REACTIONS OF TRIETHYL[1-(N-*tert*-BUTYLIMIDOYL)-2-PYRROLINYL]BORATE WITH ELECTROPHILES

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Abstract —— The reaction of triethyl[1-(N-*tert*-butylimidoyl)-2-pyrrolinyl)borate (2) with alkyl halides, allylic bromides, alkenyliodonium salt, and N-carbophenoxypyridinium chloride in the absence or the presence of copper(I) ion were investigated.

Remarkable alterations on the reaction mode of various trialkylheteroarylborates with electrophiles could be brought about by the presence of copper(I) ion. Particularly, the effect of copper(I) ion on the reaction of trialkyl(2-indolyl)-borates having a characteristic α-trialkylborylated enamine moiety was noticeable.[1] These observations prompt us to investigate further the reaction of this system, which, to our knowledge, has been scarcely studied.[2]

Enamidine (1a) was an enamine of choice in the present study, because of the ready formation of α-lithioenamine (1b) with butyllithium.[3] Borate (2) was generated *in situ* from triethylborane and 1b, and subjected to subsequent reactions.

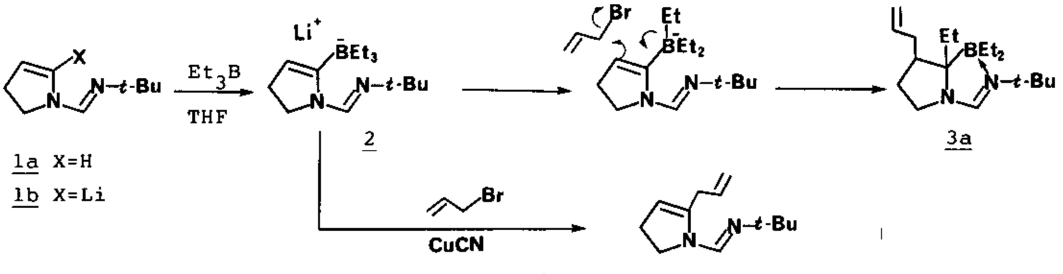


Chart 1

When treated with allyl bromide, 2 afforded 3a in 75% yield in the absence of copper(I) ion. An analogous reaction path recognized for the electrophilic substitution of trialkyl(2-indolyl)borates would be held for the formation of 3a,[1,2] where the elimination of boryl group should be hampered by a proper intramolecular interaction between amidine and boryl group (Chart 1). On the other hand, the presence of copper(I) ion promoted selective allylation at the α-position of 2 leading to 4a in 60% yield (Chart 1). The presence of copper(I) ion was also shown to be essential to force the reaction of 2 with alkenyliodonium salt (5a)[4] to give 4e in 61% yield, whereas any coupling product could not be detected without copper(I) ion. As evident from Table 1, these intriguing differences of the reactivities of 2 were also found in additional instances. In all attempted coupling reactions between 2 and other iodonium salts (5b, 5c),[5,6] the presence of copper(I) ion had no appreciable effect on the reactions, resulting in the recovery of 1a (Chart 2).

