Макрогетероциклы
http://macroheterocycles.isuct.ru

DOI: 10.6060/mhc170937a

Chiral BINAM–Containing Macrocycles with Endocyclic 1,8– and 1,5–Disubstituted Anthraquinone Structural Fragments

Olga K. Grigorova, Alexei D. Averin,@ Olga A. Maloshitskaya, and Irina P. Beletskaya

The article is dedicated to the anniversary of Academician Professor A. Yu. Tsivadze. Authors cordially congratulate the jubilee and wish him all the best and a plenty of new interesting discoveries!

Lomonosov Moscow State University, Department of Chemistry, 119991 Moscow, Russia
@Corresponding author E-mail: alexaveron@yandex.ru

A series of nitrogen- and oxygen-containing macrocycles with endocyclic (S)-2,2'-diamino-1,1'-binaphthalene (BINAM) moieties and 1,8- or 1,5-diaminoanthraquinone chromophores was synthesized using Pd(0)-catalyzed amination with a number of oxadiamines via 2,2'-bis(chloroanthraquinon-1-yl) BINAM derivatives. The dependence of the compounds yields on the structure of starting reagents was established. One exemplary macrocycle was tested as an enantioselective detector for a number of chiral aminoalcohols and 1,2-diphenylethylenediamine and was shown to be able to distinguish between enantiomers of leucinol, 2-amino-1-propanol, 2-amino-1,2-diphenylethanol, and 1,2-diphenylethylenediamine by an increase in the emission in the presence of one enantiomer. It was also shown to detect In(III) among 20 metals tested by emission enhancement.

Keywords: Macrocycles, chirality, anthraquinone, chemosensors, catalysis, amination.

Хиральные BINAM–содержащие макроциклы с эндоциклическими 1,8– и 1,5–дизамещенными структурными фрагментами антрахинона

О. К. Григорова, А. Д. Аверин,@ О. А. Малошицкая, И. П. Белецкая

Московский государственный университет им. М.В. Ломоносова, 119991 Москва, Россия
@E-mail: alexaveron@yandex.ru

С использованием Pd(0)-катализируемого аминирования 2,2'-бис(хлороантрахинон-1-ил) производных BINAM рядом оксадиаминов получены азот- и кислородсодержащие макроциклы с эндоциклическими фрагментами (S)-2,2'-диамино-1,1'-бинафталина и с 1,8- или 1,5-диаминоантрахиноновыми хромофорами. Установлена зависимость выходов продуктов от строения исходных соединений. Один из синтезированных макроциклов протестирован в качестве энантиоселективного детектора для ряда оптически активных аминоспиртов и 1,2-дифенилэтилендиамина. Показано, что с его помощью возможно различение энантиомеров лейцинола, 2-амино-1-пропанола, 2-амино-1,2-дифенилэтанола и 1,2-дифенилэтилендиамина посредством увеличения интенсивности флуоресценции в присутствии одного из энантиомеров. Также показано, что данный макроцикл детектирует катионы индия(III) из общего количества 20 протестированных катионов переходных и непереходных металлов.

Ключевые слова: Макроциклы, хиральность, антрахинон, хемосенсоры, катализ, аминирование.

Introduction

The role of individual enantiomers in various fields of science and technology, first of all in the production of drugs, agrochemicals, chiral catalysts, in biological investigations and environmental control has been intensively increasing. At present time there are many methods of detecting enantiomers, among them liquid and gas phase chromatography, nmR, ESI mass spectrometry, colorimetric methods. The use of the fluorescence to produce the analytical signal allows an increase in sensitivity, selectivity and accuracy of the method. Chiral macrocyclic compounds bearing fluorescent moieties are capable of a better binding of polar organic molecules and ions due to a number of coordinating sites and possible template effect what leads to a more selective response of the chemosensor. Beginning from 1978, when the effect of chiral amines on the fluorescent properties of 1,1'-bi-2,2'-naphthol (BINOL) was established,[1] systematic studies of this valuable molecule combining inherent *C2*-chirality and fluorescent properties resulted in the construction of a variety of enantioselective detectors on its basis. Up to date several general reviews have been already published describing various types of fluorescent chemosensors,[2-5] in some works the application of macrocycles[6,7] or supramolecular, organometallic and nanosize systems[7,8] has been considered.

One of the first chiral macrocyclic systems reported were those containing two BINOL and two chiral 1,2-diaminocyclohexane moieties.[9] BINOL was also combined with different macrocycles, *e.g.* for tartrate ions detection *bis*(triazacyclononanyl) derivative of BINOL was used,[10] this moiety was introduced in the side chain of calix[4] crown ether[11] and in a chiral crown ether which was used for recognition of chiral amines and amino acids.[12] BINOL-derived crown ethers containing additional dinitrophenyl chromophore[13] or exocyclic anthracene fluorophore[14] were reported. The latter compound can be used both for detecting Hg(II), Cu(II) и Zn(II) and chiral alkylammonium salts. Two BINOLs and two face-to-face organized porphyrin moieties were combined in one cryptand.[15] Quite recently BINOL-containing macrocycle for amino acids detection was proposed,[16] another macrocycle with this chiral fluorophore was invented for carboxylates enantiomeric excess determination.[17] A macrocyclic chemosensor combining BINOL and deoxycholic acid moieties gives a selective response to Hg(II) coordination, and the resulting complex can be used for amino acids enantiomers detection.[18]

It should be noted that the nitrogen-containing analogue of BINOL, namely 2,2'-diamino-1,1'-binaphthalene (BINAM) was once studied as a potential fluorescent enantioselective chemosensor and even demonstrated a better efficiency in α-phenylethylamine determination.[19] However, it was not further developed unlike BINOL, and there are only scarce notes in the literature about its application as chemosensor. It was attempted to detect tryptophan enantiomers,[20] BINAM with two chiral thiourea side arms was used for mandelic acid sensing,[21] chiral polymers containing BINOL and BINAM were used for phenylalaninol detection by fluorescence enhancement.[22] These facts strongly support the necessity to further investigate BINAM derivatives as prospective enantioselective detectors. In this work the emphasis is made on the synthesis of the macrocyclic derivatives of BINAM with endocyclic diaminoanthraquinone moieties known as potent chromophores. The combination of fluorophore and chromophore groups in one molecule can be regarded as a useful approach allowing bimodal sensing of analytes.

Experimental

NMR spectra were registered using Bruker Avance 400 spectrometer, MALDI-TOF spectra were obtained with Bruker Autoflex II spectrometer using 1,8,9-trihydroxyanthracene as matrix and PEGs as internal standards. UV-vis spectra were recorded with Cary 60 spectrophotometer in MeCN, spectra of fluorescence were obtained with Hitachi 2700 spectrofluorometer in MeCN. (*S*)-BINAM, 1,8- and 1,5-dichloroanthraquinones, dioxa- and trioxadiamines, *rac*-BINAP and DavePhos ligands, cesium carbonate, were purchased from Aldrich and used without further purification, $Pd(dba)_2$ was synthesized according to the method described.[23] Dioxane was distilled over NaOH followed by the distillation over sodium under argon, petroleum ether, dichloromethane and methanol were used freshly distilled.

