

Allylic boron and zinc derivatives in synthesis and transformations of nitrogen heterocycles*

Yu. N. Bubnov^{†,1}, E. V. Klimkina², I. V. Zhun², F. V. Pastukhov¹,
and I. V. Yampolsky¹

¹A. N. Nesmeyanov Institute of Organoelement Compounds,
Russian Academy of Sciences, 28 ul. Vavilova, 117813 Moscow, Russian
Federation; ²N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of
Sciences, 47 Leninsky prosp., 117913 Moscow, Russian Federation

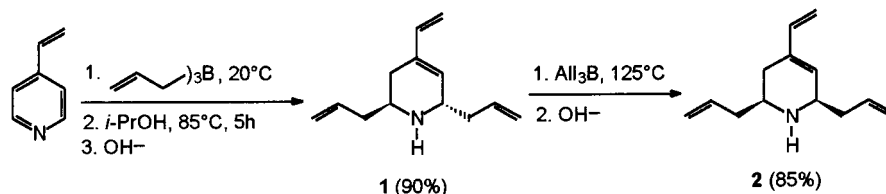
Dedicated to Prof. Dr. Henning Hopf on the occasion of his 60th birthday.

Abstract: Reductive allylation of certain nitrogen heterocycles (indoles, isoquinoline, 4-vinylpyridine, and lactams) with allylic boron and zinc derivatives is presented.

1,2-Addition reactions of organometallic compounds to the C=N bond belong to well-developed type of transformations. Thus, allylboration [1–2] and allylzincation [3] of imines present a convenient way to various butenylamines. Certain aromatic heterocycles (e.g., quinolines and phenanthridine) also react with allylic boranes at 0–20 °C via 1,2-addition to the C=N bond to give the corresponding α -allylated dihydro heterocycles [4]. Pyridines [5,6] and pyrrole [7] undergo the reductive *trans*- α,α' -diallylation on consequent treatment with allylic triorganoborane and alcohol. Allylboration of 1-lithio-2-alkyl-1,2-dihydropyridine has been used as a key step in the total syntheses of piperidine [8] and indolizidine [9] alkaloids.

In this presentation, reductive allylation of certain nitrogen heterocycles with allylic boron and zinc derivatives is presented.

4-Vinylpyridine is transformed stereoselectively into *trans*-2,6-diallyl-1,2,3,6-tetrahydropyridine **1** on heating with triallylborane in the presence of isopropanol (4 equiv) [10].



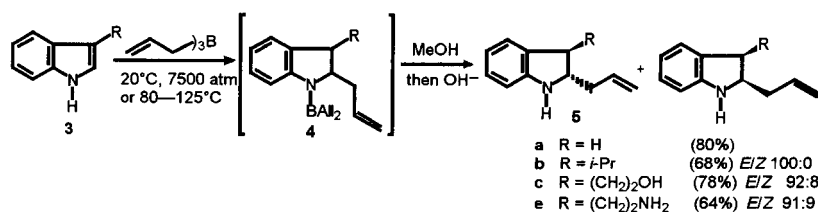
Scheme 1

Trans-amine **1** is cleanly converted into the *cis*-isomer **2** on heating with AlI_3B at 125 °C 2 h followed by deboration of aminoborane formed (Scheme 1).

Indoles **3** undergo the reductive 1,2-allylboration upon treatment with triallylborane to furnish *N*-borylated amines **4**, deboration of which leads to the *trans*-2-allyl-3-*R*-indolines **5** as the major or sole products (Scheme 2) [11].

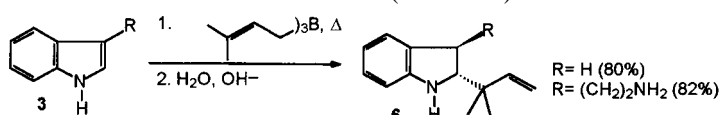
*Lecture presented at the 13th International Conference on Organic Synthesis (ICOS-13), Warsaw, Poland, 1–5 July 2000. Other presentations are published in this issue, pp. 1577–1797.

[†]Corresponding author: Fax: +7(095) 135 5085; E-mail: dir@ineos.ac.ru



Scheme 2

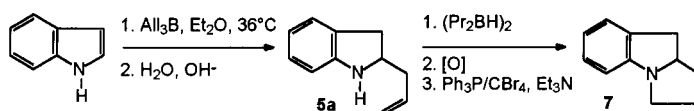
Reaction of 1-deuterioindole with AlI₃B (Et₂O, 36 °C, 8 h) afforded a 1:1 mixture of *cis*- and *trans*-2-allyl-3-deuterioindolines. Prenylboration of indole (115–120 °C, 1.5 h) and triptamine (120–130 °C, 8 h) led to indolines **6** with a terminal double bond (Scheme 3).