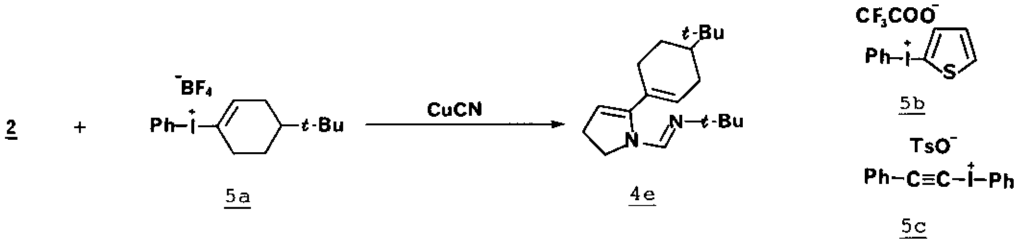


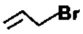
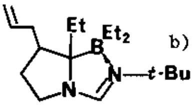
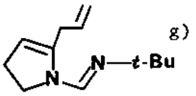
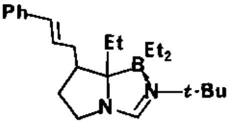
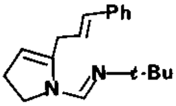
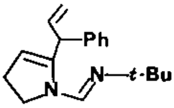
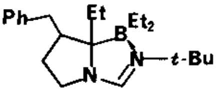
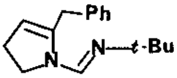
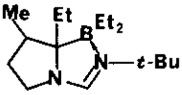
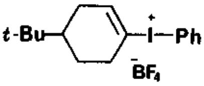
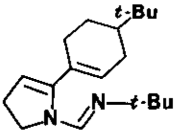
Chart 2

The results observed on the reactions of 2 with electrophiles in the presence of copper(I) ion seem to be explicable by the intermediacy of organocopper species produced from 2 and copper(I) cyanide.[7]

Likewise, treatment of 2 with N-carbophenoxypyridinium chloride (6) in the absence of copper(I) ion gave the compound (7)[8] in 15% yield, presumably through a similar reaction path to above. Under the action of copper(I) ion on the reaction, however, unexpected formation of the compound (7) was observed in 24% yield as a sole isolable product. Accordingly, in a reverse order, 1b was initially treated with copper(I) cyanide (-20°C, 20 min), followed by the addition of triethylborane (-20°C, 20 min), and then, the mixture was subjected to the reaction with 6 in the same manner. Again, there was obtained the compound (7) in 22% yield, where the borate (9) arising through a reversible interconversion ($8 \rightleftharpoons 9$) seems likely to react with 6 leading to 7.

Understanding of the difference between the reaction mode of 2 with pyridinium salt and those with other electrophiles employed must await further studies.

Table 1 Reactions of 2 with electrophiles

Electrophiles	Product in the absence of CuCN (Yield %)[a]	Product in the presence of CuCN (Yield %)[a]
	 b) 3a (75)	 g) 4a (60)
	 3b (60) mp 66-68°C c)	 4b (30) h)  4c (30) i)
	 3c (61) mp 113-115°C d)	 4d (50) j)
Me—I	 3d (68) mp 49-51°C e)	—— k)
	—— f)	 4e (61) l)

a) Yields are based on 2 b) High-Mass m/z : Calcd for $C_{16}H_{30}BN_2$ ($M^+-C_2H_5$) 261.25002. Found: 261.24902 c) Recryst. from hexane-AcOEt; Anal. Calcd for $C_{24}H_{39}BN_2$: C, 78.67; H, 10.73; N, 7.64. Found: 78.76; H, 10.72; N, 7.66 d) Recryst. from hexane-AcOEt; Anal. Calcd for $C_{22}H_{37}BN_2$: C, 77.63; H, 10.96; N, 8.23. Found: C, 77.60; H, 10.94; N, 8.25 e) Recryst. from hexane; Anal. Calcd for $C_{16}H_{33}BN_2$: C, 72.72; H, 12.58; N, 10.60. Found: C, 72.74; H, 12.53; N, 10.35 f) Recovery of 1a g) Ref. 3 h) High-Mass m/z: Calcd for $C_{18}H_{24}N_2$ 268.19374. Found: 268.19480 i) High-Mass m/z: Calcd for $C_{18}H_{24}N_2$ 268.19374. Found: 268.19564 j) High-Mass m/z: Calcd for $C_{16}H_{22}N_2$ 242.17828. Found: 242.17988 k) Complex mixture l) High-Mass m/z: Calcd for $C_{19}H_{32}N_2$ 288.25648. Found: 288.25468