*Typical procedure for the synthesis of 2,2'-bis(8-anthraquinon-1-yl) derivatives of (S)-BINAM **3** and **9**.* A two-neck flask equipped with a condenser and magnetic stirrer, flushed with dry argon, was charged with $Pd(dba)_2$ (23 mg, 4 mol%), BINAP (28 mg, 4.5 mol%), (*S*)-BINAM (284 mg, 1 mmol), 1,8- or 1,5-dichloroanthraquinone (609 mg, 2.2 mol), absolute dioxane (10 ml) was added followed by Cs_2CO_3 (1.304 g, 4 mmol), the reaction mixture was stirred at reflux for 8 h. After cooling the reaction mixture down to room temperature, the reaction mixture was diluted with CH_2Cl_2 (10 ml), the solution was filtered, evaporated *in vacuo*, dissolved in CH_2Cl_2 (10 ml), washed with an equal volume of water and dried over molecular sieves. After evaporating the solvent, target compounds were isolated by column chromatography as deep-red solids using a sequence of eluents: petroleum ether/CH_2Cl_2 4:1 – 1:4, CH_2Cl_2.

*8,8'-(1,1'-Binaphthyl-2,2'-diylbis(azanediyl))bis(1-chloroanthracene-9,10-dione) (**3**)*. Eluent: petroleum ether/CH_2Cl_2 (1:2). Yield 153 mg (20 %). M.p. 179–181 °C. (MALDI-TOF) found: 765.1402. $C_{48}H_{27}Cl_2N_2O_4$ requires 765.1348 $[M+H]^+$. ^{1}H NMR δ_H ppm ($CDCl_3$, 298 K): 7.30 (2H, t, ^3J=7.9 Hz), 7.33–7.42 (6H, m), 7.46 (2H, t, ^3J=7.1 Hz), 7.51 (2H, d, ^3J=7.5 Hz), 7.54 (2H, d, ^3J=8.0 Hz), 7.79 (4H, d, ^3J=8.3 Hz), 7.94 (2H, d, ^3J=8.1 Hz), 8.00 (2H, d, ^3J=8.8 Hz), 8.04 (2H, d, ^3J=7.7 Hz), 10.77 (2H, s). ^{13}C NMR δ_C ppm ($CDCl_3$, 298 K): 115.9 (2C), 117.4 (2CH), 121.1 (2CH), 121.9 (2CH), 125.1 (2CH), 125.3 (2CH), 125.6 (2C), 126.0 (2CH), 127.2 (2CH), 128.3 (2CH), 129.5 (2CH), 130.5 (2C), 131.3 (2C), 132.5 (2CH), 133.2 (2C), 133.8 (2C), 134.2 (2CH), 134.4 (2C), 135.1 (2C), 136.3 (2C), 137.5 (2CH), 147.4 (2C), 182.3 (2C), 183.5 (2C).

*1,1'-[(9,10-Dioxoanthracene-1,8-diyl)bis(imino-1,1'-binaphthalene-2',2-diylimino)]bis(8-chloroanthra-9,10-quinone) (**4**)* was obtained as the second product in the synthesis of compound **3**. Eluent: petroleum ether/CH_2Cl_2 (1:4). Yield 104 mg (16 %). (MALDI-TOF) found: 1253.2946. $C_{82}H_{47}Cl_2N_4O_6$ requires 1253.2873 $[M+H]^+$. ^{1}H NMR δ_H ppm ($CDCl_3$, 298 K): 7.08 (2H, dd, ^3J=8.3 Hz, ^4J=1.1 Hz), 7.23–7.46 (14H, m), 7.48 (2H, dd, ^3J=7.5 Hz, ^4J=1.0 Hz), 7.53–7.57 (4H, m), 7.59 (2H, dd, ^3J=7.8 Hz, ^4J=1.1 Hz), 7.62 (2H, dd, ^3J=7.5 Hz, ^4J=1.1 Hz), 7.74 (2H, d, ^3J=9.1 Hz), 7.76 (2H, d, ^3J=9.1 Hz), 7.81 (2H, d, ^3J=8.8 Hz), 7.93 (2H, d, ^3J=8.3 Hz), 7.97–8.03 (6H, m), 8.07 (2H, dd, ^3J=7.7 Hz, ^4J=1.3 Hz), 10.69 (2H, s), 10.77 (2H, s).

*5,5'-(1,1'-Binaphthyl-2,2'-diylbis(azanediyl))bis(1-chloroanthracene-9,10-dione) (**9**)*. Eluent: petroleum ether/CH_2Cl_2 (1:2). Yield 219 mg (29 %). M.p. 193 °C (decomp.) (MALDI-TOF)

found: 765.1387. $C_{48}H_{27}Cl_2N_2O_4$ requires 765.1348 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 7.17 (2H, t, ^3J=8.0 Hz), 7.30–7.40 (8H, m), 7.45–7.49 (4H, m), 7.52 (2H, d, ^3J=8.3 Hz), 7.73 (2H, d, ^3J=8.7 Hz), 7.85 (2H, d, ^3J=7.8 Hz), 7.94 (2H, d, ^3J=8.2 Hz), 7.99 (2H, d, ^3J=8.8 Hz), 10.77 (2H, s). ^{13}C NMR δ_c ppm ($CDCl_3$, 298 K): 113.7 (2C), 118.1 (2CH), 119.5 (2CH), 122.7 (2CH), 125.3 (2CH), 125.5 (2CH), 126.0 (2CH), 126.3 (2C), 127.2 (2CH), 128.3 (2CH), 128.8 (2C), 129.4 (2CH), 131.3 (2C), 133.1 (2CH), 133.9 (2C), 134.2 (2C), 134.7 (2CH), 135.1 (2C), 136.0 (2C), 136.4 (2CH), 136.9 (2C), 147.7 (2C), 181.7 (2C), 182.9 (2C).

*1,1'-[(9,10-Dioxoanthracene-1,5-diyl)bis(imino-1,1'-binaphthalene-2',2-diylimino)]bis(5-chloroanthra-9,10-quinone) (**10**)* was obtained as the second product in the synthesis of compound **9**. Eluent: petroleum ether/CH_2Cl_2 (1:2). Yield 152 mg (15 %). (MALDI-TOF) found: 1253.2781. $C_{82}H_{47}Cl_2N_4O_6$ requires 1253.2873 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 7.02 (2H, t, ^3J=8.0 Hz), 7.12 (2H, t, ^3J=8.1 Hz), 7.17 (2H, d, ^3J=7.3 Hz), 7.27–7.36 (10H, m), 7.41–7.51 (10H, m), 7.59 (2H, d, ^3J=8.0 Hz), 7.68 (4H, d, ^3J=8.6 Hz), 7.89 (2H, d, ^3J=7.8 Hz), 7.91–8.00 (8H, m), 10.71 (2H, s), 10.81 (2H, s). ^{13}C NMR δ_c ppm ($CDCl_3$, 298 K): 113.8 (2C), 114.3 (2C), 117.2 (2CH), 118.1 (2CH), 118.9 (2CH), 119.7 (2CH), 122.8 (2CH), 122.9 (2CH), 125.3 (2CH), 125.4 (2CH), 125.5 (2CH), 126.1 (2C), 126.2 (2CH), 126.6 (2C), 127.1 (4CH), 127.2 (2C), 128.3 (2CH), 128.4 (2CH), 129.1 (2C), 129.3 (2CH), 129.4 (2CH), 129.5 (2C), 131.3 (2C), 131.5 (2C), 133.2 (2CH), 133.9 (2CH), 134.0 (2CH), 134.3 (2C), 134.8 (2CH), 135.2 (2C), 135.4 (2C), 136.0 (2C), 136.4 (2CH), 136.5 (2C), 137.1 (2C), 147.6 (2C), 147.9 (2C), 182.0 (2C), 183.0 (2C), 184.5 (2C).

