate and then tellurium-lithium exchange reaction proceeded at the 2-position, and compound **6b** was generated. For dihalopyridines, the

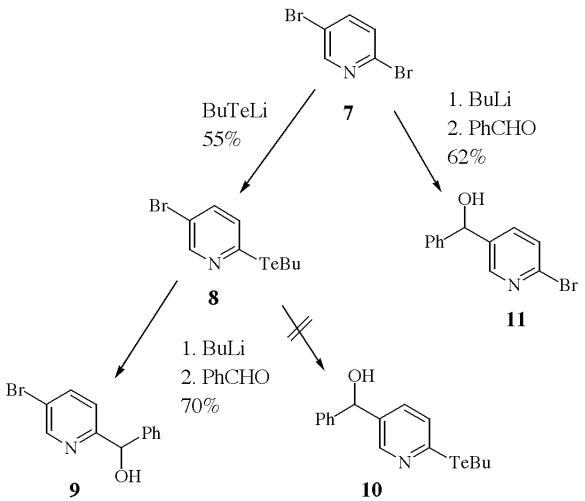
Table 2
Reactions of *n*-Butyl 2-pyridinyl Telluride **2**

Metalating reagent	Reaction temp./°C	Reaction time	Electrophile	E	Product	Yield (%)
BuLi	-78	5 min	PhCHO	CH(OH)Ph	**3a**	73
BuLi	-78	5 min	PhCONMeOMe	COPh	**3b**	64
BuLi	-78	5 min	ICH_2CH_2I	I	**3c**	50
$Me_2Cu(CN)Li_2$	-20	1.5 h	PhCHO	CH(OH)Ph	**3a**	67
$Me_2Cu(CN)Li_2$	-20	1.5 h	2-Cyclohexen-1-one	3-oxocyclohexyl	**3d**	41

Scheme 3



Scheme 4



regioselectivity of the halogen-metal exchange reaction is of importance. For example, the halogen-metal exchange reaction of 2,5-dibromopyridine **7** is known to proceed at the 5-position and 2-bromo-5-lithiopyridine are generated [7]. On the other hand, the 2-position selective halogen-metal exchange reaction of compound **7** has been scarcely known [8]. In order to develop a new method for regioselective functionalization of 2,5-dibromopyridine, we investigated the preparation of 5-bromo-2-lithiopyridine and 2-bromo-5-lithiopyridine. For 5-bromo-2-lithiopyridine, the preparation and reaction of *n*-butyl 5-bromo-2-pyridinyl telluride **8** was carried out (Scheme 4). Compound **8** was prepared by a similar manner to the preparation of compound **2** and treated with *n*-butyllithium in tetrahydrofuran at -78 °C and then benzaldehyde, to give compound **9**, which was functionalized selectively at the 2-position. The tellurium-metal exchange reaction is considered to proceed faster than the halogen-metal exchange reaction because compound **10** was not detected. And for 2-bromo-5-lithiopyridine, compound **7** was treated with *n*-butyllithium in tetrahydrofuran at -100 °C and then with benzaldehyde, to give compound **11**, in which the 5-position was selectively functionalized.

In summary, 2-pyridinyl tellurides were prepared easily from 2-halopyridines and the tellurium-metal exchange reaction is now available for the selective preparation of 2-metalopyridines. As for dihalopyridine, it has been possible to prepare the desired monolithiopyridine by using the tellurium-lithium exchange reaction of *n*-butyl halopyridinyl tellurides, which can be easily prepared by the substitution of lithium *n*-butanetellurolate.

EXPERIMENTAL

THF was distilled from sodium/benzophenone ketyl before use. *n*-Butyllithium and methyllithium were titrated using 2,5-dimethoxybenzylalcohol before use. Melting points were determined on a Yazawa micro melting point apparatus and are uncorrected. The infrared spectra were taken on a JASCO IR-810 spectrophotometer. The ^1H nmr spectra were recorded on a Varian Gemini-2000 (300 MHz) spectrometer in deuteriochloroform solution and chemical shifts are reported in δ (ppm) values relative to tetramethylsilane as an internal standard. Mass

spectra and high resolution mass spectra were recorded on a JMX-DX303 and a JMX-AX500 mass spectrometer. Elemental analyses were carried out on a yanaco CHN CORDER MT-5 apparatus.

n-Butyl 2-Pyridinyl Telluride **2**.

Typical Procedure.

