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Palladium-catalyzed amination in the synthesis of novel fluorescent sensors based on 3,3′-diamino substituted 1,1′-bi(2-naphthol)

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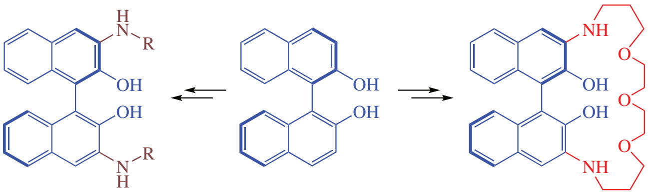
The first example of palladium-catalyzed Buchwald–Hartwig amination of 3,3′-dibromo-1,1′-bi(2-naphthol) is reported. Linear and macrocyclic derivatives of *N,N′*-disubstituted 3,3′-diamino-1,1′-bi(2-naphthols) thus obtained are able to detect metal cations when using UV and fluorescence spectroscopy.



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Development of fluorescent chemosensors is an important task of organic chemistry. Application of the fluorescence spectroscopy for detecting metal cations,[1,2] inorganic acids anions,[3,4] and organic molecules[5,6] has become a renowned and widely used method as it guarantees high sensitivity and selectivity, quick response to coordination of the analyte with detector. A special case of the fluorescent detectors comprises those with enantioselective properties which can distinguish between two enantiomers. These chiral compounds are mainly derivatives of 1,1′-bi(2-naphthol) (BINOL) which possesses inherent C_2-chirality and fluorescent properties. Various derivatives of BINOL were elaborated, additional substituents including chiral moieties[7] were introduced into the structure, especially at 3,3′ and 6,6′ positions.[8,9] The BINOL fragment was incorporated in the macrocyclic structures as well.[10–12] Our previous research was aimed at the development of enantioselective fluorescent detectors based on BINOL analogue, *i.e.* 2,2′-diamino-1,1′-binaphthalene (BINAM). We found out that its *N,N′*-diaryl derivatives containing additional chiral and fluorophore moieties could be employed for detecting enantiomers of amino alcohols.[13–17] A crucial tool for constructing C–N bonds in such compounds was Pd-catalyzed amination.[18]

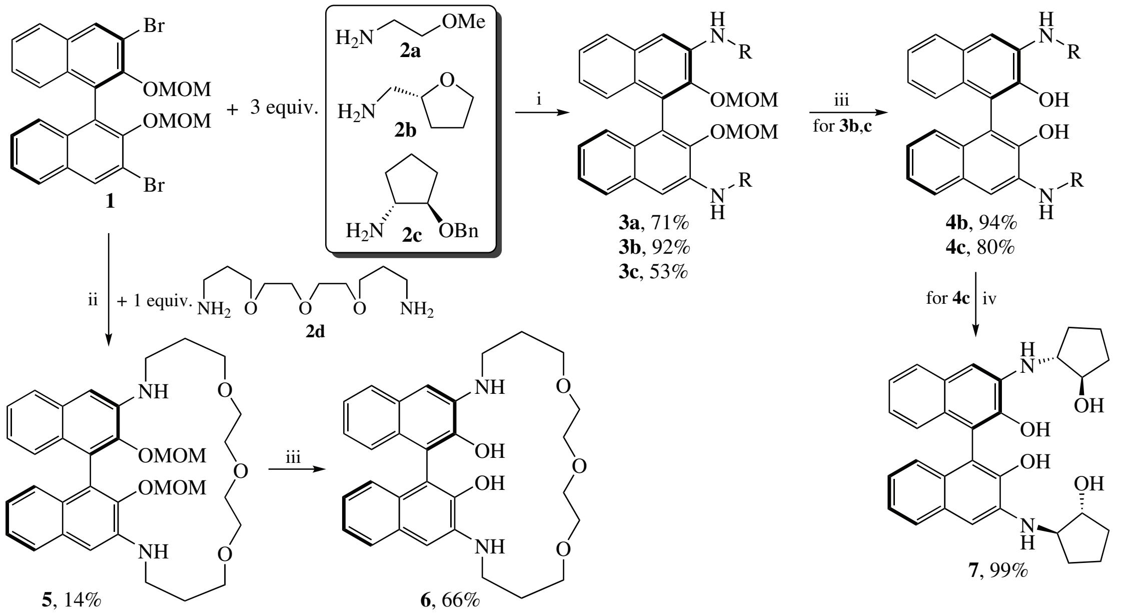
In the present research we decided to introduce several *N,O*-containing substituents at positions 3 and 3′ of BINOL also using Pd-catalyzed amination reactions, an approach which was not previously employed for BINOL modifications. It is important to retain free hydroxy groups in the target molecules to ensure the formation of hydrogen bonds with chiral analytes and provide enantioselectivity. Therefore, compound **1** with methoxymethyl (MOM) protections was chosen for further modification. It was synthesized according to a described three-step procedure from free (*R*)-BINOL.[19]