*Typical procedure for the synthesis of macrocycles **6a-c, 11a-c and 13***. A two-neck flask equipped with a condenser and magnetic stirrer, flushed with dry argon, was charged with $Pd(dba)_2$ (16 mol%), BINAP (18 mol%), BINAM derivative **3** or **9** (1 equiv.), absolute dioxane was added followed by appropriate oxadiamine **5a-c** (1 equiv.) and Cs_2CO_3 (4 equiv.), the reaction mixture was stirred at reflux for 40 h. After cooling the reaction mixture down to room temperature, the reaction mixture was diluted with CH_2Cl_2 (5 ml), the solution was filtered, evaporated *in vacuo*, dissolved in CH_2Cl_2 (5 ml), washed with an equal volume of water and dried over molecular sieves. After evaporating the solvent, target compounds were isolated by column chromatography as deep-red solids using a sequence of eluents: CH_2Cl_2, CH_2Cl_2/MeOH 200:1 – 50:1.

*11,21,22,23,24,26,27,28,29,31,32,33,34,44-Tetradecahydro-15,17:38,40-dimethanotetrabenzo-[f,i,q,t]dinaphtho[1,2-n:2',1'-l][1,26,5,11,16,22]dioxatetraazacyclotriacontine-16,39,47,48-tetrone (**6a**)*. Obtained from compound **3** (77 mg, 0.1 mmol), dioxadiamine **5a** (20 mg, 0.1 mmol) in the presence of $Pd(dba)_2$ (10 mg, 16 mol%), BINAP (12 mg, 18 mol%) in 2.5 ml dioxane. Eluent: CH_2Cl_2/MeOH (200:1). Yield 36 mg (40 %). M.p. 172–174 °C. (MALDI-TOF) found: 897.3604. $C_{58}H_{49}N_4O_6$ requires 897.3652 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 1.14 (4H, br. s), 1.72–1.82 (2H, m), 1.95–2.04 (2H, m), 2.84–2.90 (2H, m), 2.90–2.96 (2H, m), 3.18–3.35 (8H, m), 7.15 (2H, ddd, ^3J=8.2 Hz, ^3J=7.6 Hz, ^4J=1.1 Hz), 7.23 (2H, d, ^3J=8.3 Hz), 7.25 (2H, d, ^3J=8.6 Hz), 7.29–7.33 (2H, m), 7.37–7.43 (2H, m), 7.48–7.52 (2H, m), 7.62 (2H, d, ^3J=7.3 Hz), 7.65 (2H, d, ^3J=7.3 Hz), 7.72 (2H, d, ^3J=8.0 Hz), 7.81–7.85 (4H, m), 8.03 (2H, d, ^3J=8.8 Hz), 9.50 (2H, br. s), 11.26 (2H, s). ^{13}C NMR δ_c ppm ($CDCl_3$, 298 K): 24.8 ($2CH_2$), 27.8 ($2CH_2$), 40.2 ($2CH_2$), 66.4 ($2CH_2$), 68.7 ($2CH_2$), 114.5 (2C), 115.7 (2CH), 115.9 (2C), 117.6 (2CH), 118.9 (2CH), 120.0 (2CH), 121.7 (2CH), 124.9 (2C), 125.0 (2CH), 125.3 (2CH), 126.9 (2CH), 128.1 (2CH), 129.4 (2CH), 131.0 (2CH), 133.5 (2CH), 133.7 (2C), 133.8 (2C), 134.1 (2C), 134.5 (2CH), 137.2 (2C), 147.2 (2C), 150.5 (2C), 183.8 (2C), 188.0 (2C).

*11,22,23,25,26,28,29,32,33,43-Decahydro-15,17:37,39-dimethanotetrabenzo[k,n,v,y]dinaphtho[1,2-s:2',1'-q][1,4,7,10,16,21,27]trioxatetraazacyclononacosine-16,38,46,47(21H,31H)-tetrone (**6b**)*. Obtained from compound **3** (77 mg, 0.1 mmol), trioxadiamine **5b** (19 mg, 0.1 mmol) in the presence of $Pd(dba)_2$ (10 mg, 16 mol%), BINAP (12 mg, 18 mol%) in 2.5 ml dioxane. Eluent: CH_2Cl_2/MeOH (200:1). Yield 20 mg (22 %). M.p. 150 °C (decomp.) (MALDI-TOF) found: 885.3343. $C_{56}H_{45}N_4O_7$ requires 885.3288 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 3.21–3.50 (12H, m), 3.60–3.65 (4H, m), 7.04 (2H, d, ^3J=8.5 Hz), 7.06–7.11 (2H, m), 7.15–7.20 (2H, m), 7.25 (2H, d, ^3J=8.3 Hz), 7.33–7.37 (2H, m), 7.39 (2H, d, ^3J=8.6 Hz), 7.41–7.47 (4H, m), 7.52 (2H, d, ^3J=7.2 Hz), 7.73 (2H, d, ^3J=8.7 Hz), 7.82 (2H, d, ^3J=8.1 Hz), 7.93 (2H, d, ^3J=8.8 Hz), 9.50 (2H, br. s), 11.21 (2H, s). ^{13}C NMR δ_c ppm ($CDCl_3$, 298 K): 43.0 ($2CH_2$), 69.3 ($2CH_2$), 70.7 ($2CH_2$), 71.1 ($2CH_2$), 114.5 (2C), 115.2 (2CH), 115.9 (2C), 117.3 (2CH), 118.3 (2CH), 120.6 (2CH), 123.4 (2CH), 125.0 (2CH), 125.7 (2C), 125.8 (2CH), 126.6 (2CH), 128.0 (2CH), 129.4 (2CH), 131.2 (2C), 132.9 (2CH), 133.7 (4C), 133.8 (2C), 134.1 (2CH), 137.2 (2C), 147.5 (2C), 151.1 (2C), 184.1 (2C), 188.0 (2C).

*Cyclodimer **7b***. Obtained as the second product in the synthesis of compound **6b**. Eluent: CH_2Cl_2/MeOH (100:1). Yield 4 mg (4.5 %). (MALDI-TOF) found: 1769.61. $C_{112}H_{89}N_8O_{14}$ requires 1769.65 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 3.32 (8H, t, ^3J=5.8 Hz), 3.50–3.62 (24H, m), 6.87 (4H, d, ^3J=8.3 Hz), 6.95 (4H, t, ^3J=8.0 Hz), 7.23 (4H, d, ^3J=8.5 Hz), 7.29–7.44 (16H, m), 7.61 (4H, d, ^3J=8.6 Hz), 7.80–7.85 (8H, m), 10.84 (4H, s), four NH protons were not unambiguously assigned.

*11,21,22,23,24,26,27,29,30,32,33,34,35,45-Tetradecahydro-15,17:39,41-dimethanotetrabenzo[l,o,w,z]-dinaphtho[1,2-t:2',1'-r][1,4,7,11,17,22,28]trioxatetraazacyclohentriacontine-16,40,48,49-tetrone (**6c**)*. Obtained from compound **3** (77 mg, 0.1 mmol), trioxadiamine **5c** (22 mg, 0.1 mmol) in the presence of $Pd(dba)_2$ (10 mg, 16 mol%), BINAP (12 mg, 18 mol%) in 2.5 ml dioxane. Eluent: CH_2Cl_2/MeOH (200:1). Yield 34 mg (37 %). M.p. 145 °C (decomp.) UV-Vis (CH_3CN): λ_{max} nm (lgε): 322 (4.43), 352 (4.35), 556 (4.30). (MALDI-TOF) found: 913.3665. $C_{58}H_{49}N_4O_7$ requires 913.3601 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 1.66–1.75 (2H, br. m), 1.91–2.00 (2H, br. m), 2.98–3.05 (2H, m), 3.16 (4H, br. s), 3.18–3.38 (10H, m), 7.20–7.25 (4H, m), 7.39 (2H, ddd, ^3J=8.1 Hz, ^3J=6.1 Hz, ^4J=2.3 Hz), 7.42–7.48 (4H, m), 7.57 (2H, t, ^3J=8.0 Hz), 7.63–7.68 (4H, m), 7.77–7.82 (4H, m), 7.87 (92H, d, ^3J=8.2 Hz), 8.01 (2H, d, ^3J=8.8 Hz), 11.21 (2H, s), two NH protons were not unambiguously assigned. ^{13}C NMR δ_c ppm ($CDCl_3$, 298 K): 27.9 (2C), 43.5 br (2C), 67.9 (2C), 70.0 (2C), 70.1 (2C), 115.8 (2C), 116.9 br (2C), 118.3 (2C), 118.7 br (2C), 121.4 (2C), 121.8 br (2C), 122.0 (2C), 125.3 (2C), 125.5 (2C), 125.9 (2C), 127.1 (2C), 128.1 (2C), 129.6 (2C), 131.3 (2C), 133.7 (2C), 133.9 (2C), 134.1 (2C), 134.2 br (2C), 134.7 (2C), 136.9 (2C), 147.5 br (2C), 147.9 (2C), 183.2 (2C), 187.7 (2C) (some signals are substantially broadened, thus tertiary and quaternary carbons are not indicated).