Under an argon atmosphere, commercial *n*-butyllithium in *n*-hexane (1.39 *M*; 1.50 ml, 2.09 mmoles) was added to a mixture of commercial tellurium (274 mg, 2.14 mmoles) and dry tetrahydrofuran (8 ml) at room temperature and the mixture was stirred at room temperature for 10 minutes. 2-Bromopyridine (317 mg, 2.01 mmoles) was added to the mixture at -78 °C and stirred at -78 °C for 10 minutes, and then the mixture was refluxed for 92 hours. The mixture was diluted with water (50 ml) and extracted with diethyl ether (50 ml x 3). The organic layer was dried over dry magnesium sulfate. The solvent was removed and the residue was purified by silica gel column chromatography using *n*-hexane:ethyl acetate (4:1) as a solvent. The solvent was removed to give **2** (368 mg, 70%) as a viscous oil; ^{1}H nmr: δ 0.93 (t, *J* = 7.3 Hz, 3H), 1.43 (sextet, *J* = 7.3 Hz, 2H), 1.89 (quintet, *J* = 7.3 Hz, 2H), 3.14 (t, *J* = 7.3 Hz, 2H), 7.01 (ddd, *J* = 1.1, 5.0 and 7.7 Hz, 1H), 7.32 (ddd, *J* = 1.8, 7.7 and 7.7 Hz, 1H), 7.46-7.49 (m, 1H), 8.46-8.48 (m, 1H); hrms: *m/z* 265.0111 (M^+), calcd. $C_9H_{13}N^{130}Te$: 265.0109.

Phenyl(2-pyridinyl)methanol (**3a**).

via Tellurium-Lithium Exchange Reaction: Representative Procedure A.

Under an argon atmosphere, commercial *n*-butyllithium in *n*-hexane (1.35 *M*; 0.60 ml, 0.81 mmole) was added to a mixture of telluride **2** (210 mg, 0.80 mmole) and dry tetrahydrofuran (10 ml) at -78 °C and the mixture was stirred at -78 °C for 5 minutes. Benzaldehyde (120 mg, 1.13 mmoles) was added to the mixture at -78 °C and stirred at -78 °C for 10 minutes, and then the mixture was allowed to warm gradually to room temperature and stirred at room temperature for 20 hours. The mixture was diluted with water (50 ml) and extracted with dichloromethane (50 ml x 3). The organic layer was dried over dry magnesium sulfate. The solvent was removed and the residue was purified by silica gel column chromatography using *n*-hexane:ethyl acetate (4:1) as a solvent. The solvent was removed to give **3a** (109 mg, 73%) as colorless prisms, mp 74 °C; ^{1}H nmr: δ 5.27 (1H, brs), 5.75 (1H, s), 7.14-7.38 (7H, m), 7.60 (1H, ddd, *J* = 1.4, 7.7, 7.7 Hz), 8.54-8.55 (1H, m); hrms: *m/z* 185.0842 (M^+), calcd. $C_{12}H_{11}NO$: 185.0840.

Anal. Calcd. for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.79; H, 6.16; N, 7.49.

Phenyl (2-Pyridinyl) Ketone **3b** *via* Tellurium-Lithium Exchange Reaction.

According to the representative procedure A, **3b** was given in 64% yield as a colorless oil; ^{1}H nmr: δ 7.44-7.64 (4H, m), 7.86-8.12 (4H, m), 8.70-8.76 (1H, m); hrms: *m/z* 183.0691 (M^+), calcd. $C_{12}H_9NO$: 183.0684.

Anal. Calcd. for $C_{12}H_9NO$: C, 78.67; H, 4.95; N, 7.65. Found: C, 78.70; H, 4.84; N, 7.64.

2-Iodopyridine **3c** *via* Tellurium-Lithium Exchange Reaction.

According to the representative procedure A, **3c** was given in 50% yield as a colorless oil; ^{1}H nmr: δ 7.26-7.34 (2H, m), 7.72-7.75 (1H, m), 8.37-8.39 (1H, m); hrms: *m/z* 204.9398 (M^+), calcd. C_5H_4IN: 204.9387.

Anal. Calcd. for C_5H_4IN: C, 29.30; H, 1.97; I, 61.91; N, 6.86. Found: C, 29.26; H, 1.94; I, 61.82; N, 6.66.

Phenyl(2-pyridinyl)methanol (**3a**).

via Tellurium-Copper Exchange Reaction: Representative Procedure B.