The Buchwald–Hartwig Pd-catalyzed amination was carried out with achiral 2-methoxyethylamine **2a** and two chiral amines such as (*R*)-tetrahydrofurfurylamine **2b** and (1*R*,2*R*)-2-benzyloxycyclopentylamine **2c**. The reactions were performed using standard Pd(dba)$_2$/BINAP catalytic system and 3 equiv. of the corresponding amine. The target MOM-protected compounds **3a–c** were obtained in 53–92% yields (Scheme 1).

Additionally, catalytic macrocyclization reaction was performed with linear trioxadiamine **2d** in a more dilute solution (C = 0.02 M) with equimolar ratio of reagents. The yield of the macrocycle **5** was 14%. Standard procedure was employed to deprotect OH groups in the MOM-containing compounds **3**, **5** (HCl/MeOH). As a result, non-cyclic BINOL 3,3′-diamino derivatives **4b**,**c** were obtained in 94 and 80% yields, respectively, and macrocyclic derivative **6** was obtained in 66% yield (see Scheme 1). Debenzylation of compound **4c** was conducted under usual conditions (H_2, 10% Pd/C in MeOH at 60 °C) to give product **7** in 99% yield.

With several BINOL derivatives in hand, we undertook investigations of their sensing abilities. The experiments with enantiomers of the model amino alcohols (alaninol, 2-amino-1-butanol, valinol, leucinol, *tert*-leucinol, prolinol, 2-phenylglycinol), which previously were used with BINAM derivatives,[15,16] have not yet brought much success. The response of all compounds to the addition of these analytes was insufficient, unlike it was in the case of BINAM-based detectors. The changes in the spectra of fluorescence were tiny even with great excesses of amino alcohols (up to 1000 equiv.). Taking into consideration moderate fluorescence intensity of the BINOL derivatives, parasite interference of the luminescent admixtures in amino alcohols, taken in large excess, was notable which hampered reliable detection of amino alcohol enantiomers. On the contrary, the experiments with detection of metal cations were much more successful. A standard experiment was carried out by adding 5 equiv. of the corresponding metal perchlorate to the solution of the compound under investigation in acetonitrile. Spectra of absorbance and emission were recorded in each case. Discussion of UV-VIS spectra and their changes is given in Online Supplementary Materials. Spectra of fluorescence of the studied 3,3′-diamino BINOLs are characterized by an emission band with a maximum at *ca.* 380 nm, except for macrocycle **5** which shows emission maximum at 400 nm (Table 1).

