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Plant Coumarins: V.* Palladium-Catalyzed Amination of 2-(1,3-Dibromopropan-2-ylidene)oreoselone

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Abstract—Palladium-catalyzed amination of 2-(1,3-dibromopropan-2-ylidene)-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione with various amines and amino acid derivatives led to the formation of the corresponding 2-(1,3-diaminopropan-2-ylidene)-substituted oreoselones. The yields depended on the catalytic system, base, and amine structure. Di- and polyazamacrocyclic furocoumarin derivatives were obtained by reactions of 2-(1,3-dibromopropan-2-ylidene)-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione with linear di- and polyamines (hexamethylenediamine, spermine, spermidine, and 3,6-dithiaoctane-1,8-diamine), catalyzed by palladium complexes.

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Linear furocoumarins are widely used in therapy of skin diseases (PUVA therapy) [2], which is based on the joint action of psoralen drugs (furocoumarin derivatives) and long-wave ultraviolet irradiation. Photoinitiated cycloaddition of psoralens in the excited triplet state to thymine bases of DNA is the main factor determining therapeutic effect of these compounds. On the other hand, a number of serious side effects were revealed, in particular possible cross-linking of two DNA molecules with one psoralen molecule, which could give rise to genotoxicity, keratoses, skin cancer, and other oncological diseases [2]. At present, extensive studies are performed on the synthesis of new psoralen derivatives and design of photosensitizers for PUVA therapy so that to avoid the above side effects. Fusion of a cyclopentane, cyclohexane, benzene, or pyridazine ring at the furan fragment of the psoralen skeleton and introduction of a (dimethylamino)propoxy group into position *5* or *8* (to improve solubility in water) resulted in change of phototoxicity, and in the case of fused pyridazine derivatives, in considerable increase of photoantiproliferative activity [3].

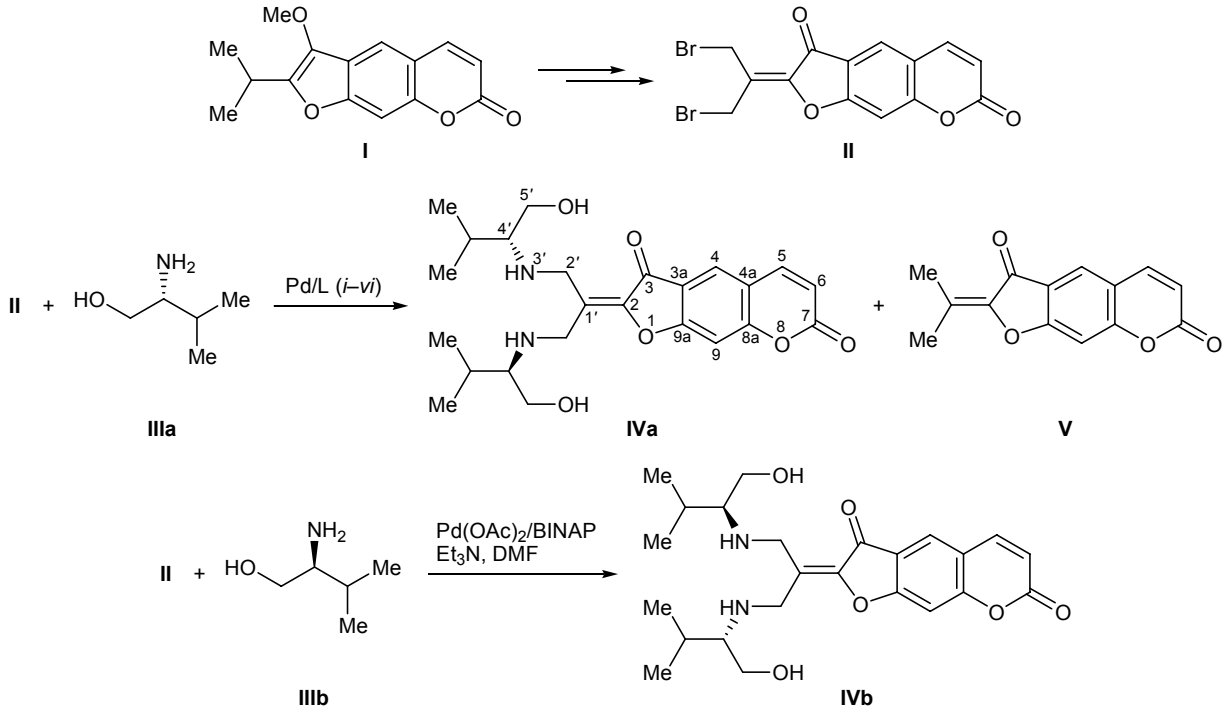
Taking into account the above stated, it seemed reasonable to synthesize and examine new furocoumarin derivatives with various nitrogen-containing substituents on the furan ring.

