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Stereospecific synthesis of aryltetraline lignan analogues using 1,6-bis(dipropylboryl)hexa-2,4-diene

Mikhail E. Gurskii,[a] Maxim I. Zuev,[a] Artur V. Eshtukov,[b] Dmitry A. Cheshkov,[b] Sergey V. Baranin*[a] and Yurii N. Bubnov[a]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: svbar@ioc.ac.ru*
[b] *State Scientific Research Institute of Chemistry and Technology of Organoelement Compounds, 105118 Moscow, Russian Federation*

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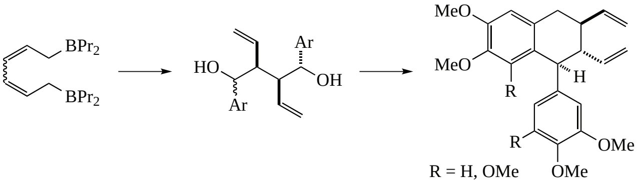
A novel convenient two-stage synthesis of aryltetraline lignan analogues from aromatic aldehydes and diallyl diboron derivatives on the basis of intramolecular Friedel–Crafts reaction has been developed.



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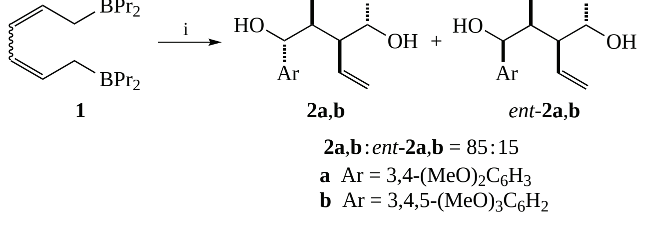
The allylboration reaction is currently a powerful synthetic tool which is widely used to prepare organic and organoelement compounds of various classes, including natural substances and their analogues.[1–3] Many reactions involving allylboranes proceed regio-, stereo- and enantioselectively with the formation of one or more new C–C or carbon–heteroatom bonds.[4–12] The purpose of this study was to expand the scope of application of β,γ-unsaturated boron derivatives containing two allylboron fragments for the construction of lignans analogues of aryltetrahydronaphthalene and 2,5-diaryltetrahydrofuran series. Earlier, we obtained 1,6-bis(dipropylboryl)hexa-2,4-diene **1**, a compound with an unusual structure containing in the molecule two boron atoms in the allylic positions[13–15] (Scheme 1). Double allylboration of aromatic aldehydes with this diboron derivative **1** afforded two diastereomeric diols **2a**,**b** and *ent*-**2a**,**b** in ratio 85 : 15 and in total yields 70–80%.[16,17] It was found[16] that new C–C bonds were formed in positions 3 and 4 of the hexadiene system stereoselectively, however they differed in the configuration of alcohol centres. The diastereomers **2** and *ent*-**2** were separated by column chromatography.

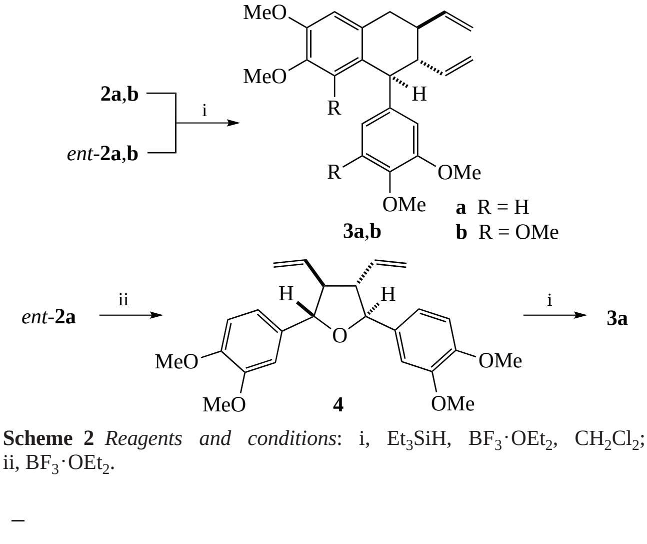
On the basis of compounds **2a**, a new effective synthesis of furofuran lignans was developed, including the ozonation of diene diols **2a** followed by reduction. As a result, six racemic furofuran lignans were obtained, namely, diaeudesmin, epiasarinin, diayangambin, epidiaeudesmin, asarinin, and epiyangambin.[17] Note that lignans are secondary metabolites produced by vascular plants, formed by oxidative dimerization of two C_6C_3 phenylpropane units, and they have a wide range of biological activity.[18–25] The allylboration products **2a**,**b** contain two arylpropane fragments connected by the β-atom of the side chain and, therefore, they may serve as synthetic blocks for the construction of various types lignan structures.[22]