A common feature of all studied 3,3′-diamino BINOLs is their response to the addition of Al^{III} and Cr^{III} cations. In the case of non-cyclic compounds **4b**,**c**, **7** and macrocycle **6**, a significant increase in the emission intensity is observed (up to 8 times),



Scheme 1 *Reagents and conditions*: i, $Pd(dba)_2$/BINAP (8/9 mol%), Bu^tONa, 0.1 M in 1,4-dioxane, inert atmosphere, reflux; ii, $Pd(dba)_2$/BINAP (8/9 mol%), Bu^tONa, 0.02 M in 1,4-dioxane, inert atmosphere, reflux; iii, HCl, MeOH, 60 °C; iv, H_2 bubbling, 10% Pd/C, MeOH, 60 °C.

Table 1 Basic optical properties of studied 3,3′-diamino BINOLs.

Entry	Sample	C/M[a]	λ_{abs}/nm	lgε	λ_{em}/nm[b]
1	**4b**	1.03×10^{-5}	278 289 338	4.26 4.25 4.09	380
2	**4c**	1.56×10^{-5}	279 290 344	4.03 4.06 3.92	382
3	**5**	9.51×10^{-6}	278 289 349	4.11 4.16 3.84	400
4	**6**	1.79×10^{-5}	279 290 339	4.06 4.07 3.91	384
5	**7**	1.22×10^{-5}	278 289 334	4.21 4.20 3.92	382

[a] All solutions were prepared in UHPLC-grade acetonitrile. [b] Excitation wavelength was 290 nm for all samples.

accompanied by a hypsochromic shift of 20 nm. This effect was noted even after adding only 1 equiv. of these metals and the detection limit of Al^{III} and Cr^{III} can be estimated as *ca.* 2×10^{-7} M. Further increase in the amount of the metal cation did not significantly change the emission [Figure 1(*a*),(*b*),(*d*),(*e*)]. Thus, these compounds can be proposed as fluorescent molecular probes for these two cations.

The addition of Cu^{II} cations to compounds **5**, **4c**, **7** led to full or partial quenching of the fluorescence with the hypsochromic shift [Figure 2(*a*)]. On the contrary, the emission of the macrocyclic compound **6** in the presence of Cu^{II} (1 equiv.) increased with a similar hypsochromic shift, but further addition of this metal resulted in a gradual emission quenching [Figure 2(*b*)].

The addition of Hg^{II} perchlorate to non-cyclic derivatives led to a hypsochromic shift of the emission maximum, in the case of the macrocycle **6** a similar hypsochromic shift was accompanied by a twofold fluorescence quenching [see Figure 1(*d*)] while with its MOM-protected analogue **5** quenching was much more pronounced [Figure 1(*c*)].

The spectral behaviour of the macrocyclic derivative **6** in the presence of Zn^{II} cations is unique: the addition of 1 equiv. of zinc perchlorate led to a partial emission quenching at 380 nm and the second emission band at 460 nm emerged [Figure 3(*a*)]. Further addition of Zn^{II} cations resulted in a steady increase of the emission intensity at 355 nm, while the emission at 460 nm remained almost at the same level after adding 4 equiv. of Zn^{II}. To note, changes in the fluorescence spectra were not accompanied by notable changes in the UV spectra. Thus, compound **6** can be regarded as a potential fluorescent chemosensor for Zn^{II} cations. To elucidate the composition and stability constants of the complexes formed, spectrofluorimetric titration of this compound with $Zn(ClO_4)_2$ was undertaken in the