An accessible source of fourocoumarins is *Peucedanum morisonii* Bes which is widespread in West Siberia; its main metabolite is peucedanin (**I**) which can be isolated from the root of the plant in up to 4% yield (calculated on the dry raw material) [4]. In continuation of our studies on peucedanin modifications [1, 5], in the present work we made an attempt to synthesize diamino-substituted furocoumarins via palladium-catalyzed amination of 2-(1,3-dibromopropan-2-ylidene)-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (**II**) which was prepared as described previously [1].

The reaction conditions were selected using the amination of dibromide **II** with L-valinol (**IIIa**) as model reaction (Scheme 1). Initially, the reaction was carried out in the presence of $Pd(dba)_2$/BINAP (8/9 mol %) since this catalytic system ensured good results in the amination of 3,24-bis(haloaryloxy)cholanes (sodium *tert*-butoxide was used as base and dioxane was used as solvent) [6]. The target amination product **IVa** was obtained in a poor yield (23%), whereas the major product was that resulting from reduction of dibromide **II**, 2-(1-methylethylidene)oreoselone (**V**, yield 52%) [5, 7]. When the amounts of the catalyst and ligand were reduced to 1/3 mol % and the reaction was carried out in boiling toluene (i.e., under the conditions described in [8]), compound **IVa** was formed in 25% yield. Replacement of $Pd(dba)_2$ by $Pd_2(dba)_3$ did not change the reaction outcome to

* For communication IV, see [1].

Scheme 1.



Reagents and conditions: *i*: $Pd(dba)_2$, BINAP, *t*-BuONa, dioxane, 100°C; *ii*: $Pd(dba)_2$, BINAP, *t*-BuONa, toluene, 80°C; *iii*: $Pd_2(dba)_3$, BINAP, *t*-BuONa, toluene, 80°C; *iv*: $Pd(OAc)_2$, $(o\text{-}MeC_6H_4)_3P$, Et_3N, DMF, 110°C; *v*: $Pd(OAc)_2$, BINAP, Et_3N, DMF, 110°C; *vi*: $Pd(OAc)_2$, Xantphos, Et_3N, DMF, 110°C.

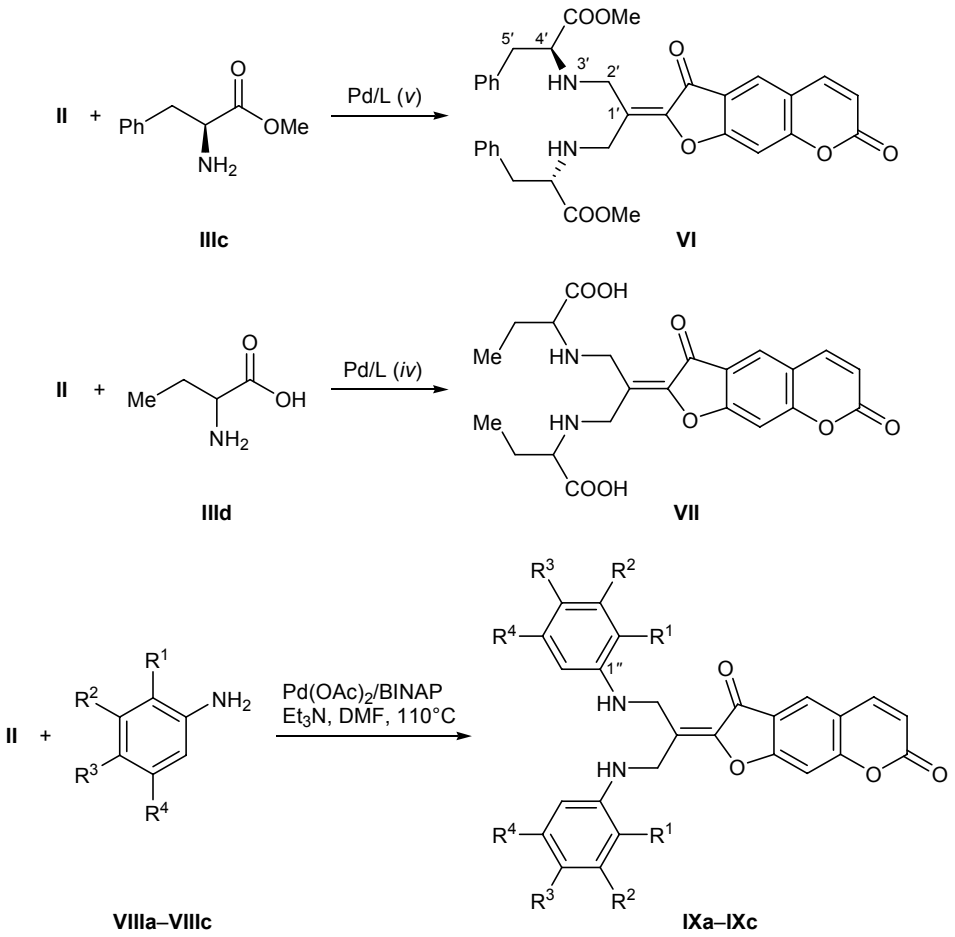
an appreciable extent: the yield of **IVa** was 18%. We succeeded in raising the yield of **IVa** to 45% by carrying out the amination of **II** with L-valinol (**IIIa**) in the presence of $Pd(OAc)_2$/$(o\text{-}MeC_6H_4)_3P$ (2/8 mol %) as catalytic system and triethylamine (1.3 equiv) as base in dimethylformamide; in this case, the yield of **V** did not exceed 10%. The use of BINAP as ligand was more effective. At the optimal $Pd(OAc)_2$/BINAP ratio (4/8 mol %) amination product **IVa** was isolated in 72% yield, and its optical rotation was twice as large. The same catalytic system ensured formation of 64% of optically active stereoisomer **IVb** in the amination of dibromofurocoumarin **II** with D-valinol (**IIIb**). Inhibition of racemization was observed previously in palladium-catalyzed coupling of aryl bromides with various optically active amines in the presence of BINAP as ligand [9].