Scheme 3

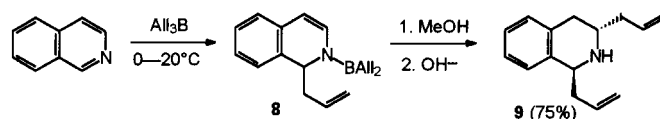
These results show clearly that 1,2-allylboration of indoles proceeds with full rearrangement of allylic moiety.

2-Allylated indolines thus obtained are valuable precursors for many organic compounds. Thus, benzo[*f*]pyrrolizidine **7** was synthesized from **5a** via hydroboration-oxidation-cyclization sequence (Scheme 4) [12].



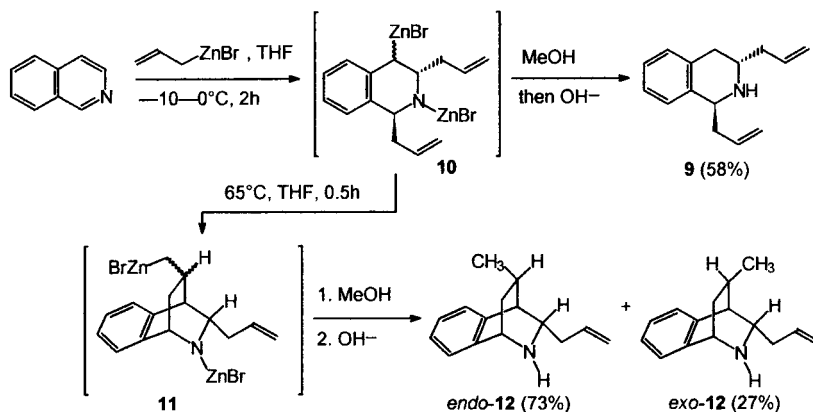
Scheme 4

Isoquinoline reacts with AlI₃B to give 1,2-allylboration product **8** treatment of which with methanol and base produces *trans*-1,3-diallyl-1,2,3,4-tetrahydroisoquinoline **9** (Scheme 5) [5ab,13].



Scheme 5

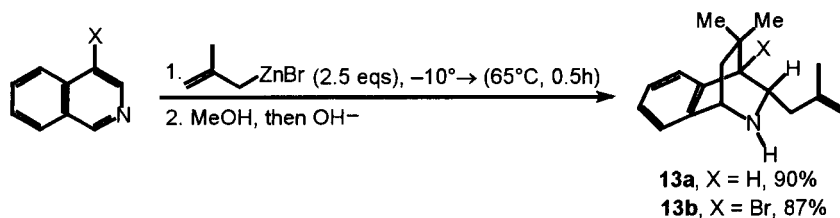
Amine **9** was also prepared in 58% yield by the reaction of isoquinoline with allylzinc bromide (1:2.5) in THF (–10–0 °C for 0.5 h) followed by dezincation with methanol and base [10a].



Scheme 6

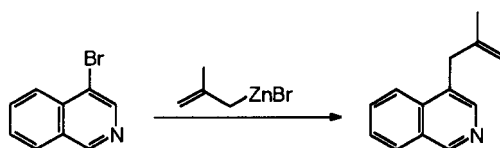
When an intermediate dizinc derivative **11** was heated in THF under reflux for 0.5 h and worked up with MeOH and base, a 7:3 mixture of the isoquinolidine isomers, *endo*-**12** and *exo*-**12**, was obtained in 88% overall yield [10]. Transformation of **10** into tricyclic compounds **11** seems to proceed by the addition of the benzylzinc fragment to the double bond of the 1-allyl group. The predominant formation of *endo*-**12** is most likely caused by the electronic effect of the benzene ring on the orientation of the double bond and the 4-ZnBr group in the transition state (Scheme 6).

The usefulness of this novel reaction was demonstrated in the one-pot synthesis of the isoquinolidine derivatives **13ab** from methallylzinc bromide (Scheme 7) [10b].



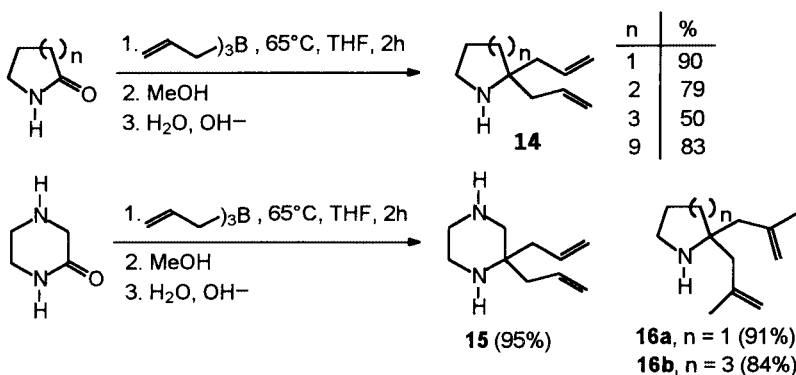
Scheme 7

It should be noted that 4-methallylisoquinoline was obtained in 83% yield, instead of **13a**, when a solution of methallylzinc bromide in THF (2.4 M) was added to 3-bromoisoquinoline at 70°C (Scheme 8) [10b].