Here we report a general strategy for the stereoselective one-pot transformation of diols **2a**,**b** into structural lignan analogues of aryltetraline and 2,5-diaryl-3,4-disubstituted tetrahydrofuran series (for examples of natural lignans structures of furofuran, aryltetrahydronaphthalene and 2,5-diaryltetrahydrofuran series, that can be obtained from diols **2a**,**b**, see Online Supplementary Materials). In our experiments, sequential treatment of both (1*R**,2*S**,3*S**,4*R**)-diols **2a**,**b** with triethylsilane and $BF_3 \cdot OEt_2$ in CH_2Cl_2 at ~20 °C led to (1*R**,2*R**,3*R**)-tetrahydronaphthalenes **3a**,**b** as individual diastereomers in high yields (Scheme 2). The same diastereomers **3a**,**b** were also obtained from (1*R**,2*S**,3*S**,4*S**)-diols *ent*-**2a**,**b**.

The structure of compounds **3a**,**b** was confirmed by ^{1}H and ^{13}C NMR using 2D NMR experiments (COSY, HSQC, HMBC,



Scheme 1 *Reagents and conditions*: i, ArCHO (2 equiv.), –78 → 20 °C; ii, H_2O_2/OH^-, 5 °C.



Scheme 2 *Reagents and conditions*: i, Et_3SiH, $BF_3 \cdot OEt_2$, CH_2Cl_2; ii, $BF_3 \cdot OEt_2$.

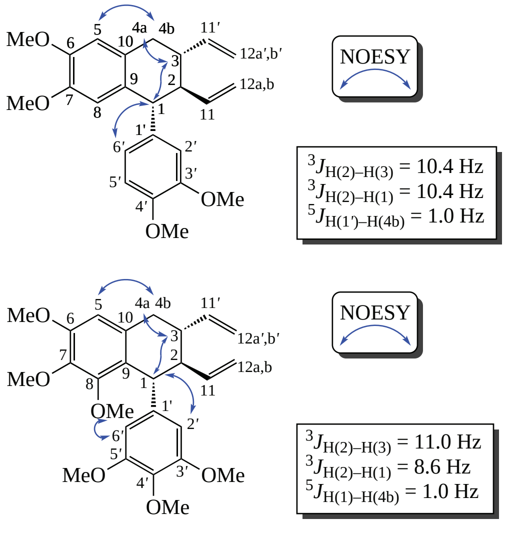
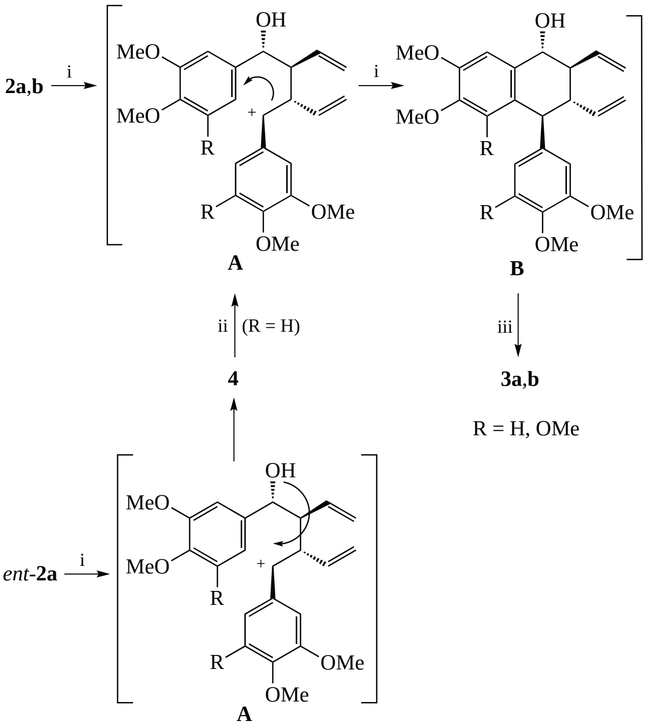


Figure 1 Key NOESY correlations for determination of the compounds **3a**,**b** structures.

and NOESY). Their configuration was determined based on the $^3J_{H(2)–H(3)}$ and $^3J_{H(2)–H(1)}$ values and NOE correlations between H(3), H(1), and H(3), H(4α) (Figure 1). Large values of the vicinal constants and NOE interactions between H(1) and H(3) clearly indicate the pseudo-axial orientation of the H(1), H(2) and H(3) protons. The high-resolution mass spectra of compounds **3a**,**b** contain peaks $[M+H]^+$.