Catalytic systems Pd/Xantphos were effectively used to build up C–N bonds [10]. We found that the yield of amination product **IVa** decreased (45%) while the yield of compound **V** increased (30%) when the reaction of furocoumarin **II** with L-valinol **IIIa** was carried out in the presence of $Pd(OAc)_2$/Xantphos (2/8 mol %) as catalytic system. Thus, the best yields of the amination products in the reactions of dibromofurocoumarin **II** with L- and D-valinols **IIIa** and **IIIb** were obtained in the presence of $Pd(OAc)_2$/BINAP.

By amination of dibromofurocoumarin **II** with L-phenylalanine methyl ester (**IIIc**) in the presence of $Pd(OAc)_2$/BINAP and triethylamine (1.3 equiv) in DMF we obtained optically active coumarin derivative **VI** (yield 66%; Scheme 2). In the reaction of **II** with 2-aminobutanoic acid (**IIId**) in the presence of $Pd(OAc)_2$/$(o\text{-}MeC_6H_4)_3P$ (2/8 mol %) diaminoisopropylidene derivative **VII** was formed in 48% yield. Compound **II** reacted with substituted anilines [4-fluoroaniline (**VIIIa**), 2-piperidinoaniline (**VIIIb**), and 3,4,5-trimethoxyaniline (**VIIIc**)] in DMF in the presence of $Pd(OAc)_2$/BINAP (4/8 mol %) as catalytic system and triethylamine as base to afford the corresponding bis-anilino derivatives **IXa**–**IXc** which were isolated in 48–54% yield.

The reactions of cyclic secondary amines, morpholine (**X**) and *N*-methylpiperazine (**XI**), with dibromide **II** were characterized by lower yields of the amination products (Scheme 3). These reactions were carried out using $Pd(OAc)_2$/$(o\text{-}MeC_6H_4)_3P$ (2/8 mol %) as catalytic system, and the yields of amination products **XIIa**

Scheme 2.

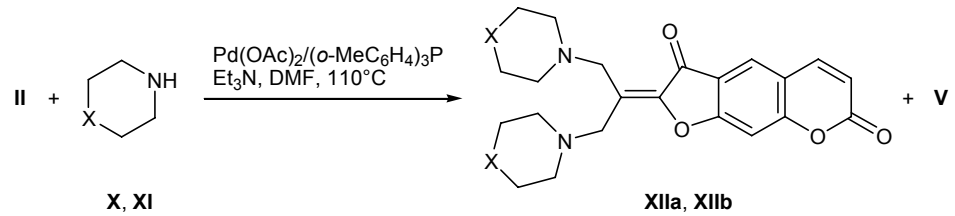


$R^1 = R^2 = R^4 = H$, $R^3 = F$ (**a**); R^1 = piperidino, $R^2 = R^3 = R^4 = H$ (**b**); $R^1 = H$, $R^2 = R^3 = R^4 = MeO$ (**c**).

and **XIIb** were 22 and 34%, respectively. Increase of the amount of catalyst (4/8 mol %), as well as addition of morpholine (**X**) in 30 min after mixing the initial furocoumarin, catalyst, and base (in keeping with the recommendations given in [8]), did not improve the yield of amination products **XIIa** and **XIIb**. In addition, 32–42% of **V** was isolated in each case.