Scheme 8

Lactams containing an N–H bond are transformed into the corresponding 2,2-diallylated nitrogen heterocycles (**14** and **15**) on heating with triallylborane in THF followed by deboration with methanol and base (Scheme 9) [14].



Scheme 9

The amines **16** are similarly obtained starting from trimethylaluminum [14]. With only one exception (reaction of Al_3B with caprolactam) the 2,2-diallylated heterocycles **14–16** were obtained in 80–95% yield.

This work was supported by the Russian Foundation for Basic Research (grant N 99-03-33125a and 00-15-97378), and Ministry of Science and Technology (N 402-19-/22.3/23.1(00)-P).

REFERENCES

1. (a) Y. Yamamoto and N. Asao. *Chem. Rev.* **93**, 2207 (1993); (b) A. Meller and G. Gerger. *Monatsh. Chem.* **105**, 684 (1974); (c) R. W. Hoffmann, G. Eichler, A. Endesfelder. *Lieb. Ann. Chem.* 2000 (1983); (d) A. A. El-Shehawy, M. Y. Abdelaal, K. Watanabe, K. Ito, S. Itsuno. *Tetrahedron: Asymmetry* **8**, 1731 (1997).
2. (a) Yu. N. Bubnov, V. C. Bogdanov, B. M. Mikhailov. *Zh. Obshch. Khim.* **38**, 260 (1968) [CA 69•52200j]; (b) Yu. N. Bubnov, V. I. Zheludeva, T. Yu. Rudashevskaya, T. S. Kuznetsova. *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, **38**, 1073 (1989) (Engl. Transl.); (c) L. I. Lavrinovich, A. V. Ignatenko, Yu. N. Bubnov. *Bull. Russ. Acad. Sci., Div. Chem. Sci.* **41**, 2051 (1992) (Engl. Transl.); (d) M. E. Gurskii, S. B. Golovin, A. V. Ignatenko, Yu. N. Bubnov. *Bull. Russ. Acad. Sci., Div. Chem. Sci.* **41**, 1724 (1992) (Engl. Transl.); (e) M. E. Gurskii, T. V. Potapova, Yu. N. Bubnov. *Russ. Chem. Bull.* **47**, 1410 (1998) (Engl. Transl.).
3. (a) P. Knochel and R. D. Singer. *Chem Rev.* **93**, 2117 (1993); (b) M. Nakamura, A. Hirai, E. Nakamura. *J. Am. Chem. Soc.* **118**, 8489 (1996).
4. Yu. N. Bubnov, S. V. Evchenko, A. V. Ignatenko. *Bull. Russ. Acad. Sci., Div. Chem. Sci.* **41**, 2239 (1992) (Engl. Transl.).
5. (a) Yu. N. Bubnov. *Pure Appl. Chem.* **66**, 235 (1994); (b) Yu. N. Bubnov. *Russ. Chem. Bull.* **44**, 1156 (1995) (Engl. Transl.); (c) Yu. N. Bubnov. In *Adv. Boron Chemistry*, W. Siebert (Ed.), pp. 123–138, The Royal Society of Chemistry, Thomas Graham House, Cambridge (1997).
6. Yu. N. Bubnov, E. E. Demina, A. V. Ignatenko. *Russ. Chem. Bull.* **46**, 1306 (1997) (Engl. Transl.).
7. Yu. N. Bubnov, E. V. Klimkina, L. I. Lavrinovich, A. Yu. Zykov, A. V. Ignatenko. *Russ. Chem. Bull.* **48**, 1696 (1999) (Engl. Transl.).
8. Yu. N. Bubnov, E. V. Klimkina, A. V. Ignatenko. *Russ. Chem. Bull.* **47**, 451 (1998) (Engl. Transl.).
9. Yu. N. Bubnov, E. V. Klimkina, A. V. Ignatenko. *Russ. Chem. Bull.* **47**, 941 (1998) (Engl. Transl.).
10. (a) Yu. N. Bubnov, F. V. Pastukhov, A. V. Ignatenko. *Russ. Chem. Bull.* **46**, 1975 (1997); (b) Yu. N. Bubnov and F. V. Pastukhov. Unpublished results.
11. Yu. N. Bubnov, I. V. Zhun', E. V. Klimkina, A. V. Ignatenko, Z. A. Starikova. *Eur. J. Org. Chem.* (2000) in press.
12. Yu. N. Bubnov, M. E. Gurskii, T. V. Potapova. *Russ. Chem. Bull.* **45**, 2665 (1996) (Engl. Transl.).
13. Yu. N. Bubnov, S. V. Evchenko, A. V. Ignatenko. *Russ. Chem. Bull.* **42**, 1268 (1993) (Engl. Transl.).
14. Yu. N. Bubnov, F. V. Pastukhov, I. V. Yampolsky, A. V. Ignatenko. *Eur. J. Org. Chem.* 1503 (2000).