A NOVEL 1,2-ALKYL MIGRATION OF TRIALKYL(4-PYRIDYL)BORATES

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Abstract——The reaction of lithium trialkyl(4-pyridyl)borates with Lewis acids or acylating agents produced 4-alkylpyridines via 1,2-alkyl migration from boron to pyridine ring.

Tetracoordinated organoborates which are adjacent to an electron deficient carbon atom are known to be readily accompanied by 1,2-migration of an organyl group from boron to carbon.[1] To our knowledge, the only one example of this type of 1,2-alkyl migration reaction from boron to pyridine ring was reported by Nozaki, i.e., trialkyl(6-bromo-2-pyridyl)borates underwent the 1,2-alkyl shift from boron to 2-position of pyridine with concerted cleavage of pyridine ring to give 5-alkyl-5-dialkylboryl-2,4-pentadienenitriles.[2]
In the course of our studies on pyridylborane compounds,[3] we found that 4-alkylpyridines (2) could be produced from trialkyl(4-pyridyl)borates (1) via the 1,2-alkyl migration sequence in the presence of Lewis acids or acylating agents, as shown in Chart 1.

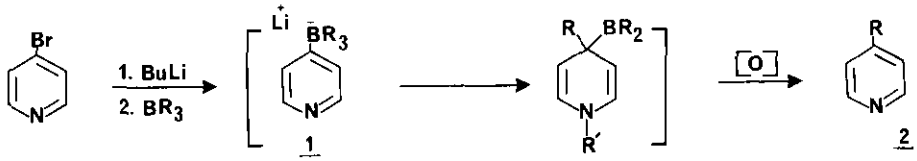

Chart 1

Reaction of 4-lithiopyridine, derived from 4-bromopyridine (1 mol eq) and BuLi (1 mol eq) in Et_2O,[4] with tributylborane (1 mol eq) under nitrogen atmosphere at -70°C produced lithium tributyl(4-pyridyl)borate (1, R=Bu) in situ, which decomposed on being allowed to stand at room temperature overnight to give a resinous substance.

An attempted reaction of 1 (R=Bu) with alkyl halides (MeI, $PhCH_2Br$) (-70°C ⟶ room temperature) overnight gave no isolable product. Alternatively, substantial amount of 4-butylpyridine was obtained on treatment of 1 (R=Bu) with 2 mol eq of BF_3OEt_2 or $(CF_3CO)_2O$ in Et_2O under nitrogen atmosphere at -70°C, and then room temperature overnight, followed by the oxidation with alkaline hydrogen peroxide. Table summarizes the results of brief studies of the 1,2-alkyl migration reaction of 1 in the presence of Lewis acids or acylating agents.

Table 1,2-Alkyl migration reaction of 1

BR_3 of 1	Reagent	Yield(%)[a] of 2	BR_3 of 1	Reagent	Yield(%)[a] of 2
BBu_3	BF_3OEt_2	58[b]	$B(sec\text{-}Bu)_3$	BF_3OEt_2	48[c]
	$B(OMe)_3$	38		$TiCl_4$	42
	$AlCl_3$	20		$(CF_3CO)_2O$	44
	$TiCl_4$	45		$(CH_3CO)_2O$	15
	$(CF_3CO)_2O$	56		PhCOCl	34
	$(CH_3CO)_2O$	33	$B(Hex)_3$	BF_3OEt_2	59[d]
	PhCOCl	40		$(CF_3CO)_2O$	52
Bu-9-BBN	BF_3OEt_2	23	$B(cyc\text{-}Hex)_3$	BF_3OEt_2	26[e]
	$(CF_3CO)_2O$	20		$(CF_3CO)_2O$	23

a) Isolated yield by flash chromatography (SiO_2/hexane:AcOEt=4:1) based on 4-bromopyridine b) 4-Butylpyridine [bp 91°C/18 mmHg (lit.[5] 84°C/8 mmHg)] c) 4-sec-Butylpyridine [bp 85°C/18 mmHg (lit.[5] 197°C)] d) 4-Hexylpyridine [bp 140°C/18 mmHg (lit.[5] 110°C/5 mmHg)] e) 4-Cyclohexylpyridine [bp 135°C/15 mmHg; picrate, mp 148-151°C (lit.[6] mp 150-151°C)]

Next, the reaction of 1 with 3-indolylacetyl chloride was undertaken. Borate (1; R=Bu, sec-Bu) was reacted with 3-indolylacetyl chloride (1 mol eq) in Et_2O under nitrogen atmosphere (-70°C ⟶ room temperature, overnight). After concentration of the reaction mixture in vacuo, the residue was directly subjected to flash chromatography (SiO_2/hexane:AcOEt=4:1) to afford small amount of fairly unstable dieneamide (5a, 10%; 5b, 10%)[7] together with substantial amount of 4-alkylpyridine (2: R=Bu, 44%; R=sec-Bu, 37%). The formation of dieneamide (5) may be explained by sequences (3 ⟹ 4 ⟹ 5) depicted in Chart 2. The structure of 5 was further confirmed by the immediate conversion to amide (6)[8] by catalytic hydrogenation over PtO_2 in EtOH under atmospheric pressure.