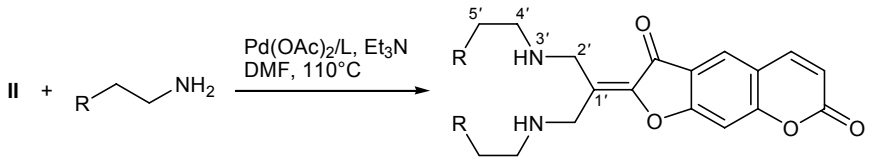
Dibromide **II** readily reacted with linear amines, such as 2-aminoethanol (**XIIIa**), 3-aminopropan-1-ol (**XIIIb**), and ethylenediamine (**XIIIc**) (Scheme 4). The reaction of coumarin **II** with aminopropanol **XIIIb** in the presence of $Pd(OAc)_2$/(o-$MeC_6H_4)_3P$ gave 42% of 2-[1,3-bis(2-hydroxypropylamino)propan-2-ylidene]-oreoselone (**XIVb**). By reactions of compound **II** with 2-aminoethanol (**XIIIa**) and ethylenediamine (**XIIIc**) in the presence of $Pd(OAc)_2$/BINAP (4/8 mol %) we obtained amination products **XIVa** and **XIVc** in 36–38% yield. 2-[1,3-Bis(2-aminoethylamino)propan-2-ylidene]oreoselone (**XIVc**) was also formed in the amination of dibromide **II** with excess (2 equiv) of

Scheme 3.



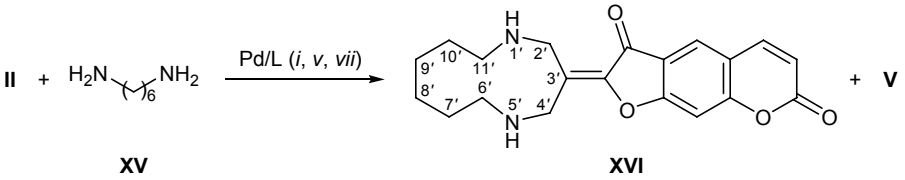
X, **XIIa**, X = O; **XI**, **XIIb**, X = NMe.

Scheme 4.



R = OH (**a**), CH_2OH (**b**), NH_2 (**c**).

Scheme 5.



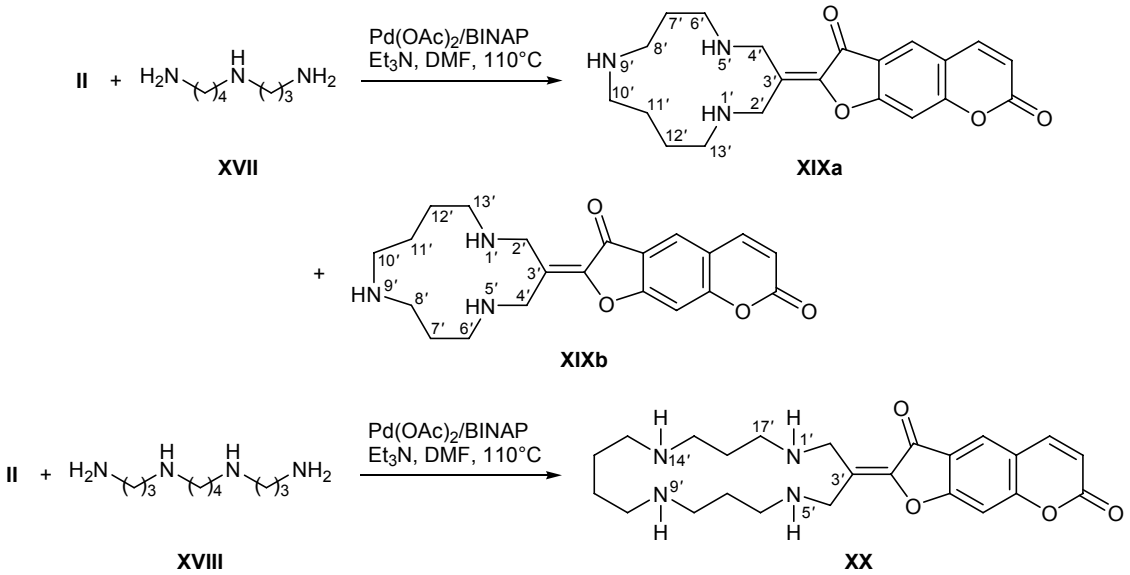
Reagents and conditions: *i*: $Pd(dba)_2$, BINAP, *t*-BuONa, dioxane, 100°C; *v*: $Pd(OAc)_2$, BINAP, Et_3N, DMF, 110°C; *vii*: $Pd(dba)_2$, BINAP, Cs_2CO_3, toluene, 80°C.

diamine **XIIIc**; no formation of dicoumarin derivatives or cyclization products was observed.