Under an argon atmosphere, commercial methyllithium in diethyl ether (1.07 *M*; 1.50 ml, 1.61 mmoles) was added to a mixture of copper(I) cyanide (70.5 mg, 0.78 mmole) and dry tetrahydrofuran (5 ml) at -78 °C and the mixture was stirred at 0 °C for 30 minutes. Telluride **2** (211 mg, 0.80 mmole) was added to the mixture at -20 °C and stirred at -20 °C for 1.5 hours. Benzaldehyde (84.9 mg, 0.80 mmole) was added to the mixture at -20 °C and stirred at -20 °C for 10 minutes, and then the mixture was allowed to warm gradually to room temperature and stirred at room temperature for 20 hours. The mixture was diluted with water (50 ml) and extracted with dichloromethane (50 ml x 3). The organic layer was dried over dry magnesium sulfate. The solvent was removed and the residue was purified by silica gel column chromatography using *n*-hexane-ethyl acetate (4:1) as a solvent. The solvent was removed to give **3a** (99.1 mg, 67%) as colorless prisms.

3-(2-Pyridinyl)cyclohexanone **3d** *via* Tellurium-Copper Exchange Reaction.

According to the representative procedure B, **3d** was given in 41% yield as a colorless oil; ir (neat): ν 1708; ^{1}H nmr: δ 1.72-3.24 (9H, m), 7.14-7.18 (2H, m), 7.64 (1H, ddd, *J*=1.9, 7.7, 7.7 Hz), 8.56-8.57 (1H, m); hrms: *m/z* 175.0987 (M^+), calcd. $C_{11}H_{13}NO$: 175.0996.

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 74.90; H, 7.64; N, 7.90.

n-Butyl 6-Chloro-2-pyridinyl Telluride (**5a**).

Representative Procedure C.

Under an argon atmosphere, commercial *n*-butyllithium in *n*-hexane (1.35 *M*; 8.00 ml, 10.8 mmoles) was added to a mixture of commercial tellurium (1.40 g, 11.0 mmoles) and dry tetrahydrofuran (40 ml) at room temperature and the mixture was stirred at room temperature for 10 minutes 2,6-Dichloropyridine (1.49 g, 10.0 mmoles) was added to the mixture at -78 °C and stirred at -78 °C for 10 minutes, and then the mixture was stirred at room temperature for 24 hours. The mixture was diluted with water (100 ml) and extracted with diethyl ether (100 ml x 3). The organic layer was dried over dry magnesium sulfate. The solvent was removed and the residue was purified by silica gel column chromatography using *n*-hexane:ethyl acetate (4:1) as a solvent. The solvent was removed to give **5a** (1.28 g, 43%) as a viscous oil; ^{1}H nmr: δ 0.94 (3H, t, *J* = 7.4 Hz), 1.43 (2H, sextet, *J* = 7.4 Hz), 1.90 (2H, quintet, *J* = 7.4 Hz), 3.15 (2H, t, *J* = 7.4 Hz), 7.02-7.05 (1H, m), 7.24-7.29 (1H, m), 7.37-7.39 (1H, m); hrms: *m/z* 298.9753 (M^+), calcd. $C_9H_{12}{}^{35}ClN^{130}Te$: 298.9720.

Phenyl(6-chloro-2-pyridinyl)methanol (**6a**).

Representative Procedure D.

Under an argon atmosphere, commercial *n*-butyllithium in *n*-hexane (1.35 *M*; 0.76 ml, 1.03 mmoles) was added to a mixture of telluride **5a** (313 mg, 1.05 mmoles) and dry tetrahydrofuran (10 ml)

at -78 °C and the mixture was stirred at -78 °C for 5 minutes. Benzaldehyde (130 mg, 1.22 mmoles) was added to the mixture at -78 °C and stirred at -78 °C for 10 minutes, and then the mixture was allowed to warm gradually to room temperature and stirred at room temperature for 20 hours. The mixture was diluted with water (50 ml) and extracted with dichloromethane (50 ml x 3). The organic layer was dried over dry magnesium sulfate. The solvent was removed and the residue was purified by silica gel column chromatography using *n*-hexane:ethyl acetate (1:4) as a solvent. The solvent was removed to give **6a** (179 mg, 77%) as a viscous oil; ^{1}H nmr: δ 4.53 (1H, brs), 5.73 (1H, s), 7.09-7.12 (1H, m), 7.18-7.21 (1H, m), 7.25-7.39 (5H, m), 7.55 (1H, dd, *J* = 7.8, 7.8 Hz); hrms: *m/z* 219.0442 (M^+), calcd. $C_{12}H_{10}{}^{35}ClNO$: 219.0450.

n-Butyl 3-Chloro-2-pyridinyl Telluride (**5b**).