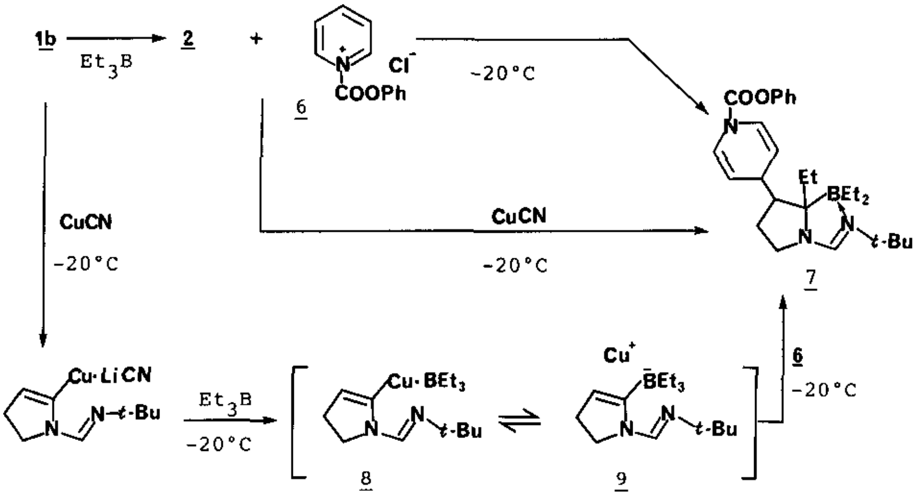


Chart 3

EXPERIMENTAL

All melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected.

Tetrahydrofuran was distilled from sodium benzophenone ketyl before use.

The ir spectra were recorded with a Hitachi 270-30 spectrometer. The nmr spectra were determined with a JEOL FX-90Q or a JEOL GX-270 spectrometer. *Chemical shifts are given in δ-value down field from tetramethylsilane.* Tetramethylsilane (in ^{1}H-nmr) and the $CDCl_3$ resonance at 77.1 ppm (in ^{13}C-nmr) were used as internal references. Coupling constants are reported in Hertz and splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Mass spectra were recorded on a JEOL JMS-QH100 or a JEOL JMS-D300 spectrometer.

Flash and medium pressure liquid chromatography (MPLC) were performed on silica gel (230-400 mesh ASTM, Merck) and a Merck lobar column (LiChroprep Si60) under pressure (around 4 kg/cm^2), respectively.

Typical procedure: The reaction of 2 with allyl bromide in the absence of copper(I) cyanide

Lithioenamine (1b) was generated from 1a (270 mg, 1.77 mmol) and butyllithium (1.5 M solution in hexane, 1.4 ml, 2.1 mmol) in tetrahydrofuran (10 ml) under an argon atmosphere according to the literature.[3] Triethylborane (1 M solution in hexane, 2.1 ml, 2.1 mmol) was added to 1b at -20°C under an argon atmosphere, and stirred for 1 h. After addition of allyl bromide (302 mg, 2.5 mmol) at -20°C, the whole was gradually warmed to room temperature, and stirred overnight. The mixture was treated with 10% aqueous sodium hydroxide (5 ml) and 30% aqueous hydrogen peroxide (1 ml) solutions under ice-cooling, and extracted with ethyl acetate (60 ml). The extract was washed with brine (30 ml), and dried over magnesium sulfate. The solvent was removed, and the residue was subjected to MPLC with hexane:ethyl acetate=30:1 to give 390 mg (75% yield) of 3a.

Reactions of 2 with alkyl halides, allylic bromides, 5a, and 6 in the absence of copper(I) cyanide were carried out in a similar manner as above. Spectral data of 3 are summarized in Table 2.