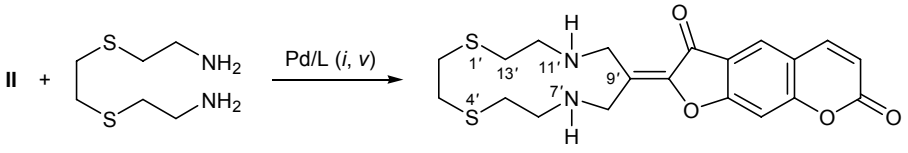
The reaction of dibromide **II** with hexamethylenediamine (**XV**, 2 equiv) in DMF in the presence of $Pd(OAc)_2$/BINAP (4/8 mol %) and triethylamine on heating to 110°C (6 h) resulted in the formation of cyclization product **XVI** (yield 56%, Scheme 5). The same product was obtained when increased amount of amine **XV** was used. The yield of amination product **XVI** sharply decreased (to 26%) when the reaction of **II** with diamine **XV** was carried out using a larger amount of the catalyst [$Pd(dba)_2$/BINAP, 8/9 mol %; *t*-BuONa; heating in boiling dioxane over a period of 7 h] [6]. In this case, the major product was 2-(1-methylethylidene)oreoselone (**V**, yield 50%). In order to reduce the yield of side product **V** and obtain acyclic polyamine derivatives, sodium *tert*-butoxide as base was replaced by cesium carbonate, the catalytic system being $Pd(dba)_2$/BINAP [11]. By contrast, the yield of **V** increased even to a stronger extent (68%), while amination product **XVI** was isolated in 14% yield. Thus the reaction of **II** with diamine **XV** gives only macrocyclic furocoumarin derivative **XVI**.

Taking into account interest in hybrid nitrogen-containing macrocyclic compounds, including natural ones [12], we examined the possibility for synthesizing

Scheme 6.



Scheme 7.



i: $Pd(dba)_2$, BINAP, *t*-BuONa, dioxane, 100°C; *v*: $Pd(OAc)_2$, BINAP, Et_3N, DMF, 110°C.

polyamines possessing a coumarin fragment via amination of dibromide **II** with polyamines, in particular with spermidine (**XVII**) and spermine (**XVIII**) (Scheme 6). The reaction of **II** with spermidine (**XVII**) [$Pd(OAc)_2$/BINAP (4/8 mol %)–Et_3N] on heating in DMF gave a mixture of *E*/*Z*-isomeric macrocyclic compounds **XIXa** and **XIXb** in an overall yield of 55%. Isomers **XIXa** and **XIXb** were formed at a ratio of 1:1 which was determined from the intensity ratio of the singlet signals from 2′-H and 4′-H of each isomer in the ^{1}H NMR spectrum. We failed to separate the isomer mixture. By reaction of **II** with spermine (**XVIII**) under analogous conditions we obtained 60% of macrocyclic compound **XX**. The yield of **XX** in the reaction of dibromide **II** with diamine **XVIII** was considerably lower (35%) in the presence of $Pd(OAc)_2$)–(o-$MeC_6H_4)_3P$ (2/8 mol %) as catalytic system.

High yields of macrocyclic furocoumarin derivatives stimulated our further study on the amination of compound **II** with heteroatom-containing diamines. The reaction of **II** with dithia diamine **XXI** [13] was carried out using $Pd(OAc)_2$/BINAP (4/8 mol %) as catalytic system (Scheme 7), and the only amination product was macrocyclic compound **XXII** which was isolated in 44% yield. In the reaction of **II** with diamine **XXI** in the presence of $Pd(dba)_2$/BINAP (8/9 mol %) and sodium *tert*-butoxide [6] the yield of **XXII** was 28%. No acyclic polyamino-substituted coumarin derivatives were detected among the amination products in the reactions of dibromide **II** with di- and polyamines **XVI**, **XIX**, **XX**, and **XXII**.