*Macrocycle **11a***. Obtained from compound **9** (135 mg, 0.17 mmol), dioxadiamine **5a** (35 mg, 0.17 mmol) in the presence of $Pd(dba)_2$ (16 mg, 16 mol%), BINAP (20 mg, 18 mol%) in 4.5 ml dioxane. Eluent: CH_2Cl_2/MeOH (200:1). Yield 27 mg (18 %). (MALDI-TOF) found: 897.3728. $C_{58}H_{49}N_4O_6$ requires 897.3652 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 1.93–2.00 (4H, br. m), 2.00–2.07 (4H, br. m), 3.44–3.60 (6H, m), 3.61–3.68 (2H, m), 3.69–3.76 (4H, m), 6.55 (2H, t, ^3J=8.0 Hz), 6.94 (2H, d, ^3J=8.6 Hz), 6.99 (2H, d, ^3J=8.5 Hz), 7.12 (4H, d, ^3J=8.0 Hz), 7.20–7.26 (4H, m), 7.40 (2H, t, ^3J=8.0 Hz), 7.43 (2H, t, ^3J=7.7 Hz), 7.70 (2H, d, ^3J=8.7 Hz), 7.96 (2H, d, ^3J=8.1 Hz), 8.00 (2H, d, ^3J=8.8 Hz), 9.92 (2H, t, ^3J=4.9 Hz) 10.82 (2H, s). ^{13}C NMR δ_c ppm ($CDCl_3$, 298 K): 26.1 ($2CH_2$), 27.9 ($2CH_2$), 40.5 ($2CH_2$), 68.5 ($2CH_2$), 71.2 ($2CH_2$), 112.8 (2C), 114.4 (2CH), 116.4 (2CH), 116.6 (2CH), 117.4 (2CH), 117.6 (2C), 124.5 (2CH), 124.8 (2C), 125.2 (2CH), 126.6 (2CH), 126.7 (2CH), 128.1 (2CH), 128.9 (2CH), 131.4 (2C), 133.5 (2CH), 134.7 (2CH), 134.9 (2C), 135.9 (2C), 136.0 (2C), 136.3 (2C), 147.9 (2C), 151.1 (2C), 184.0 (2C), 185.7 (2C).

*Macrocycle **11b***. Obtained from compound **9** (77 mg, 0.1 mmol), trioxadiamine **5b** (19 mg, 0.1 mmol) in the presence of $Pd(dba)_2$ (10 mg, 16 mol%), BINAP (12 mg, 18 mol%) in 2.5 ml dioxane. Eluent: CH_2Cl_2/MeOH (200:1). Yield 34 mg (38 %).

M.p. 184–186 °C. (MALDI-TOF) found: 885.3329. $C_{56}H_{45}N_4O_7$ requires 885.3288 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 3.42–3.48 (2H, br. m), 3.56–3.69 (2H, br. m), 3.80–3.92 (8H, m), 4.05–4.10 (4H, m), 6.45 (2H, dd, ^3J=8.3 Hz, ^3J=7.6 Hz), 6.94 (2H, d, ^3J=8.3 Hz), 6.95 (2H, d, ^3J=8.6 Hz), 7.02 (2H, dd, ^3J=7.5 Hz, ^4J=1.0 Hz), 7.11 (92H, dd, ^3J=8.6 Hz, ^4J=0.9 Hz), 7.20 (2H, ddd, ^3J=8.3 Hz, ^3J=6.8 Hz, ^4J=1.3 Hz), 7.26 (2H, dd, ^3J=7.3 Hz, ^4J=0.9 Hz), 7.43 (2H, dd, ^3J=8.7 Hz, ^3J=7.7 Hz), 7.45 (2H, ddd, ^3J=8.0 Hz, ^3J=6.8 Hz, ^4J=1.0 Hz), 7.69 (2H, ^3J=8.7 Hz), 7.96 (2H, ^3J=8.1 Hz), 7.99 (2H, d, ^3J=8.8 Hz), 9.97 (2H, br. s,), 10.74 (2H, s). ^{13}C NMR δ_c ppm ($CDCl_3$, 298 K): 43.0 ($2CH_2$), 69.3 ($2CH_2$), 71.1 ($2CH_2$), 72.3 ($2CH_2$), 113.2 (2C), 114.1 (2C), 114.7 (2CH), 116.4 (4CH), 117.4 (2CH), 125.0 (2C), 125.1 (2CH), 125.2 (2CH), 126.6 (2CH), 126.9 (2CH), 128.1 (2CH), 128.8 (2CH), 131.4 (2C), 133.6 (2CH), 134.8 (2CH), 135.1 (2C), 135.8 (2C), 136.1 (4C), 147.9 (2C), 150.9 (2C), 184.2 (2C), 185.6 (2C).

Cyclodimer ***12b***. Obtained as the second product in the synthesis of compound **11b**. Eluent: CH_2Cl_2/MeOH (100:1). Yield 6 mg (7 %). (MALDI-TOF) found: 1769.68. $C_{112}H_{89}N_8O_{14}$ requires 1769.65 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 3.36 (8H, t, ^3J=5.4 Hz), 3.68–3.72 (8H, m), 3.72–3.77 (16H, m), 6.85 (4H, d, ^3J=8.5 Hz), 6.89 (4H, t, ^3J=8.1 Hz), 7.17 (4H, d, ^3J=8.5 Hz), 7.21 (4H, d, ^3J=7.1 Hz), 7.25–7.37 (16H, m), 7.50 (4H, t, ^3J=7.8 Hz), 7.64 (4H, d, ^3J=8.7 Hz), 7.94 (4H, d, ^3J=8.2 Hz), 7.96 (4H, d, $^3J_{obs}$=6.8 Hz), 10.79 (4H, s), four NH protons were not unambiguously assigned.

