AN ALTERNATIVE SYNTHESIS OF DIALKYLPYRIDYLBORANES

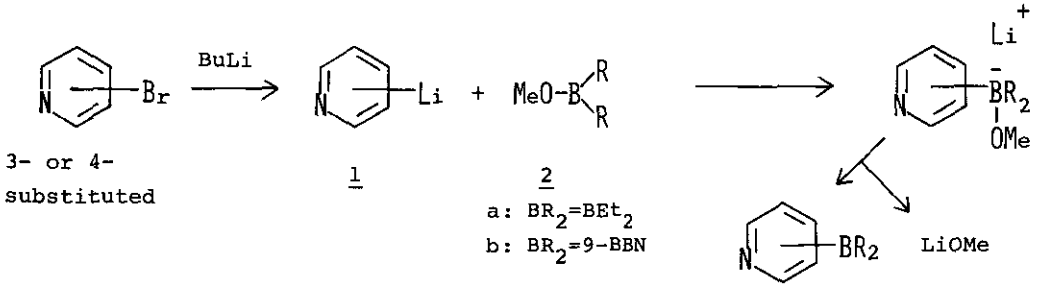
Minoru Ishikura, Tsutomu Mano, Izumi Oda, and Masanao Terashima*
Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen University,
Ishikari-Tobetsu, Hokkaido 061-02, Japan

Abstract ——— The reaction of lithiopyridines and dialkylmethoxyboranes gave an alternative route to the preparation of dialkylpyridylboranes.

In our previous report, the reaction of 3-lithiopyridine with trialkylboranes followed by treatment with iodine has been shown to give dialkyl(3-pyridyl)boranes in high yields.[1]

There were two other reports on the preparation of dialkylheteroarylboranes, which involve the reaction of heteroaryllithiums(i.e., lithiothiophenes, 2-lithio-1-methylpyrrole) or 5-alkyl-2-iodothiophenes with dialkylhaloboranes.[2] However, special care must be exercised in handling haloboranes and the yields of these methods are less satisfactory.

Now we wish to report an alternative and versatile approach to the preparation of dialkylpyridylboranes by the reaction of lithiopyridines(1) with dialkylmethoxyboranes(2) which are readily accessible from trialkylboranes or dialkylboranes with methanol.[3]



3- or 4-substituted

1

2
a: BR_2=BEt_2
b: BR_2=9-BBN

3

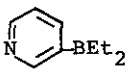
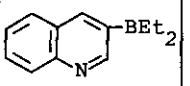
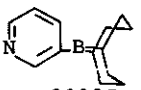
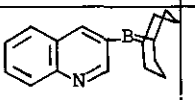
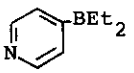
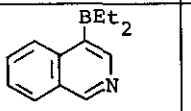
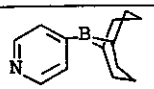
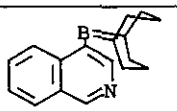
Chart 1

Reactions were simply carried out by the addition of 2(2.1 mol eq.) to an ethereal solution of 1(1 mol eq.), formed from bromopyridines and BuLi in situ, at -70°C, then the mixture being stirred at room temperature overnight. Isolation of the

products was performed by column chromatography(silica gel, benzene) after the organic phase was washed with brine, dried and concentrated, or by filtration of the precipitates liberated in the reaction medium.

In the synthesis of diethyl(4-pyridyl)borane, the present method was found to be more effective than the previous one,[1] as shown in Table. Similarly, benzo-fused pyridylboranes(i.e., quinolyl- and isoquinolylboranes) could be obtained in moderate yields.

