REACTION OF TRIALKYL(3-PYRIDYL)BORATES WITH ALLYLIC BROMIDES IN THE PRESENCE OF COPPER(I) SALTS. A NEW PROCEDURE FOR THE PREPARATION OF 3-ALLYLPYRIDINE DERIVATIVES

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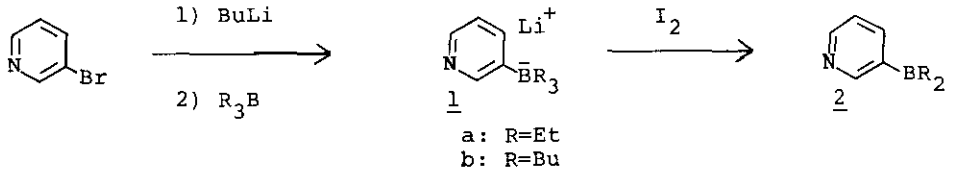
Abstract ——— *The reaction of lithium trialkyl(3-pyridyl)borates with allylic bromides in the presence of copper(I) salts was found to give 3-allylpyridine derivatives regioselectively.*

In the previous paper, we reported that the treatment of lithium trialkyl(3-pyridyl)borates(1), derived from 3-lithiopyridine and trialkylboranes *in situ*, with iodine afforded dialkyl(3-pyridyl)boranes(2) in good yields[1] (Chart 1).



1

a: R=Et
b: R=Bu

2

Chart 1

Recently, the effective activation of C-B bond of alkyl- or alkenylborate complexes with copper(I) in their coupling reactions has been demonstrated.[2] It might be conceivable, then, that a similar activation of C-B bond would be permitted upon treatment of borates(1) with electrophiles in the presence of copper(I).

We wish to report here that copper(I) trialkyl(3-pyridyl)borates, generated from lithium trialkyl(3-pyridyl)borates(1) and copper(I) salts *in situ*, reacted with allylic bromides to attain regioselective allylation at the 3-position of pyridine.

At first, we examined the reaction of lithium triethyl(3-pyridyl)borate(1a) with allyl bromide. From previous observation,[1] it was expected that nitrogen of 1a

would also exhibit sufficient nucleophilicity. Thus, the reaction of 1a with allyl bromide without copper(I) in THF under nitrogen atmosphere at room temperature resulted in the N-allylation to produce betaine(3) as a viscous oil[3] in 64% yield based on 3-bromopyridine. On the other hand, the presence of copper(I) salt(2.1 mol eq.), 1 mol eq. of which should be consumed by the coordination to nitrogen, elicited the remarkable change on the reaction path of 1a, i.e., the exclusive formation of 3-allylpyridine(5) presumably via copper(I) borate(4),[2] as shown in Chart 2.

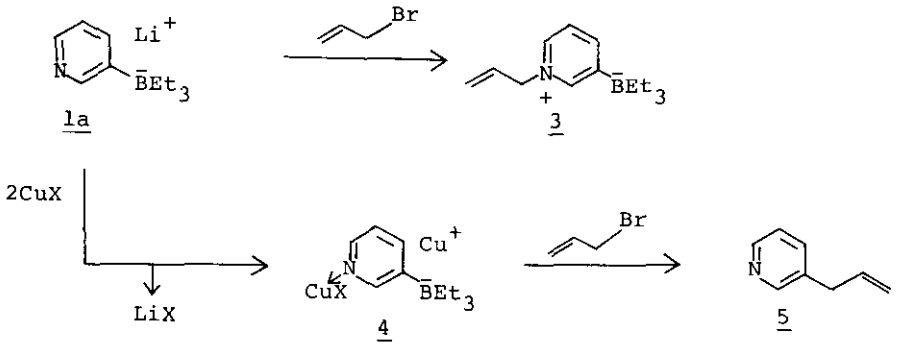


Chart 2

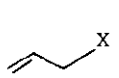
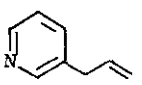
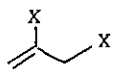
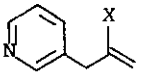
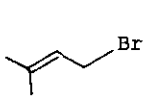
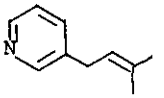
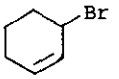
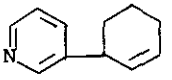
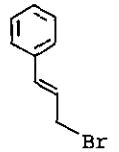
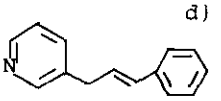
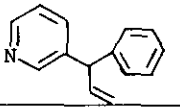
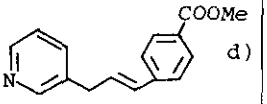
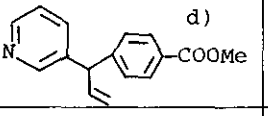
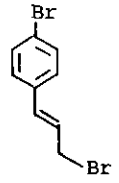
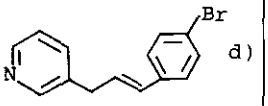
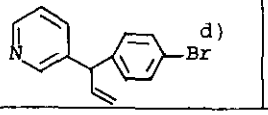
After brief examination of the reaction of 1 with allyl bromide(1.1 mol eq.) in the presence of copper(I) salt(2.1 mol eq.), it was finally settled to use lithium tributyl(3-pyridyl)borate(1b) and copper(I) cyanide for further exploration of the reaction, as summarized in Tables 1 and 2.