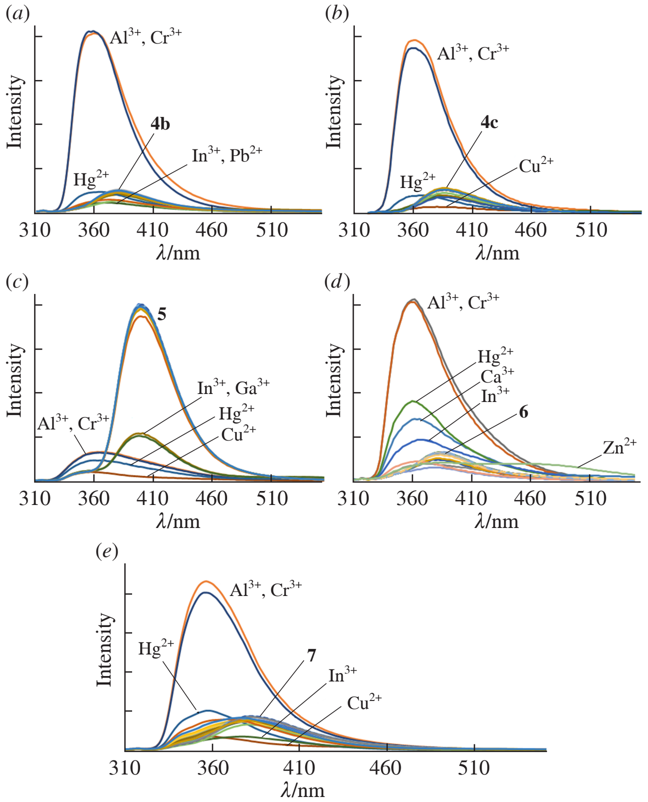


Figure 1 Spectra of fluorescence of 3,3′-diamino substituted BINOLs in the presence of metal cations (5 equiv.) in MeCN, $\lambda_{ex} = 290$ nm: (*a*) compound **4b**, (*b*) compound **4c**, (*c*) compound **5**, (*d*) compound **6**, and (*e*) compound **7**.

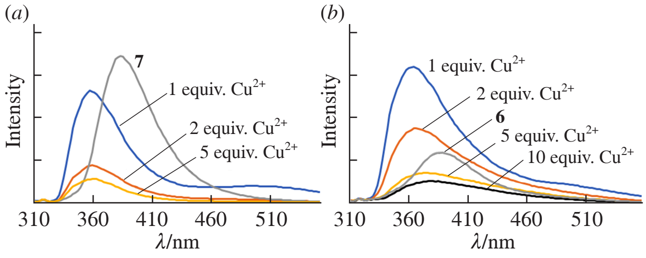


Figure 2 Spectra of fluorescence of (*a*) compound **7** and (*b*) compound **6** in MeCN in the presence of Cu^{II} cations, $\lambda_{ex} = 290$ nm.

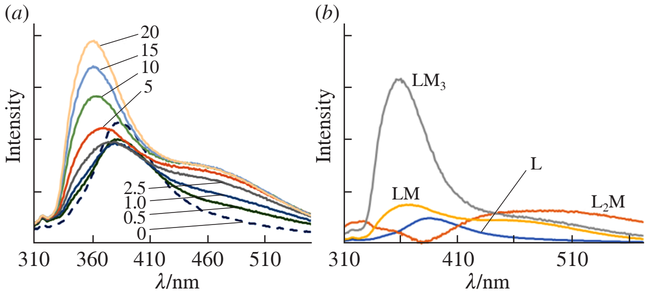


Figure 3 (*a*) Spectrofluorimetric titration of compound **6** with $Zn(ClO_4)_2$ (MeCN, $C_L = 1.79\times10^{-5}$ M, $\lambda_{ex} = 290$ nm, increment 0.1–1 equiv., range 0–20 equiv. Zn^{II}). Some spectra are omitted for clarity. (*b*) Calculated fluorescence spectra of complexes of compound **6** with Zn^{II}.

range of 0–20 equiv. The results were processed with HypSpec program.[20] The best fit of experimental and calculated data was obtained for the model comprising three complexes L_2M (logβ 9.18 ± 0.01), LM (logβ 4.44 ± 0.01), LM_3 (logβ 11.15 ± 0.01). The emission at 460 nm was found to be a feature of L_2M complex which is characterized by the presence of the two maxima. Increase in the fluorescence intensity with a hypsochromic shift (355 nm) on increasing Zn^{II} content is associated with the formation of LM and mainly of LM_3 complexes [see Figure 3(*b*)]. The detection limit of Zn^{II} with this ligand was estimated as 6×10^{-7} M.