The structure of the obtained compounds was determined on the basis of their spectral parameters, elemental compositions, and molecular weight measurement. The IR spectra of bis-amino derivatives **IVa**, **IVb**, **VII**, **XIIa**, and **XIIb** characteristically contained absorption bands belonging to stretching vibrations of the N–H bonds and carboxy groups in the regions 1604–1695 and 1700–1746 cm^{-1}, as well as broad bands due to associated hydroxy groups at 2340–2470 and 3430–3520 cm^{-1}. In the ^{1}H NMR spectra of these compounds we observed signals typical of protons in the coumarin fragment and those of the corresponding substituents on the nitrogen atoms. Compounds **IVa**, **IVb**, **VI**, and **VII** were characterized by magnetic nonequivalence of the 2′-H protons which had different chemical shifts and showed geminal coupling. In the ^{1}H NMR spectra of **IXa**–**IXc**, **XIIa**, **XIIb**, **XIVa**–**XIVc**, **XVI**, **XIXa**, **XIXb**, **XX**, and **XXII**, methylene protons neighboring to the nitrogen atoms resonated as a broadened singlet. The latter was located most upfield in the spectra of macrocyclic compounds **XVI**, **XIXa**, **XIXb**, **XX**, and **XXII** (δ 2.68–2.92 ppm). Diamino derivatives **XIIa**, **XIIb**, and **XIVa**–**XIVc** displayed 2′-H signals in a weaker field, at δ 3.03–3.24 ppm, and the most downfield position of these signals (δ 3.93–4.04 ppm) was typical of bis-anilino derivatives **IXa**–**IXc**. The structure of macrocyclic coumarin derivatives **XVI**, **XIXa**, **XIXb**, **XX**, and **XXII** and compound **XIVc** was also confirmed by determination of their molecular weights.

To conclude, we have developed catalytic procedures for the synthesis of various 2-(1,3-aminoprop-2-ylidene)-substituted oreoselone derivatives and nitrogen- and sulfur-containing macrocyclic furocoumarin derivatives. The results of the catalytic amination are determined by the reaction conditions and amine structure. The best catalytic system for the amination of 2-(1,3-dibromoprop-2-ylidene)furocoumarin **II** with various amines is $Pd(OAc)_2$/BINAP.

EXPERIMENTAL

The NMR spectra were recorded on Bruker AV-300 (300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C), AV-400 (400.13 MHz for ^{1}H and 100.78 MHz for ^{13}C), and AV-600 spectrometers (600.30 MHz for ^{1}H and 150.96 MHz for ^{13}C) from solutions in $CDCl_3$. Signals in the NMR spectra were assigned using several proton–proton and carbon–proton shift correlation techniques (COSY, COXH, COLOC). Multiplicity of ^{13}C signals was determined from the *J*-modulation spectra. The IR spectra were measured in KBr on a Vector-22 instrument. The UV spectra were recorded

on an HP 8453 UV Vis spectrophotometer from solutions in ethanol. The optical rotations $[\alpha]_D^{20}$ were measured on a PolAAr3005 polarimeter. The molecular weights of compounds **XIVc**, **XVI**, **XIXa**, **XIXb**, **XX**, and **XXII** were determined using a Knauer vapor pressure osmometer. The elemental compositions were determined on a Carlo Erba 1106 CHN analyzer.

The products were isolated by column chromatography on silica gel (0.035–0.070 mm, Acros Organics) or aluminum oxide using chloroform and chloroform–ethanol (50:3) as eluents. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using chloroform–ethanol (3:1), benzene, or benzene–ethyl acetate (1:1) as eluent; spots were visualized by treatment with iodine vapor or under UV light.

The solvents (dioxane, toluene, DMF), triethylamine, 2-aminoethanol, 3-aminopropan-1-ol, and ethylenediamine were distilled in a stream of argon just before use. Commercial L- and D-valinol, L-phenylalanine methyl ester, 2-aminobutanoic acid, 2-piperidinoaniline, 4-fluoroaniline, and 3,4,5-trimethoxyaniline (from Alfa Aesar), morpholine, spermine, and spermidine (from Aldrich), and *N*-methylpiperazine (from Acros) were used without additional purification.

Palladium(II) acetate was synthesized according to the procedure described in [14]; $Pd(dba)_2$ was prepared as reported in [15] and was not subjected to additional recrystallization; $Pd_2(dba)_3$, $(o\text{-}MeC_6H_4)_3P$, (*R*)-(+)-BINAP, and Xantphos were commercial products (from Alfa Aesar).

Amination of 2-(1,3-dibromoprop-2-ylidene)-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (II). *i*. Dibromide **II**, 300 mg (0.75 mmol), was dissolved in 4 ml of anhydrous dioxane, 34 mg (8 mol %) of $Pd(dba)_2$, 46 mg (9 mol %) of BINAP, 210 mg (3 equiv) of *t*-BuONa, and 310 mg (3 mmol) of L-valinol (**IIIa**) or 2 mmol of diamine **XIV** or **XX** were added in succession under argon, and the mixture was heated for 10 h at 100°C until the initial compound (**II**) disappeared (according to the TLC data). The mixture was evaporated, and the residue was subjected to column chromatography on silica gel to isolate fractions containing amination product **IVa**, **XV**, or **XXI** and compound **V**. The main portion of compound **V** was separated by recrystallization from acetone, the precipitate of **V** was filtered off, the mother liquor was evaporated, and the residue was subjected again to chromatography on silica gel to isolate chromatographically pure compound **IV**, **XV**, or **XXI**.