Macrocycle ***11c***. Obtained from compound **9** (65 mg, 0.08 mmol), trioxadiamine **5c** (19 mg, 0.08 mmol) in the presence of $Pd(dba)_2$ (8 mg, 16 mol%), BINAP (10 mg, 18 mol%) in 2 ml dioxane. Eluent: CH_2Cl_2/MeOH (100:1). Yield 12 mg (16 %). M. p. 175–177 °C. (MALDI-TOF) found: 913.3543. $C_{58}H_{49}N_4O_7$ requires 913.3601 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 2.04–2.12 (2H, br. m), 2.30–2.38 (2H, br. m), 3.30–3.55 (4H, br. m), 3.56–3.72 (4H, br. m), 3.75–3.88 (4H, br. m), 3.91–3.98 (2H, m), 3.98–4.05 (2H, m), 6.67 (2H, t, ^3J=7.9 Hz), 7.07 (2H, d, ^3J=8.5 Hz), 7.11 (2H, d, ^3J=8.2 Hz), 7.22 (2H, d, ^3J=7.2 Hz), 7.25–7.52 (10H, m), 7.66 (2H, d, ^3J=8.7 Hz), 7.98 (2H, d, ^3J=7.8 Hz), 8.03 (2H, d, ^3J=8.9 Hz), 10.86 (2H, s), two NH protons were not unambiguously assigned. ^{13}C NMR δ_c ppm ($CDCl_3$, 298 K): 28.2 (2C), 43.0 br. (2C), 70.3 (2C), 70.5 (2C), 70.8 (2C), 115.6 (2C), 117.0 (2C), 117.6 (2C), 118.0 (2C), 118.8 (2C), 123.9 (2C), 125.2 (2C), 126.5 (2C), 126.8 (2C), 128.2 (2C), 128.3 (2C), 129.1 (2C), 131.3 (2C), 133.7 (2C), 134.9 (2C), 135.2 (2C), 135.6 (2C), 135.9 (2C), 136.4 (2C), 147.9 (2C), 150.0 br (2C), 184.2 (2C), 185.3 (2C) (some signals are substantially broadened, thus tertiary and quaternary carbons are not indicated).

Macrocycle ***13***. Obtained from compound **10** (147 mg, 0.12 mmol), trioxadiamine **5c** (26 mg, 0.12 mmol) in the presence of $Pd(dba)_2$ (11mg, 16 mol%), BINAP (13 mg, 18 mol%) in 3 ml dioxane. Eluent: CH_2Cl_2/MeOH (120:1). Yield 21 mg (12 %). M. p. 195–196 °C. (MALDI-TOF) found: 1401.5038. $C_{92}H_{69}N_6O_9$ requires 1401.5126 $[M+H]^+$. ^1H NMR δ_H ppm ($CDCl_3$, 298 K): 2.03 (4H, br. s), 3.43 (4H, br. s), 3.71 (8H, br. s), 3.77 (4H, br. s), 6.91 (2H, d, ^3J=7.6 Hz), 7.00 (2H, d, ^3J=8.7 Hz), 7.12–7.18 (4H, m), 7.19–7.52 (18H, m), 7.46 (2H, d, ^3J=9.1 Hz), 7.50 (2H, d, ^3J=7.2 Hz), 7.69 (2H, d, ^3J=8.5 Hz), 7.72 (2H, d, ^3J=9.1 Hz), 7.88 (2H, d, ^3J=7.2 Hz), 7.93 (2H, d, ^3J=8.8 Hz), 7.97 (4H, d, ^3J=7.5 Hz), 9.78 (2H, br. s), 10.81 (2H, s), 10.84 (2H, s). ^{13}C NMR δ_c ppm ($CDCl_3$, 298 K): 28.9 (2C), 40.0 (2C), 67.1 (2C), 68.9 (2C), 70.7 (2C), 114.4 (2C), 114.9 (2C), 116.3 (2C), 117.1 (2C), 117.3 (2C), 118.8 (2C), 119.5 (2C), 122.8 (2C), 123.0 (2C), 125.1 (2C), 125.3 (2C), 125.5 (2C), 125.6 (2C), 126.9 (2C), 127.1 (2C), 128.2 (2C), 128.3 (4C), 129.2 (4C), 131.2 (2C), 131.3 (2C), 134.0 (2C), 134.1 (2C), 134.2 (2C), 134.9 (2C), 135.5 (2C), 135.8 (2C), 136.0 (2C), 136.4 (2C), 136.6 (2C), 136.9 (2C), 147.6 (2C), 147.8 (2C), 151.3 (2C), 184.6 (2C), 184.8 (2C), 185.2 (2C) (six quaternary carbon atoms were not unambiguously assigned, some signals are substantially broadened, thus tertiary and quaternary carbons are not indicated).

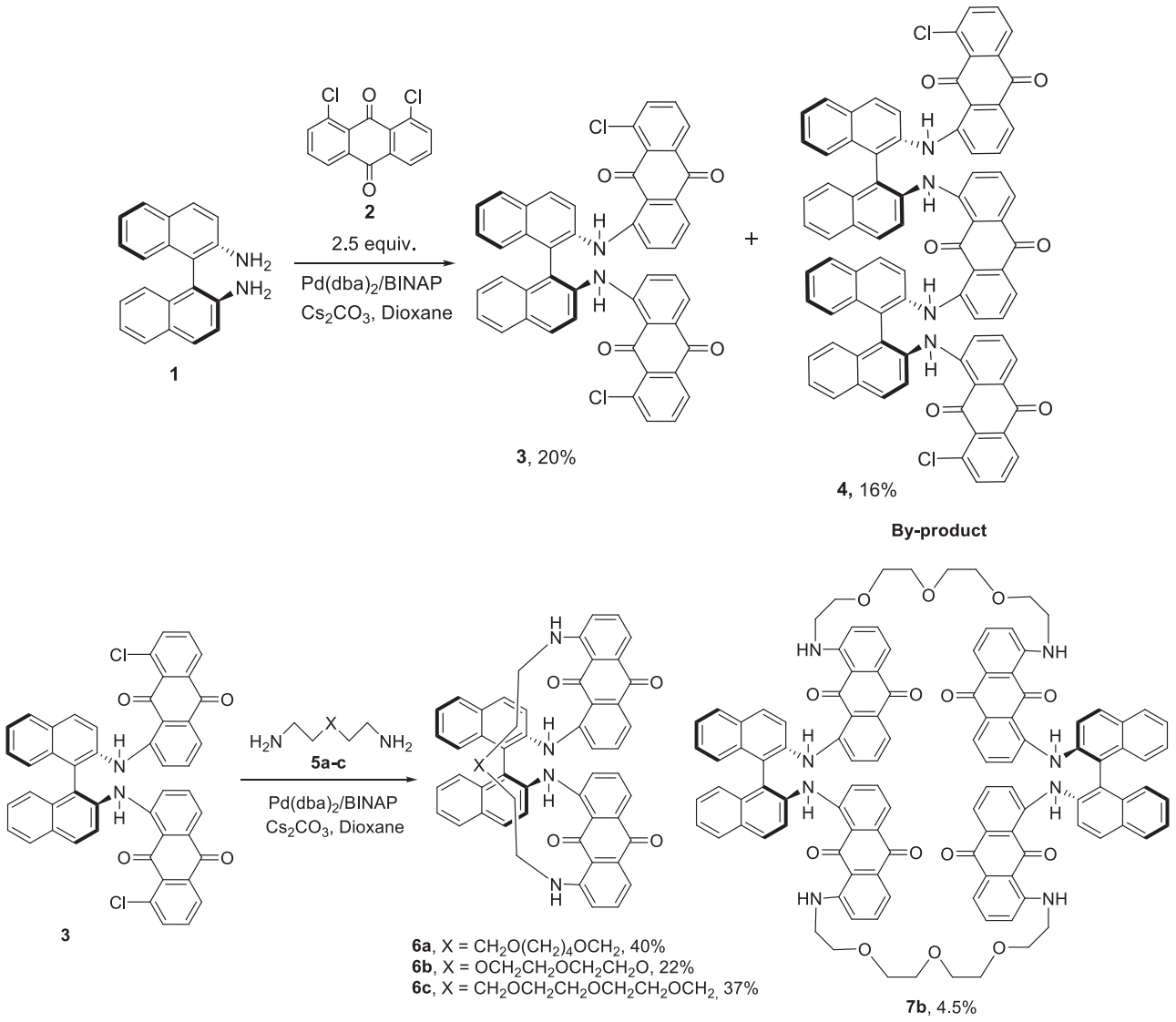
The investigations of the spectral properties of the macrocycle **6c** in the presence of different chiral molecules were carried out in a following manner: 3 ml of the solution of **6c** (*C*=8.33 μM) in MeCN was placed in a spectrofluorimetric cuvette, solutions of appropriate chiral compounds (*S*)- and (*R*)-leucinol, (*S*)- and (*R*)-*tert*-leucinol, (*S*)- and (*R*)-phenylglycinol, (*S*)- and (*R*)-2-amino-1-propanol, (*S*)- and (*R*)-2-amino-1-butanol, (*1S,2R*)- and (*1R,2S*)-2-amino-1,2-diphenylethanol, (*1S,2S*)- and (*1R,2R*)-1,2-diphenylethylenediamine) in MeCN (*C*=0.2 M) were added sequentially (100, 200, 500, 1000 equiv.) and after each addition UV-Vis and fluorescence spectra were recorded. Also the solutions of Li(I), Na(I), K(I), Mg(II), Ca(II), Ba(II), Al(III), Fe(II), Mn(II), Co(II), Ni(II), Cr(III), Cu(II), Zn(II), Cd(II), Pb(II), Hg(II) perchlorates and Ga(III), In(III), Y(III) nitrates in MeCN (*C*=0.01 M) were added sequentially to the solution of macrocycle **6c** in MeCN (1, 2, and 5 equiv.) and after each addition UV-Vis and fluorescence spectra were recorded.