Typical procedure: The reaction of 2 with allyl bromide in the presence of copper(I) cyanide

Borate (2) was generated from 1a (228 mg, 1.5 mmol) and butyllithium (1.5 M solution in hexane, 1.2 ml, 1.8 mmol) in tetrahydrofuran (10 ml) under an argon atmosphere, followed by treatment with triethylborane (1 M solution in hexane, 1.8 ml, 1.8 mmol) in a similar manner as above. Copper(I) cyanide (196 mg, 2.2 mmol) was added to 2 at -20°C, and stirred for 20 min. Allyl bromide (242 mg, 2 mmol) was added, and the mixture was gradually warmed to room temperature, then stirred overnight. The mixture was treated with 10% aqueous sodium hydroxide (5 ml) and 30% aqueous hydrogen peroxide (1 ml) solutions under ice-cooling, and extracted with ethyl acetate (60 ml). The extract was washed with brine (30 ml), and dried over magnesium sulfate. The solvent was removed, and the residue was subjected to flash chromatography with hexane:triethylamine=100:7 to give 173 mg (60% yield) of 4a.

Reactions of 2 with alkyl halides, allylic bromides, 5a, and 6 in the presence of copper(I) cyanide were carried out in a similar manner as above. Spectral data of 4 are summarized in Table 2.

Table 2 Spectral data of 3 and 4

Compd.	^{1}H-nmr ($CDCl_3$)δ	^{13}C-nmr ($CDCl_3$)δ
3a	0.40-2.30(m, 19H), 1.40(s, 9H), 2.60(dd, 1H, J=5, 10Hz), 3.27(t, 2H, J=7Hz), 4.75-5.05(m, 2H), 5.45-5.95(m, 1H), 7.16(s, 1H)	11.0(q), 11.3(q), 11.5(q), 15.0(br), 25.8(t), 28.1(t), 30.9(q), 36.6(t), 43.4(d), 45.0(t), 55.1(s), 114.7(t), 139.3(d), 155.6(d)
3b	0.30-1.00(m, 15H), 1.15-2.40(m, 4H), 1.32(s, 9H), 2.75(br d, 1H, J=11Hz), 3.30(t, 2H, J=8Hz), 6.03(ddd, 1H, J=4, 7, 13Hz), 6.31(d, 1H, J=13Hz), 7.10-7.45(m, 6H)	11.0(q), 11.3(q), 11.5(q), 15.2(br), 25.7(t), 28.2(t), 30.8(q), 35.7(t), 43.7(d), 45.0(t), 55.0(s), 125.9(d), 126.8(d), 128.5(d), 130.3(d), 131.3 (d), 137.9(s), 155.6(d)
3c	0.50-1.10(m, 13H), 1.20-1.90(m, 5H), 1.33(s, 9H), 2.20-2.60(m, 1H), 3.15-3.40(m, 1H), 3.33 (t, 2H, J=7Hz), 7.00-7.40(m, 6H)	11.1(q), 11.4(q), 11.6(q), 15.0(br), 25.8(t), 27.9(t), 31.0(q), 38.1(t), 45.2(t), 46.0(d), 55.2(s), 125.6(d), 128.3(d), 129.2(d), 143.1(s), 155.8(d)
3d	0.40-1.00(m, 16H), 1.21(s, 9H), 1.30-1.70 (m, 3H), 1.80-2.50(m, 2H), 3.28(t, 2H, J=8Hz), 7.22(s, 1H)	11.3(q), 11.5(q), 15.0(br), 19.5(q), 25.6(t), 30.9(q), 32.9(t), 37.9(d), 44.8(t), 55.0(s), 156.3(d)
4a	1.17(s, 9H), 2.40-2.70(m, 2H), 2.97(dd, 2H, J=2, 6Hz), 3.80(t, 2H, J=8Hz), 4.60-4.75(m, 1H), 4.95-5.30(m, 2H), 5.25(ddt, 1H, J=2, 10, 18Hz), 7.73(s, 1H)	27.1(t), 31.2(q), 31.2(t), 46.5(t), 53.5(s), 103.3(d), 117.3(t), 133.8(d), 141.8(s), 143.0(d)
4b	1.16(s, 9H), 2.40-2.70(m, 2H), 3.16(d, 2H, J=6Hz), 3.82(t, 2H, J=8Hz), 4.70-4.85(m, 1H), 6.12(dt, 1H, J=15, 6Hz), 6.50(d, 1H, J=15Hz), 7.15-7.45(m, 5H), 7.80(s, 1H)	27.2(t), 30.5(t), 31.2(q), 46.6(t), 53.6(s), 103.6(d), 125.9(d), 126.2(d), 127.4(d), 128.5(d), 132.6(d), 137.1(s), 142.0(s), 143.1(d)
4c	0.97(s, 9H), 2.40-2.70(m, 2H), 3.74(t, 2H, J=7Hz), 4.20(d, 1H, J=6Hz), 4.70-4.85(m, 1H), 4.97(dd, 1H, J=2, 15Hz), 5.10(ddd, 1H, J=6, 9, 15Hz), 5.15(dd, 1H, J=2, 9Hz), 7.10-7.45(m, 5H), 7.67(s, 1H)	27.1(t), 30.9(q), 46.5(t), 47.6(d), 53.3(s), 105.3(d), 116.5(t), 126.9(d), 128.0(d), 128.6(d), 137.9(d), 139.5(s), 143.9(d), 144.5(s)
4d	1.04(s, 9H), 2.40-2.80(m, 2H), 3.56(br s, 2H), 3.73(t, 2H, J=8Hz), 4.60-4.75(m, 1H), 7.10-7.40(m, 5H), 7.61(s, 1H)	27.1(t), 31.0(q), 33.3(t), 46.5(t), 53.4(s), 105.0(d), 126.6(d), 128.5(d), 137.0(s), 142.3(s), 143.3(d)
4e	0.89(s, 9H), 1.10-1.40(m, 2H), 1.18(s, 9H), 1.90-2.60(m, 1H), 2.64(dt, 2H, J=3, 9Hz), 2.20-3.40(m, 5H), 3.84(t, 2H, J=9Hz), 4.77 (t, 1H, J=3Hz), 5.75-5.95(m, 1H), 7.74(s, 1H)	24.2(t), 25.7(t), 27.2(q), 27.7(t), 29.4(t), 31.3(q), 32.3(s), 44.0(d), 46.8(t), 53.5(s), 103.0(d), 128.9(d), 129.2(s), 145.8(d), 146.9(s)