Table Preparation of dialkylpyridylboranes

2	3[a]	Yield (%)	High-MS[d] (Calcd)	2	3[a]	Yield (%)	High-MS[d] (Calcd)
2a	 mp 160-162°C (from isopropanol)	80 (80)[c]	$C_9H_{14}NB$ 147.1210 (147.1218)	2a	 mp 284°C dec.[b]	60	$C_{13}H_{16}NB$ 197.1373 (197.1375)
2b	 mp above 300°C (from benzene)	60	$C_{13}H_{18}NB$ 199.1532 (199.1528)	2b	 mp 168-170°C (from acetone-MeOH)	62	$C_{17}H_{20}NB$ 249.1668 (249.1668)
2a	 mp above 300°C (from acetone)	71 (48)[c]	$C_9H_{14}NB$ 147.1210 (147.1218)	2a	 mp above 300°C[b]	70	$C_{13}H_{16}NB$ 197.1385 (197.1375)
2b	 mp above 300°C[b]	60	$C_{13}H_{18}NB$ 199.1525 (199.1528)	2b	 mp above 300°C[b]	54	$C_{17}H_{20}NB$ 249.1672 (249.1668)

a) All compounds were fully characterized spectroscopically (^{1}H-NMR, MS). b) Severely insoluble in most organic solvents c) Yield obtained by the previously reported method[1] d) High-resolution mass spectral data

Interesting observations were obtained on the examination of the reaction of 2 with 2-lithiopyridines(5) or lithioquinolines(11).

Thus, treatment of 5a with 2a afforded borate(8a),[4,†] stable oil to an acidic treatment(10% aq.HCl in EtOH, 24h, room temperature), as a single product in 74% yield after silica gel column chromatography(hexane:benzene=1:1). Likewise, the reaction of 5a with 2b or 5b with 2a produced corresponding 8, whereas 6-methyl group of 5b seemed to have some steric effects on the reaction of 5b with 2b to give borane(7)(mp 170-175°C dec.). For the formation of diethyl(2-

pyridyl)borane(9) as a dimer(mp 205-206°C);[4] two methods were available; heating of 8a at 180°C for several minutes under reduced pressure(20 mmHg)(25% yield based on 8a) or treatment of 5a with triethylborane followed by treatment with iodine(25% yield based on 4). These reactions could be explained to proceed through the following paths, as indicated in Chart 2.

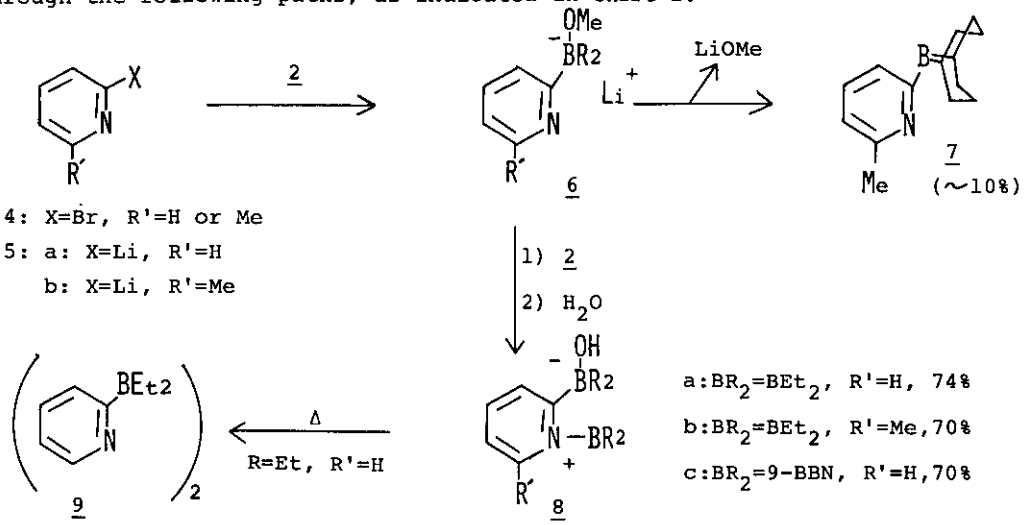


Chart 2

Next, we examined the reaction of lithioquinolines(11), formed from bromoquinolines(10) and BuLi *in situ*, with 2a under similar conditions described above, and found remarkable differences of chemical behavior between 2-, 3- and 4-isomers of 11. Thus, contrary to the smooth production of diethyl(3-quinolyl)borane(14b) from 11b and 2a as expected, the products obtained by the treatment of 11a,c with 2a were not the expected diethylquinolylboranes but corresponding ethylquinolines (13a; 20%, 13b; 16%), presumably derived from the borate(12) via migration of ethyl group from boron to carbon followed by certain oxidation processes,[5] as shown in Chart 3. The reaction of 11a with 2b under the same condition gave borane(14a) in 62% yield, while similar treatment of 11c with 2b gave no isolable products. Details of these attractive processes are under investigation and the results will be the subjects of forthcoming publications.