Unexpectedly, we have found that diastereomer *ent*-**2a** under the action of $BF_3 \cdot OEt_2$ in diethyl ether gave individual (2*R**,3*R**,4*R**,5*R**)-tetrahydrofuran **4** (see Scheme 2). The structure and configuration of compound **4** were established by NMR spectroscopy with the use of a standard set of 2D correlation experiments: $^1H,^1H$-COSY, $^1H,^{13}C$-HSQC, $^1H,^{13}C$-HMBC. The NOE contacts were examined in the $^1H,^{13}C$-HSQC-NOESY experiment without decoupling. The absence of the NOE contacts between the protons of all the substituents indicates their mutual *trans*-orientation. The values of the vicinal spin–spin coupling constants between the furan ring protons also indicate the mutual *trans*-orientation of the substituents. It should be noted that since the ^1H NMR spectrum contains non-first order multiplets, the spectrum total lineshape analysis was performed by ANATOLIA NMR software[26] to calculate the values of coupling constants. To correlate the values of the vicinal spin–spin coupling constants with the relative stereochemical configuration, qualitative quantum-mechanical calculations of all possible configurations were carried out (including geometry optimization and spin–spin coupling constants calculation[27]). Detailed information on measuring the coupling constants, their relation to stereochemistry and measurement of NOE effects, as well as elucidation of stereochemical configuration is given in the Online Supplementary Materials.

It should be noted that the cyclization of diol **2a**,**b** under milder conditions (ether, lower temperature) took a longer time, however it led to the same aryltetralines **3a**,**b** (see Scheme 2). The transformation of furan **4** into the final product **3a** in ether also required longer time, but in CH_2Cl_2 it proceeded within few minutes. Thus, the pathway of tetraline **3** formation depends upon the diol **2** diastereomeric structure and the solvent used. We assume that in CH_2Cl_2 under the action of $BF_3 \cdot OEt_2$, diols **2a**,**b** initially form intermediate cation **A** (Scheme 3). Its stability is provided by electron-donating substituents of the aromatic ring. The cation **A** rapidly undergoes intramolecular cyclization yielding an intermediate **B** which upon ionic hydrogenation ($Et_3SiH + BF_3 \cdot OEt_2$) is transformed into 1,2,3,4-tetrahydronaphthalene derivative **3a**,**b**. Presumably, the direction of the intramolecular attack on the oxygen atom of the hydroxy group of the intermediate **A** in the case of *ent*-**2a** in ether is more favourable than the occurrence of the intramolecular Friedel–Crafts reaction (which would take place for **2a**).



Scheme 3 *Reagents and conditions*: i, $BF_3 \cdot OEt_2$, Et_2O; ii, $BF_3 \cdot OEt_2$, CH_2Cl_2; iii, Et_3SiH, $BF_3 \cdot OEt_2$, Et_2O or CH_2Cl_2.

One of described general accesses to 2,5-diaryl-substituted tetrahydrofurans of type **4** involves stereoselective intramolecular cyclization of 1,4-diarylbutanediols.[28–32] Also note that the intramolecular Friedel–Crafts reaction of 2,3-substituted 1,4-diarylbutan-1-ols is a popular way to construct an aryltetraline skeleton.[23,33,34] Reported stereoselective syntheses of compounds of **3a**,**b** type are very time-consuming and multistage.[35–38] Our strategy greatly reduces this sequence.

In conclusion, a new convenient two-stage synthesis of aryltetraline lignan analogues from aromatic aldehydes and diallyl diboron derivatives has been developed. The presence of vinyl groups in tetralines **3a**,**b** opens further possibilities for their transformation into natural lignans.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.09.033.

References

1 B. M. Mikhailov and Yu. N. Bubnov, *Bororganicheskie soedineniya v orgsnicheskom sinteze (Organoboron Compounds in Organic Synthesis)*, Nauka, Moscow, 1977 (in Russian).

2 B. M. Mikhailov and Yu. N. Bubnov, *Organoboron Compounds in Organic Synthesis*, Harwood Academic Publishers, London, 1984.

3 Yu. N. Bubnov, in *Science of Synthesis*, eds. D. S. Matteson and D. Kaufmann, Georg Thieme, Stuttgart, 2004, vol. 6, pp. 945–1072.

4 A. Pelter, K. Smith and H. C. Brown, *Borane Reagents*, Academic Press, London, 1988.

5 D. S. Matteson, *Stereodirected Synthesis with Organoboranes*, Springer, Berlin, 1995.

6 Yu. N. Bubnov, *Pure Appl. Chem.*, 1987, **59**, 895.

7 Yu. N. Bubnov, *Pure Appl. Chem*., 1991, **63**, 361.

8 Yu. N. Bubnov, M. E. Gurskii and I. D. Gridnev, in *Comprehensive Heterocyclic Chemistry-II*, eds. A. R. Katrizky, C. W. Rees and E. F. Scriven, Pergamon, Oxford, 1996, vol. 8, pp. 889–931.