Table 1 Reaction of 1 with allyl bromide in the presence of CuX[a)]

CuX	1	Yield(%) of 5[b)]	CuX	1	Yield(%) of 5[b)]
CuCl	1a	39	CuCl	1b	42
CuBr	1a	48	CuBr	1b	50
CuBr·SMe_2	1a	46	CuBr·SMe_2	1b	58
CuI	1a	43	CuI	1b	45
CuCN	1a	64	CuCN	1b	75

a) Product was isolated by flash chromatography(hexane:AcOEt=2:1).
b) Isolated yield based on 3-bromopyridine

Table 2 Reaction of 4b with allylic bromides

Allylic halide	Product[a)b)]	Yield(%)[c)]	bp(°C/mmHg) or mp(°C)
		48(X=Cl)	bp 78/18
		75(X=Br)	(lit.[4] 75/15)
	 d)	9(X=Cl)	bp 110/15[e)]
		55(X=Br)	bp 130/20[e)]
	 d)	44	bp 110/18[e)]
	 d)	70	bp 125/18[e)] mp(picrate) 109-111
	 d)	40	bp 160/1[e)]
	 d)	23	bp 120/1[e)]
	 d)	38	bp 220/1[e)]
	 d)	27	bp 200/1[e)]
	 d)	41	bp 200/1[e)]
	 d)	30	bp 190/1[e)]

a) Structural assignment was deduced from spectral (IR, NMR, MS) data.
b) Isolated by flash column chromatography (silica gel, hexane:AcOEt= 2:1) c) Isolated yields based on 3-bromopyridine d) All compounds gave satisfactory combustion or high-resolution mass spectral analyses.
e) Kugelrohr distillation, bath temperature

Typical experimental procedure is as follows. Borate(1b) was prepared from 3-bromopyridine(1.41 g, 9 mmol) and BuLi(1.5M solution in hexane, 6 ml) followed by treatment with tributylborane(1M solution in hexane, 9 ml) by the previously reported method.[1] To a THF suspension(15 ml) of CuCN(1.7 g, 18.9 mmol) under nitrogen atmosphere at -30°C, a THF solution(20 ml) of 1b was added and the mixture was stirred for 20 min. Allyl bromide(1.19 g, 9.9 mmol) was added to the mixture, the whole was warmed gradually to room temperature, and then stirred overnight. After treatment with 10% NaOH(10 ml) and 30% H_2O_2(3 ml) solutions under ice-cooling, the mixture was extracted with AcOEt, and the extract was washed with brine, and dried. After removal of the solvent, the residue was purified by flash chromatography(AcOEt:hexane=1:2) to give 0.8 g(75% yield) of 3-allylpyridine(5); bp 78°C/18 mmHg (lit.[4] 75°C/15 mmHg).

As compared with the known procedure,[4] in which incorporation of sensitive functional groups is restrictive, the mildness and versatility of the present method for the preparation of 3-allylpyridine derivatives may permit various allylic bromides to be employed, as summarized in Table 2. In the cases of cinnamyl bromide derivatives, the reaction proceeded with the allylic transposition.

REFERENCES AND NOTES

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2. H. C. Brown and G. A. Molander, J. Org. Chem., 1981, 46, 645. K. Utida, K. Utimoto and H. Nozaki, Tetrahedron, 1977, 33, 2987. S. Hara, Y. Satoh and A. Suzuki, Chem. Lett., 1982, 1289.
3. 3; NMR ($CDCl_3$) δ : 0.01-0.80(m, 10H), 4.85(dd, 2H, J=1, 7Hz), 5.27(d, 1H, J=18Hz), 5.46(d, 1H, J=12Hz), 5.80-6.30(m, 1H), 7.35-7.60(m, 1H), 7.70-7.90 (m, 1H), 8.15(br s, 1H). High-resolution MS m/e: Calcd for $C_{14}H_{24}NB$ 217.2005; Found 217.2012.
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