Applications of the present method to other heteroarylborane syntheses are underway.

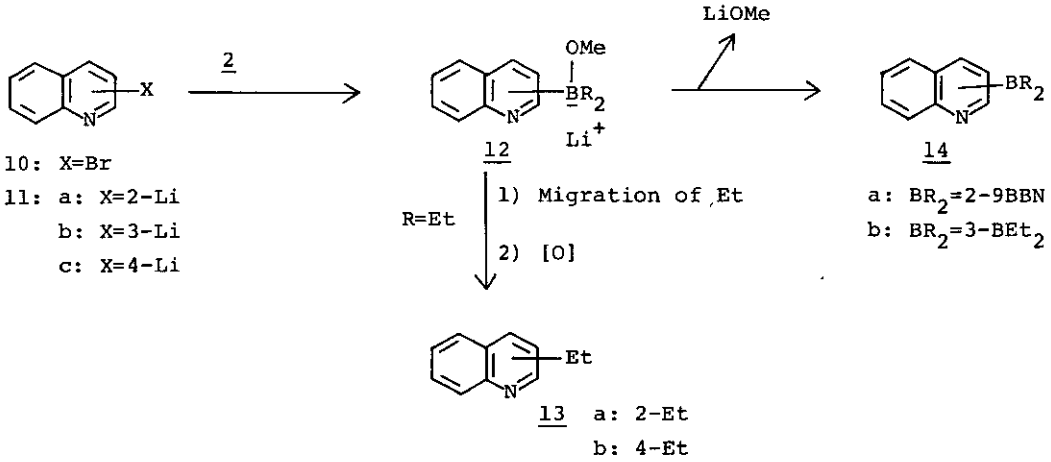


Chart 3

REFERENCES AND NOTES

1. M. Terashima, H. Kakimi, M. Ishikura and K. Kamata, Chem. Pharm. Bull., 1983, 31, 4573.

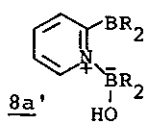
2. W. Siebert, Chem. Ber., 1970, 103, 2308. B. Wrackmeyer and H. Nöth, Chem. Ber., 1976, 109, 1075.

3. H. C. Brown, "Organic Syntheses via Boranes", John Wiley & Sons, Inc., New York, 1975, p 32. R. Köster, W. Fenzl and G. Seidel, Liebigs Ann. Chem., 1975, 352.

4. 8a; ^{1}H-NMR($CDCl_3$) δ: 0.30-1.00(m, 20H), 2.40(br s, 1H, OH), 7.15(m, 1H), 7.36(dd, 1H, J=1, 8Hz), 7.63(m, 1H), 7.90(dd, 1H, J=1, 6Hz). High-resolution MS m/z Calcd for $C_{13}H_{24}NB_2O$ 232. 2043, Found 232.2051. 9; ^{1}H-NMR($CDCl_3$) δ: 0.30-1.00(m, 20H), 7.15(m, 2H), 7.40-7.80(m, 4H), 8.33(dd, 2H, J=1, 6Hz). MS m/z 292, 293, 294(M^+). Anal. Calcd for $C_{18}H_{28}N_2B_2$; C, 73.52; H, 9.60; N, 9.53. Found C, 73.36; H, 9.65; N, 9.51.

5. K. Utimoto, K. Okada and H. Nozaki, Tetrahedron Lett., 1975, 4239. E. Negishi and R. E. Merrill, Chem. Commun., 1974, 860.

† An alternative structure(8a') could not be excluded.



8a'

Received, 13th July, 1984