Results and Discussion

In our recent work we have established the possibility to form *N*- and *O*-macrocyclic compounds containing a *C2*-chiral 2,2'-diamino-1,1'-binaphthyl fragment using our universal approach – the Pd(0)-catalyzed macrocyclization reaction of starting di(bromoaryl) substituted precursors with a variety of oxadiamines.[24] This method allowed to synthesize macrocycles with phenylene, naphthalene and benzyl spacers. Introduction of the 1,8- or 1,5-diaminoanthraquinone moiety in the macrocycle is useful for the construction of colorimetric chemosensors, as it was shown by us previously.[25,26] From this viewpoint it was considered important to explore the synthesis of chiral macrocycles comprising such structural fragments.

For this purpose first we synthesized *N,N'*-di(8-chloroanthraqinon-1-yl) substituted BINAM **3** by the reaction of the starting (*S*)-2,2'-diamino-1,1'-binaphthalene (BINAM, **1**) with 1,8-dichloroanthraquinone (**2**) (Scheme 1). The reaction was run in the presence of $Pd(dba)_2$/BINAP (4/4.5 mol%) catalytic system using Cs_2CO_3 as a base because anthraquinone backbone does not tolerate stronger sodium *tert*-butoxide which is usually used as a base in the catalytic amination. The target precursor **3** was obtained in 20 % yield and the oligomeric by-product **4** was also isolated by column chromatography in 16 % yield.

At the next step compound **3** was introduced in the Pd(0)-catalyzed macrocyclization reactions with oxadiamines **5a-c** differing by the chain length and the number of oxygen atoms, the same catalytic system being used (Scheme 1). The results with dioxadiamine **5a** and trioxadiamine **5c** were quite good and corresponding macrocycles **6a,c** were obtained in 40 and 37 % yields, respectively, while the reaction with another trioxadiamine **5b** gave a poorer yield of the macrocycle **6b** (22 %). In this reaction we also isolated a cyclic dimer **7b**, however its yield was too small (4.5 %). These data could have been explained by the fact that trioxadiamine **5b** posseses the shortest chain length (13 atoms instead of 14 and 15 in **5a** and **5c**, respectively) if it were not for quite different results of the macrocyclization with the isomeric compound **9** (*vide infra* Scheme 2). We also tried another phosphine ligand DavePhos (2-dicyclohexylphosphino-2'-dimethylaminobiphenyl) in these reactions in order to increase the yields of the target macrocycles, but



Scheme 1.

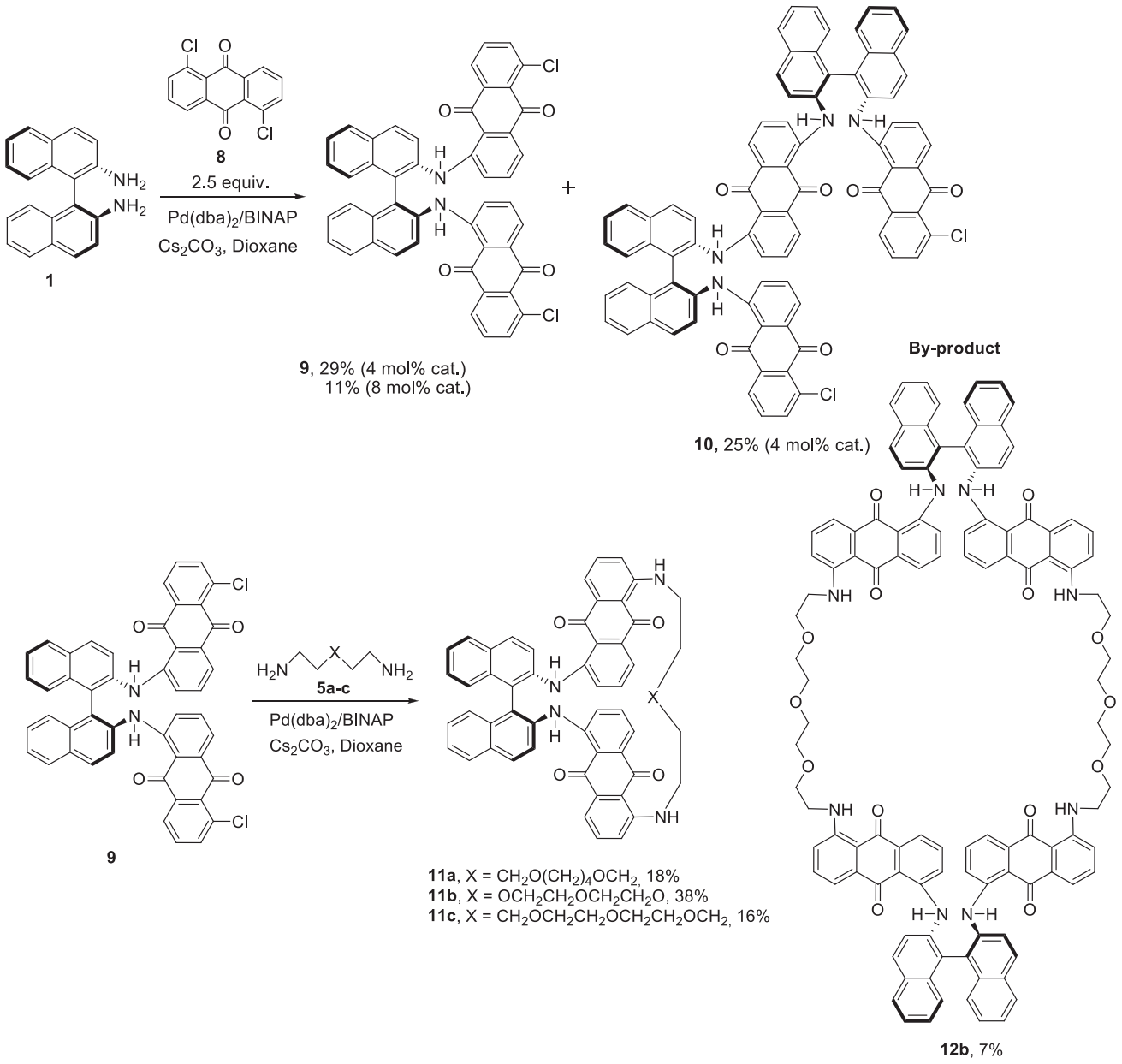
only in the case of **5c** the product **6c** was isolated in a negligible 4 % yield, thus BINAP was shown to be the appropriate ligand in this macrocyclization.