We also observed some changes (mainly hypsochromic shifts of the absorption at 335 nm) in the UV-VIS spectra of studied compounds upon addition of various metals, however, they were not characteristic for certain metals and differed only in intensity. Thus UV-VIS spectra cannot be used for metal detection in our case.[†] We have also conducted NMR titration of compound **6** with $Zn(ClO_4)_2$ in CD_3CN, which confirmed the formation of the complexes with L_2M stoichiometry by notable bends of titration curves at 0.5 equiv. (see Online Supplementary Materials).

To sum up, our investigations of 3,3′-disubstituted BINOLs reveal that compounds **4b**,**c** and **7** can be regarded as fluorescent molecular probes for Al^{III} and Cr^{III} cations by substantial increase in the emission intensity in the presence of these metals; these compounds can also be used for Hg^{II} cations detection using hypsochromic shifts of the emission maxima without notable changes in the fluorescence intensity. Macrocycle **6** can be considered as a potential fluorescent chemosensor for Zn^{II} cations based on unique changes in the emission spectrum in the presence of this metal.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.7629.

References

1 M. Formica, V. Fusi, L. Giorgi and M. Micheloni, *Coord. Chem. Rev.*, 2012, **256**, 170; https://doi.org/ 10.1016/j.ccr.2011.09.010.

2 S. Khan, X. Chen, A. Almahri, E. S. Allehyani, F. A. Alhumaydhi, M. M. Ibrahim and S. Ali, *J. Environ. Chem. Eng.*, 2021, **9**, 106381; https://doi.org/10.1016/j.jece.2021.106381.

3 N. Wu, L.-X. Zhao, C.-Y. Jiang, P. Li, Y. Liu, Y. Fu and F. Ye, *J. Mol. Liq.*, 2020, **302**, 112549; https://doi.org/10.1016/j.molliq.2020.112549.

4 H. Nawaz, J. Zhang, W. Tian, K. Jin, R. Jia, T. Yang and J. Zhang, *J. Hazard. Mater.*, 2020, **387**, 121719; https://doi.org/10.1016/j.hazmat.2019.121719.

5 Y.-X. Sun, W.-Y. Han, Z.-P. Deng, Y.-G. Sun, Y.-H. Jia, Y. Sun and S.-Z. Zhang, *Inorg. Chim. Acta*, 2023, **556**, 121643; https://doi.org/10.1016/j.ica.2023.121643.

6 S. Jeon, T.-I. Kim, H. Jin, U. Lee, J. Bae, J. Bouffard and Y. Kim, *J. Am. Chem. Soc.*, 2020, **142**, 9231; https://doi.org/10.1021/jacs.9B13982.

7 F. Yu, Y. Chen, H. Jiang and X. Wang, *Analyst*, 2020, **145**, 6769; https://doi.org/10.1039/D0AN01225D.

8 S. Nian and L. Pu, *J. Org. Chem.*, 2019, **84**, 909; https://doi.org/10.1021/ACS.JOC.8B02793.

9 Y. Wang, J. Tian, F. Zhao, Y. Chen, B. Huo, S. Yu, X. Yu and L. Pu, *Tetrahedron Lett.*, 2021, **66**, 152803; https://doi.org/10.1016/j.tetlet.2020.152803.

10 F. Zhao, Y. Wang, X. Wu, S. Yu, X. Yu and L. Pu, *Chem. – Eur. J.*, 2020, **26**, 7258; https://doi.org/10.1002/chem.202000423.

11 R. Fu, Q.-Y. Zhao, H. Han, W.-L. Li, F.-Y. Chen, C. Tang, W. Zhang, S.-D. Guo, D.-Y. Li, W.-C. Geng, D.-S. Guo and K. Cai, *Angew. Chem., Int. Ed.*, 2023, **62**, 15990; https://doi.org/10.1002/anie.202315990.