ii. Dibromide **II**, 300 mg (0.75 mmol), was dissolved in 6 ml of anhydrous toluene, 4.3 mg (1 mol %) of $Pd(dba)_2$, 15 mg (3 mol %) of BINAP, 210 mg (3 equiv) of *t*-BuONa, and 85 mg (0.825 mmol) of L-valinol (**IIIa**) were added in succession under argon, and the mixture was heated for 8 h at 80°C until initial coumarin **II** disappeared (TLC). The mixture was then cooled in a stream of argon and evaporated, and the residue was subjected to column chromatography on aluminum oxide to isolate a fraction containing compounds **IVa** and **V**. The product mixture was recrystallized from acetone to remove the main part of compound **V**, and the residue was subjected to chromatography on silica gel. A fraction containing the amination product was dissolved in diethyl ether, the solution was cooled, and the precipitate of compound **IVa** was filtered off.

iii. Dibromide **II**, 300 mg (0.75 mmol), was dissolved in 6 ml of anhydrous toluene, 7.8 mg (1 mol %) of $Pd_2(dba)_3$, 15 mg (3 mol %) of BINAP, 210 mg (3 equiv) of *t*-BuONa, and 154 mg (1.5 mmol) of L-valinol (**IIIa**) were added in succession under argon, and the mixture was heated for 8 h at 80°C and treated as described above to isolate compounds **IVa** and **V**.

iv. Compound **II**, 300 mg (0.75 mmol), was dissolved in 5 ml of anhydrous dimethylformamide, 3.2 mg (2 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of $(o\text{-}MeC_6H_4)_3P$, 0.07 ml (1.3 equiv) of Et_3N, and 1.5 mmol of amine **IIIa**, **IIId**, **X**, **XI**, or **XIIIb** were added under argon, and the mixture was heated for 5 h at 110°C (TLC). The mixture was cooled in a stream of argon and poured into a Petri dish for evaporation. The residue was subjected to chromatography first on aluminum oxide and then on silica gel. A fraction containing the amination product was dissolved in diethyl ether, the solution was cooled, and the precipitate (compound **IVa**, **VII**, **XIIa**, **XIIb**, or **XIVb**) was filtered off.

v. Compound **II**, 300 mg (0.75 mmol), was dissolved in 4 ml of anhydrous dimethylformamide, 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, 0.07 ml (1.3 equiv) of Et_3N, and 1.5 mmol of amine **IIIa**–**IIIc**, **VIIIa**–**VIIIc**, or **XIIIa** or 2.0 mmol of diamine **XIIIc**, **XV**, **XVII**, **XVIII**, or **XXI** were added under argon, and the mixture was heated for 6 h at 110°C (TLC). The mixture was then cooled in a stream of argon and poured into a Petri dish. After evaporation, the residue was subjected to column chro-

matography on aluminum oxide or silica gel to isolate amination product **IVa**, **IVb**, **VI**, **IXa**–**IXc**, **XIVa**, **XIVc**, **XVI**, **XIXa**, **XIXb**, **XX**, and **XXII**.

vi. Compound **II**, 300 mg (0.75 mmol), was dissolved in 4 ml of anhydrous dimethylformamide, 4.4 mg (4 mol %) of $Pd(OAc)_2$, 44 mg (8 mol %) of Xantphos, 0.07 ml (1.3 equiv) of Et_3N, and 154 mg (1.5 mmol) of L-valinol (**IIIa**) were added under argon, and the mixture was heated for 6 h at 110°C (TLC). The mixture was then cooled in a stream of argon and poured into a Petri dish. After evaporation, the residue was subjected to column chromatography on aluminum oxide to isolate compounds **IVa** (yield 44%) and **V** (30%).

vii. Dibromide **II**, 300 mg (0.75 mmol), was dissolved in 6 ml of anhydrous toluene, 8.6 mg (2 mol %) of $Pd(dba)_2$, 10 mg (2 mol %) of BINAP, 1200 mg (5 equiv) of Cs_2CO_3, and 174 mg (2 mmol) of hexamethylenediamine (**XV**) were added in succession under argon, and the mixture was heated for 8 h at 80°C (TLC). The mixture was then cooled in a stream of argon and evaporated, and the residue was subjected to column chromatography on aluminum oxide to isolate a fraction containing compounds **XVI** and **V**. The product mixture was recrystallized from acetone to remove the main part of compound **V**, and the residue was subjected to chromatography on silica gel. We isolated 37 mg (14%) of macrocyclic compound **XVI** and 123 mg (68%) of compound **V**.