The reaction of BINAM with the isomeric 1,5-dichloroanthraquinone (**8**) under the same conditions afforded 29 % yield of *N,N'*-diaryl derivative **9** and the second product **10** of oligomeric structure was isolated in 25 % yield (Scheme 2). We tried to increase the yield of the target product **8** by applying 8 mol% catalyst instead of 4 mol% but the yield decreased to 11 % due to undesirable formation of various oligomers *via* diamination of 1,5-dichloroanthraquinone. Previously we also noticed this effect in some catalytic amination reactions.[27]

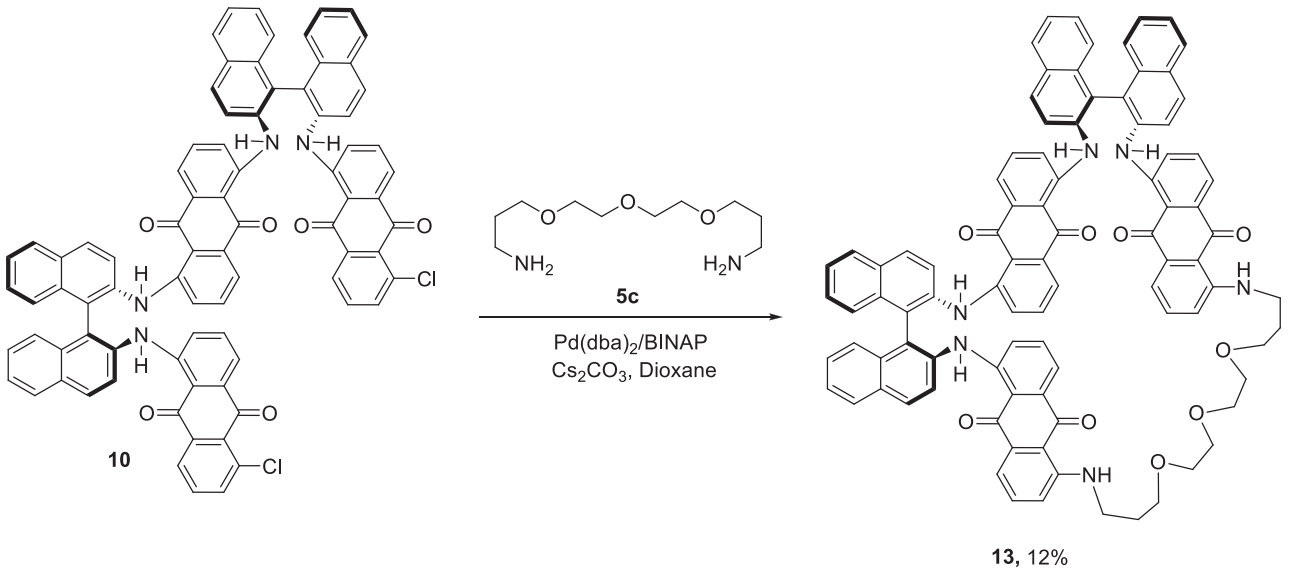
Compound **9** was introduced in the macrocyclization reaction with oxadiamines **5a-c** and corresponding macrocycles **11a-c** were obtained in 16–38 % yields (Scheme 2), however, in this series the best yield (38 %) was provided by trioxadiamine **5b**. In the reaction with this compound cyclic dimer **12b** was also obtained in individual state. All these facts clearly demonstrate the dependence of the result of the macrocyclization on the structure of both starting compounds.

Further we attempted the synthesis of a large macrocycle containing two BINAM and three anthraquinone moieties by reacting the oligomer **10** with trioxadiamine **5c** possessing the longest chain (Scheme 3). The reaction was enough successful and the desired macrocycle **13** was isolated in 12 % yield.

We investigated the ability of one exemplary macrocycle (**6c**) to detect some chiral compounds using UV-Vis and fluorescence spectrometry. This macrocyclic ligand shows three absorption bands which can be used for detection: λ_{max}=322 (lgε 4.43), 352 (lgε 4.35), 556 nm (lgε 4.30) (in MeCN). Excitation at 322 or 352 nm results in fluorescence with maximum at 396 nm. We chose the following chiral organic molecules for our preliminary test: (*S*)- and (*R*)-leucinol, (*S*)- and (*R*)-*tert*-leucinol, (*S*)- and (*R*)-phenylglycinol, (*S*)- and (*R*)-2-amino-1-propanol, (*S*)- and (*R*)-2-amino-1-butanol, (*1S,2R*)- and (*1R,2S*)-2-amino-1,2-diphenylethanol, (*1S,2S*)- and (*1R,2R*)-1,2-diphenylethylenediamine. UV-Vis and fluorescence spectra were recorded upon addition of 100, 200, 500, and 1000 equiv. of corresponding compounds to a solution of the ligand in MeCN (*C*=8.33 μM). (*S*)- and (*R*)-*tert*-leucinol, (*S*)-



Scheme 2.



Scheme 3.

and (*R*)-2-amino-1-butanol did not cause notable changes in the spectra of the ligand, (*S*)- and (*R*)-phenylglycinol produced similar changes in the fluorescence spectra: emission enhancement together with the formation of the second emission band as a shoulder at *ca.* 430 nm. The addition of (*R*)-leucinol did not lead to any change in the emission spectrum while (*S*)-leucinol caused an increase in the fluorescence intensity (twofold with 500 equiv., Figure 1).

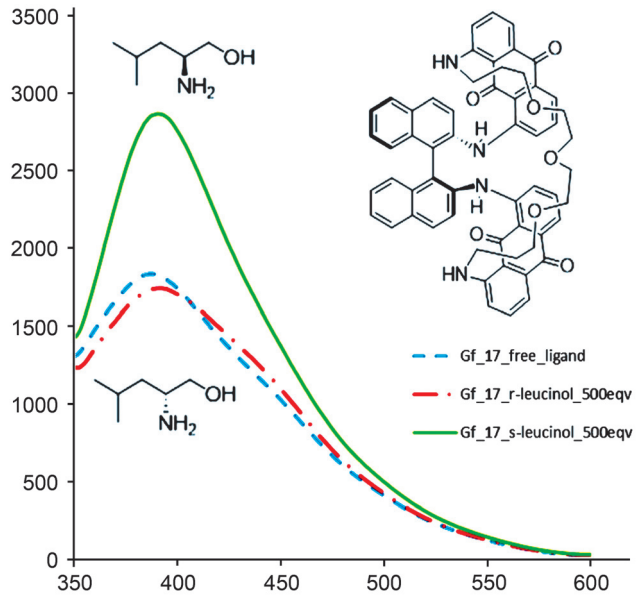


Figure 1. The emission spectra of **6c** in the presence of (*S*)- and (*R*)-leucinol.