12 X. Xu, C. O. Trindle, G. Zhang and L. Pu, *Chem. Commun.*, 2015, **51**, 8469; https://doi.org/ 10.1039/C5CC02457A.

13 O. K. Grigorova, D. I. Gusev, A. D. Averin, O. A. Maloshitskaya and I. P. Beletskaya, *Russ. Chem. Bull.*, 2019, **68**, 848; https://doi.org/10.1007/S11172-019-2495-2.

14 A. D. Averin, O. K. Grigorova, A. S. Malysheva, A. V. Shaferov and I. P. Beletskaya, *Pure Appl. Chem.*, 2020, **92**, 1367; https://doi.org/10.1515/pac-2020-0205.

15 A. V. Shaferov, A. S. Malysheva, A. D. Averin, O. A. Maloshitskaya and I. P. Beletskaya, *Sensors*, 2020, **20**, 3234; https://doi.org/10.3390/s20113234.

16 O. K. Grigorova, A. D. Averin, O. A. Maloshitskaya and I. P. Beletskaya, *Macroheterocycles*, 2017, **10**, 446; https://doi.org/10.6060/mhc170937a.

17 O. K. Grigorova, A. D. Averin, O. A. Maloshitskaya and I. P. Beletskaya, *Macroheterocycles*, 2019, **12**, 312; https://doi.org/10.6060/mhc190337a.

18 R. Dorel, C. P. Grugel and A. M. Haydl, *Angew. Chem., Int. Ed.*, 2019, **58**, 17118; https://doi.org/10.1002/anie.201904795.

19 Z. Fu, X. Cao, G. Hao, Q. Shi and H. Cai, *Chem. Pap.*, 2021, **75**, 831; https://doi.org/10.1007/s11696-020-01308-w.

20 P. Gans, A. Sabatini and A. Vacca, *Talanta*, 1996, **43**, 1739; https://doi.org/10.1016/0039-9140(96)01958-3.

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[†] *Typical experimental procedure for Pd-catalyzed amination.* 3,3′-Dibromo BINOL **1** (133 mg, 0.25 mmol), $Pd(dba)_2$ (12 mg, 8 mol%), and BINAP (14 mg, 9 mol%) were placed in a Schlenk tube (or two-necked flask) equipped with a magnetic stirring bar and a reflux condenser and flushed with dry argon. Dry dioxane (2.5 ml for compounds **3a**–**c**, 12 ml for compound **5**) was added under an argon flow, the mixture was stirred for 3 min, and then amine (0.75 mmol for compounds **3a**–**c**, 0.25 mmol for compound **5**) and sodium *tert*-butoxide (72 mg, 0.75 mmol) were added. The reaction mixture was refluxed for 36 h. After the completion of the reaction, the solvent was evaporated and the resulting dark viscous oily residue was chromatographed on silica gel using CH_2Cl_2–MeOH mixtures (0 → 30% MeOH) as the eluents. After evaporation of the eluent, target compounds were obtained as light yellow viscous oils.

Procedure for the spectrophotometric and spectrofluorimetric detection of the metal cations. Solutions of compounds **4b**,**c**, **5**, **6**, **7** in the UHPLC grade acetonitrile were placed in a spectrofluorimetric cuvette, and UV and fluorescence spectra were recorded. Then an acetonitrile solution of a metal perchlorate (Li^I, Na^I, Mg^{II}, Ca^{II}, Ba^{II}, Al^{III}, Mn^{II}, Fe^{II}, Cr^{III}, Ni^{II}, Co^{II}, Cu^{II}, Zn^{II}, Cd^{II}, Pb^{II}, Ag^I, Hg^{II}), nitrate (Ga^{III}, In^{III}, Y^{III}) or acetate (K^I) ($C = 0.01$ M) was added stepwise (to achieve 1, 2, 5, and 10 equiv.) and UV-VIS and fluorescence spectra were recorded after each addition.