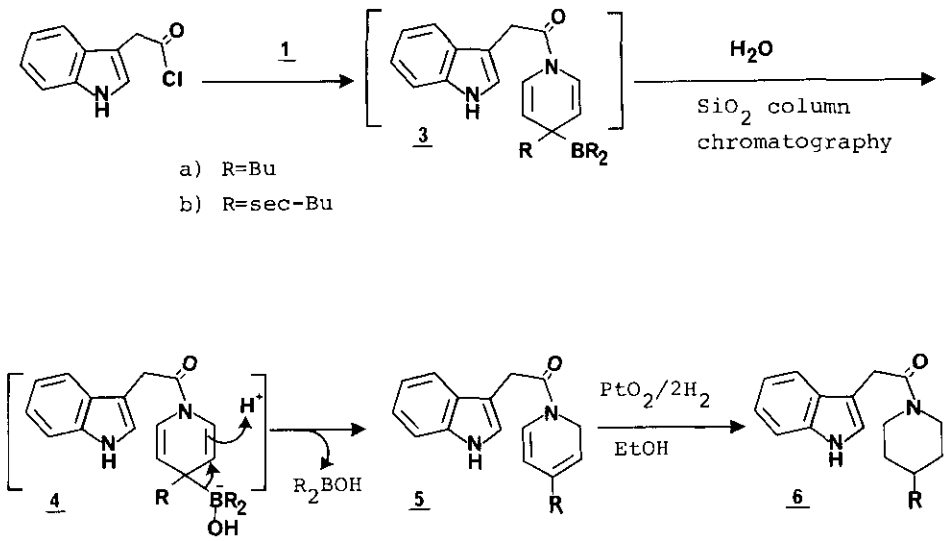

Chart 2

Typical procedure: 4-Butylpyridine———Tributylborane (1M solution in hexane, 9 ml) was added slowly to an ethereal solution (50 ml) of 4-lithiopyridine, derived from 4-bromopyridine (1.2 g, 9 mmol) and BuLi (1.5M solution in hexane, 6 ml) in Et_2O at -70°C under nitrogen atmosphere, the mixture was gradually warmed to -10°C and then cooled to -30°C. Boron trifluoride etherate (2.3 ml, 18 mmol) was added dropwise, the whole was slowly warmed to room temperature, and then stirred overnight. After treatment with 10% NaOH (20 ml) and 30% H_2O_2 (5 ml) solutions under ice-cooling, the mixture was extracted with AcOEt, the extract was dried over $MgSO_4$. The solvent was removed and the residue was purified by flash chromatography (SiO_2/hexane:AcOEt=4:1) to give 620 mg (58%) of 4-butylpyridine.

ACKNOWLEDGEMENT

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7. 5a; viscous oil. IR(neat) cm^{-1}: 3300, 3108, 1638, 1594. NMR($CDCl_3$) δ: 0.50-1.80(m, 9H), 2.50-3.00(m, 1H), 3.87(s, 2H), 4.10-4.60(m, 1H), 5.05 (d, 1H, J=9Hz), 5.20-5.50(m, 1H),6.72(d, 1H, J=9Hz), 6.80-7.80(m, 5H), 8.50 (br s, 1H). High-MS(m/z) : Calcd for $C_{19}H_{22}N_2O$: 294.17319. Found: 294.17599. 5b; viscous oil. IR(neat) cm^{-1}: 3300, 2960, 1636, 1596. NMR($CDCl_3$) δ : 0.60-1.80(m, 9H), 2.90-3.10(m, 1H), 3.60-4.00(m, 1H), 3.87(s, 2H), 4.60-5.10(m, 2H), 6.73(d, 1H, J=9Hz), 7.00-7.70(m, 5H), 8.20(br s, 1H). High-MS(m/z): Calcd for $C_{19}H_{22}N_2O$: 294.17319. Found: 294.17338.
8. 6a; syrup. IR($CHCl_3$) cm^{-1}: 3488, 3204, 1624, 1620. NMR($CDCl_3$) δ : 0.60-1.90(m, 14H), 2.30-3.20(m, 2H), 3.83(s, 2H), 3.50-3.90(m, 1H), 4.50-4.80 (m, 1H), 6.90-7.70(m, 5H), 8.20(br s, 1H). High-MS(m/z): Calcd for $C_{19}H_{26}N_2O$: 298.20447. Found: 298.20458. 6b; mp 115-116°C (AcOEt-ether). IR($CHCl_3$) cm^{-1}: 3488, 3272, 1624. NMR($CDCl_3$) δ : 0.60-1.90(m, 14H), 2.30-3.10(m, 2H), 3.84(s, 2H), 3.90-4.20(m, 1H), 4.60-4.90(m, 1H), 7.00-7.80(m, 5H), 8.15(br s, 1H). High-MS(m/z): Calcd for $C_{19}H_{26}N_2O$: 298.20447. Found: 298.20287.

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