According to the representative procedure C, **5b** was given in 55% yield as a viscous oil; ^{1}H nmr: δ 0.94 (3H, t, *J* = 7.4 Hz), 1.44 (2H, sextet, *J* = 7.4 Hz), 1.89 (2H, quintet, *J* = 7.4 Hz), 3.16 (2H, t, *J* = 7.4 Hz), 6.96 (1H, dd, *J* = 4.6, 8.9 Hz), 7.41 (1H, dd, *J* = 1.4, 8.0 Hz), 8.38-8.39 (1H, m); hrms: *m/z* 298.9728 (M^+), calcd. $C_9H_{12}{}^{35}ClN^{130}Te$: 298.9720.

Phenyl(3-chloro-2-pyridinyl)methanol (**6b**).

According to the representative procedure D, **6b** was given in 72% yield as colorless prisms, mp 70 °C; ^{1}H nmr: δ 5.32 (1H, s), 6.00 (1H, s), 7.20-7.37 (5H, m), 7.65 (1H, dd, *J* = 1.4, 8.1 Hz), 8.54 (1H, dd, *J* = 1.4, 4.7 Hz); hrms: *m/z* 219.0432 (M^+), calcd. $C_{12}H_{10}{}^{35}ClNO$: 219.0450.

Anal. Calcd. for $C_{12}H_{10}ClNO$: C, 65.61; H, 4.59; Cl, 16.14; N, 6.38. Found: C, 65.69; H, 4.80; Cl, 15.99; N, 6.62.

n-Butyl 5-Bromo-2-pyridinyl Telluride (**8**).

According to the representative procedure C, **8** was given in 55% yield as a viscous oil; ^{1}H nmr: δ 0.93 (3H, t, *J* = 7.4 Hz), 1.43 (2H, sextet, *J* = 7.4 Hz), 1.88 (2H, quintet, *J* = 7.4 Hz), 3.13 (2H, t, *J* = 7.4 Hz), 7.35-7.38 (1H, m), 7.45 (1H, dd, *J* = 2.4, 8.3 Hz), 8.55-8.56 (1H, m); hrms: *m/z* 342.9225 (M^+), calcd. $C_9H_{12}{}^{79}BrN^{130}Te$: 342.9415.

Phenyl(5-bromo-2-pyridinyl)methanol (**9**).

According to the representative procedure D, **9** was given in 70% yield as a viscous oil; ^{1}H nmr: δ 4.75 (1H, brs), 5.73 (1H, s), 7.08-7.11 (1H, m), 7.26-7.37 (5H, m), 7.74 (1H, dd, *J* = 2.2, 8.5 Hz), 8.61-8.62 (1H, m); hrms: *m/z* 262.9970 (M^+), calcd. $C_{12}H_{10}{}^{79}BrNO$: 262.9946.

Phenyl(2-bromo-5-pyridinyl)methanol (**11**).

Under an argon atmosphere, commercial *n*-butyllithium in *n*-hexane (1.39 *M*; 0.80 ml, 1.11 mmoles) was added to a mixture of 2,5-dibromopyridine (237 mg, 1.00 mmole) and dry tetrahydrofuran (5 ml) at -100 °C and the mixture was stirred at -78 °C for 3 hours. Benzaldehyde (42.9 mg, 0.40 mmole) was added to the mixture at -78 °C and stirred at -78 °C for 1 hour, and then the mixture was allowed to warm gradually to room temperature and stirred at room temperature for 20 hours. The mixture was diluted with saturated ammonium chloride (30 ml) and extracted with dichloromethane (30 ml x 3). The organic layer was dried over dry magnesium sulfate. The solvent was removed and the residue was purified by silica gel column chromatography using *n*-hexane:ethyl acetate (2:1) as a solvent. The solvent was removed to give **11** (163 mg, 62%) as colorless prisms, mp 79-80 °C; ^{1}H nmr: δ 2.20 (1H, brs), 5.84 (1H, s), 7.29-7.45 (6H, m), 7.55 (1H, dd, *J* = 2.6, 8.1 Hz), 8.39 (1H, d, *J* = 2.6 Hz); hrms: *m/z* 262.9975 (M^+), calcd. $C_{12}H_{10}{}^{79}BrNO$: 262.9946.

Anal. Calcd. for $C_{12}H_{10}BrNO$: C, 54.57; H, 3.82; Br, 30.25; N, 5.30. Found: C, 54.42; H, 3.96; Br, 30.30; N, 5.34.

Acknowledgments.

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