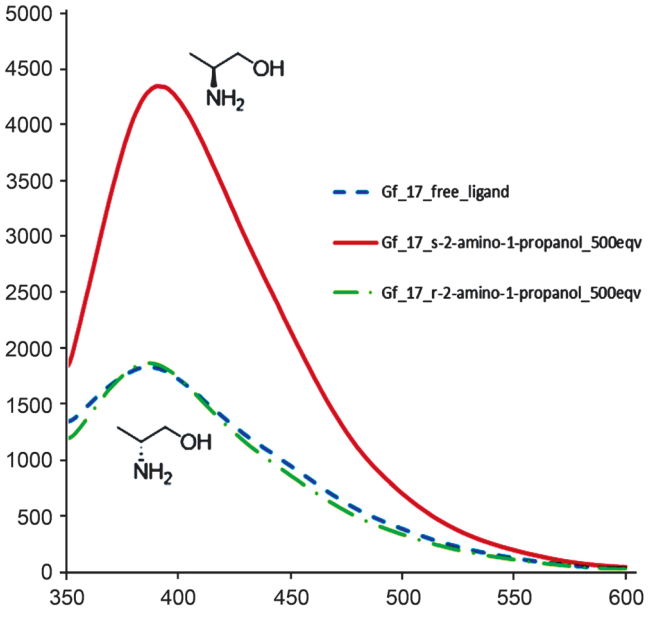


Figure 2. The emission spectra of **6c** in the presence of (*S*)- and (*R*)-2-amino-1-propanol.

Similarly, (*R*)-2-amino-1-propanol did not lead to the changes in the emission spectrum of **6c** while the addition of 500 equiv. of (*S*)-2-amino-1-propanol resulted in a threefold enhancement of the emission (Figure 2). The addition of 500 equiv. of (*1R,2S*)-2-amino-1,2-diphenylethanol to the macrocycle also led to more intensive fluorescence whereas its enantiomer, (*1S,2R*)-2-amino-1,2-diphenylethanol did not change notably the emission spectrum (Figure 3).

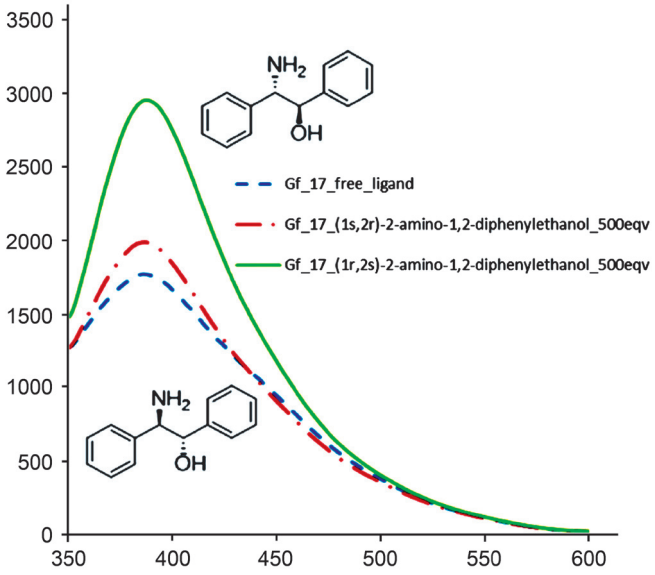


Figure 3. The emission spectra of **6c** in the presence of (*1S,2R*)- and (*1R,2S*)-2-amino-1,2-diphenylethanol.

At last, the most intensive response to coordination was achieved with (*1S,2S*)-1,2-diphenylethylenediamine, in the presence of this analyte the enhancement of fluorescence was *ca.* 7 times, while the isomeric (*1R,2R*)-1,2-diphenylethylenediamine did not cause the changes (Figure 4).

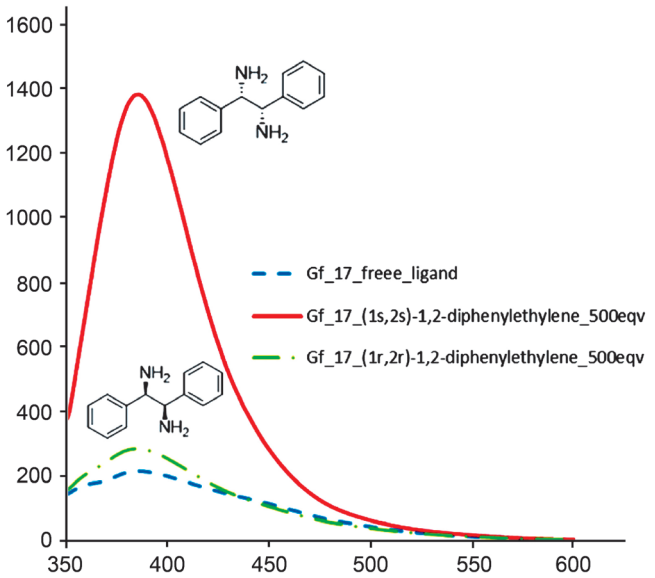


Figure 4. The emission spectra of **6c** in the presence of (*1S,2S*)- and (*1R,2R*)-1,2-diphenylethylenediamine.

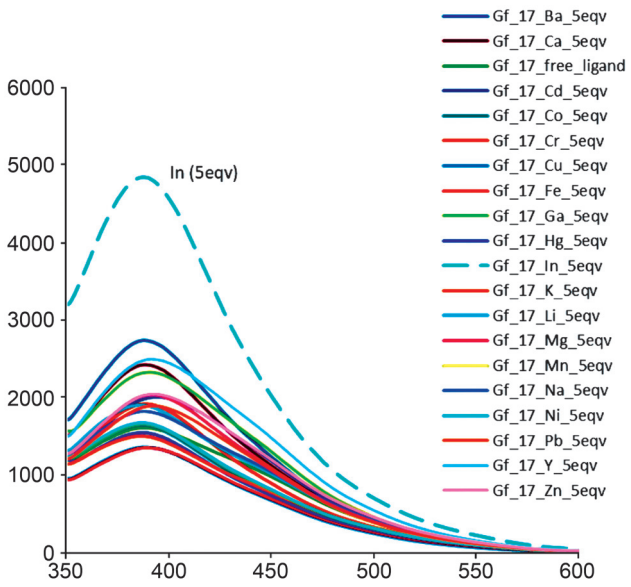


Figure 5. The emission spectra of **6c** in the presence of metal salts.

The changes in UV-Vis spectra were not notable in the region 300–600 nm for all analytes tested. We also investigated the influence of the metal cations on the absorption and emission properties of the macrocycle **6c**. For this purpose, 20 metal salts were tested: Li(I), Na(I), K(I), Mg(II), Ca(II), Ba(II), Al(III), Fe(II), Mn(II), Co(II), Ni(II), Cr(III), Cu(II), Zn(II), Cd(II), Pb(II), Hg(II) perchlorates and Ga(III), In(III), Y(III) nitrates. 1, 2, and 5 equiv. of the corresponding salts were added to the solution of **6c** in MeCN, and only in the case of In(III) *ca.* 2.5 time enhancement of the emission was noted while other metals changed the fluorescence insignificantly (Figure 5).

As in the case with chiral molecules, we did not observe changes in UV-Vis spectra, except for Cu(II) which were slight with 5 equiv. of the metal but were quite notable with 10 equiv. and resulted in the decrease of the absorption in the visible range together with bathochromic shift of this band from 556 to 510 nm.

Conclusions

To sum up, we developed the catalytic approach to previously unknown *N*- and *O*-containing macrocycles comprising chiral BINAM fragment, chromophore diaminoanthraquinone spacers and various oxadiamine chains. The dependence of the compounds yields on the structure of starting compounds was established, in some cases side products of oligomeric structure were isolated and characterized. One representative of the new series of macrocycles was tested as an enantioselective detector for a number of chiral amino alcohols and 1,2-diphenylethylenediamine and was shown to be able to distinguish between enantiomers of leucinol, 2-amino-1-propanol, 2-amino-1,2-diphenylethanol, and 1,2-diphenmylethylenediamine by increasing the emission in the presence of one enantiomer. It also detects In(III) among 20 metals tested by emission enhancement.

Acknowledgements. This work was financially supported by the RFBR grants N 15-03-04698 and 17-53-16012.

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Received 21.09.2017
Accepted 01.11.2017