9 H. C. Brown and P. K. Jadhav, *J. Am. Chem. Soc*., 1983, **105**, 2092.

10 U. S. Racherla and H. C. Brown, *J. Org. Chem*., 1991, **56**, 401.

11 H. C. Brown, *Pure Appl. Chem.*, 1994, **66**, 201.

12 W. R. Roush, *in Comprehensive Organic Synthesis*, eds. B. M. Trost, I. Fleming and C. F. Heathcock, Pergamon, Oxford, 1991, vol. 2, pp. 1–53.

13 Yu. N. Bubnov, M. E. Gurskii and A. V. Geiderikh, *Organomet. Chem. USSR*, 1989, **2**, 761 (*Metalloorg. Khim*., 1989, **2**, 1433).

14 M. E. Gursky, A. V. Geiderikh, A. V. Ignatenko and Yu. N. Bubnov, *Russ. Chem. Bull*., 1993, **42**, 144 (*Izv. Akad. Nauk, Ser. Khim*., 1993, 160).

15 M. E. Gursky, A. V. Geiderikh, S. B. Golovin, A. V. Ignatenko and Yu. N. Bubnov, *Russ. Chem. Bull*., 1993, **42**, 215 (*Izv. Akad. Nauk, Ser. Khim*., 1993, 236).

16 A. N. Anfimov, S. Yu. Erdyakov, M. E. Gurskii, A. V. Ignatenko K. A. Lyssenko and Yu. N. Bubnov, *Mendeleev Commun*., 2011, **21**, 1.

17 A. N. Anfimov, S. Yu. Erdyakov, M. E. Gurskii and Yu. N. Bubnov, *Russ. Chem. Bull., Int. Ed*., 2011, **60**, 2336 (*Izv. Akad. Nauk, Ser. Khim*., 2011, 2291).

18 W. M. Hearon and W. S. MacGregor, *Chem. Rev*., 1955, **55**, 957.

19 R. S. Ward, *Chem. Soc. Rev*., 1982, **11**, 75.

20 R. S. Ward, *Nat. Prod. Rep*., 1993, **10**, 1.

21 R. S. Ward, *Nat. Prod. Rep*., 1999, **16**, 75.

22 D. C. Ayres and J. D. Loike, *Lignans: Chemical, Biological and Clinical Properties*, Cambridge University Press, Cambridge, 1990.

23 J.-Y. Pan, S.-L. Chen, M.-H. Yang, J. Wu, J. Sinkkonen and K. Zou, *Nat. Prod. Rep*., 2009, **26**, 1251.

24 M. Saleem, H. J. Kim, M. S. Ali and Y. S. Lee, *Nat. Prod. Rep*., 2005, **22**, 696.

25 J. L. Charlton, *J. Nat. Prod*., 1998, **61**, 1447.

26 D. A. Cheshkov, K. F. Sheberstov, D. O. Sinitsyn and V. A. Chertkov, *Magn. Reson. Chem*., 2018, **56**, 449.

27 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Jr. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, *Gaussian 09*, Revision A.02, Gaussian, Wallingford, CT, 2009.

28 D. Soorukram, M. Pohmakotr, C. Kuhakarn and V. Reutrakul, *Synthesis*, 2018, **50**, 4746.

29 T. Biftu, B. G. Hazra, R. Stevenson and J. R. Williams, *J. Chem. Soc., Perkin Trans. 1*, 1978, 1147.

30 C. W. Perry, M. V. Kalnins and K. H. Deitcher, *J. Org. Chem.*, 1972, **37**, 4371.

31 P. R. Jagtap, I. Císařová and U. Jahn, *Org. Biomol. Chem*., 2018, **16**, 750.

32 B. E. Hetzler, G. Volpin, E. Vignoni, A. G. Petrovic, G. Proni, C. T. Hu and D. Trauner, *Angew. Chem., Int. Ed*., 2018, **57**, 14276.

33 J. D. Sellars and P. G. Steel, *Eur. J. Org. Chem*., 2007, 3815.

34 X. Liu, P. Chen, X. Li, M. Ba, X. Jiao, Y. Guo and P. Xie, *Bioorg. Med. Chem. Lett*., 2018, **28**, 1699.

35 X. Li, X. Jiao, X. Liu, C. Tian, L. Dong, Y. Yao and P. Xie, *Tetrahedron Lett.*, 2014, **55**, 6324.

36 B.-C. Hong, C.-S. Hsua and G.-H. Lee, *Chem. Commun*., 2012, **48**, 2385.

37 M. Coltart and J. L. Charlton, *Can. J. Chem*., 1996, **74**, 88.

38 C. E. Rye and D. Barker, *J. Org. Chem*., 2011, **76**, 6636.

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