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8. mp 124-126°C (recryst. from hexane-AcOEt). Ir (KBr) : 1720, 1692, 1616 cm^{-1}. ^{1}H-Nmr (CDCl$_3$)δ: 0.33-0.47(m, 1H), 0.91(t, 3H, J=7Hz), 1.20-1.40(m, 1H), 1.35 (s, 9H), 1.55(dq, 1H, J=20, 7Hz), 1.59-1.87(m, 9H), 1.95-2.08(m, 2H), 2.15 (ddd, 1H, J=3, 3, 6Hz), 3.29-3.40(m, 2H), 3.61(dd, 1H, J=3, 7Hz), 4.80-4.97(m, 2H), 6.80-6.94(m, 2H), 7.12(s, 1H), 7.14(dd, 2H, J=1.5, 8Hz), 7.21(d, 1H, J=7.5Hz), 7.35(dd, 2H, J=7.5, 8Hz). ^{13}C-Nmr (CDCl$_3$)δ: 11.5(q), 11.8(q), 15.5(br), 27.1(t), 28.6(t), 31.1(s), 34.6(d), 45.8(t), 52.2(s), 55.1(s), 111.0 (d), 111.5(d), 113.6(d), 114.0(d), 121.5(d), 122.2(d), 123.4(d), 125.8(d), 129.4(d), 149.9(s), 150.8(s), 154.3(d). Anal. Calcd for $C_{27}H_{40}BN_3O_2$: C, 72.15; H, 8.97; N, 9.34. Found: C, 72.17; H, 9.04; N, 9.35.

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