2-[(1*R*,3*R*)-1,3-Bis(1-hydroxy-3-methylbutan-2-ylamino)propan-2-ylidene]-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (IVa). Yield 23 (*i*), 25 (*ii*), 18% (*iii*); 45%, $[\alpha]_D^{20}$ = –7.6° (*c* = 0.5, EtOH) (*iv*); 72%, $[\alpha]_D^{20}$ = –8.8° (*c* = 0.5, $CHCl_3$) (*v*); 30%, $[\alpha]_D^{20}$ = –5.6 (*c* = 0.5°, EtOH) (*vi*); mp 135–136°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3388, 3084, 2965, 2470, 2030, 1702, 1680, 1620, 1521, 1392, 1330,1260, 1133, 1050, 970, 804, 721, 669. UV spectrum, λ_{max}, nm (logε): 202 (4.18), 259 (3.72), 306 (3.74), 345 (3.48). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.89 d and 0.97 d [6H each, $(CH_3)_2CH$, *J* = 7.0], 1.84 m [2H, $CH(CH_3)_2$], 2.57 d.d (2H, 4′-H, *J* = 6.6, 2.2), 3.15 d.d.d (2H, 5′-H, *J* = 10.6, 1.8, 1.5), 3.30 d.d (2H, NH, *J* = 2.2, 1.8), 3.34 m (2H, OH), 3.32 d.d (2H, 2′-H, *J* = 12.0, 1.0), 3.38 d (2H, 2′-H, *J* = 12.0), 6.25 d (1H, 6-H, *J* = 9.8), 6.98 s (1H, 9-H), 7.55 d (1H, 5-H, *J* = 9.8), 7.95 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 17.18 q and 20.28 q [$CH(CH_3)_2$], 28.68 d [$CH(CH_3)_2$], 44.19 t ($C^{2'}$), 60.28 d ($C^{4'}$), 66.41 d ($C^{5'}$), 101.23 d (C^9), 112.80 d (C^6), 113.49 s (C^{4a}), 115.60 s (C^{3a}), 119.56 s ($C^{1'}$), 123.53 d (C^4), 143.26 d (C^5), 144.19 s (C^2), 157.62 s (C^{8a}), 161.82 s (C^{9a}), 171.35 s (C^7), 198.79 s (C^3). Found, %: C 64.62; H 6.83; N 5.94. $C_{24}H_{32}N_2O_6$. Calculated, %: C 64.85; H 7.26; N 6.30.

2-[(1*S*,3*S*)-1,3-Bis(1-hydroxy-3-methylbutan-2-ylamino)propan-2-ylidene]-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (IVb) was synthesized from 300 mg (0.75 mmol) of compound **II** and 154 mg (1.5 mmol) of D-valinol in the presence of 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et_3N in 4 ml of DMF. Yield 213 mg (64%), $[\alpha]_D^{20}$ = +7.2 (*c* = 0.5, $CHCl_3$), mp 135–136°C (from Et_2O). The spectral parameters of **IVb** were similar to those of its stereoisomer **IVa**.

Dimethyl *N*,*N*′-[2-(3,7-dioxo-7*H*-furo[3,2-*g*]-chromen-2-ylidene)propane-1,3-diyl]bis[(2*S*)-2-amino-3-phenylpropanoate] (VI) was synthesized from 300 mg (0.75 mmol) of compound **II** and 324 mg (1.5 mmol) of phenylalanine methyl ester (**IIIc**) in the presence of 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et_3N in 4 ml of anhydrous DMF (*v*). Yield 295 mg (66%), $[\alpha]_D^{20}$ = –10.8° (*c* = 0.5, $CHCl_3$), mp 231–233°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3420, 3220, 3171, 3029, 1737, 1698, 1680, 1656, 1621, 1590, 1392, 1353, 1297, 1143, 1130, 906, 839, 752, 740, 702, 586. UV spectrum, λ_{max}, nm (logε): 237 (3.59), 276 (4.17), 307 (4.40), 355 (3.52). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.84 d.d.d (2H, 5′-H, *J* = 11.6, 6.6, 2.0), 3.05 d.d.d (2H, 5′-H, *J* = 11.6, 3.8, 1.0), 3.20 d (2H, 2′-H, *J* = 12.0), 3.34 d (2H, 2′-H, *J* = 12.0), 3.61 s (6H, OCH_3), 3.67 d.d.d (2H, 4′-H, *J* = 6.6, 3.8, 1.5), 6.23 d (1H, 6-H, *J* = 9.8), 6.95 s (1H, 9-H), 7.12 m (4H, *o*-H), 7.23–7.28 m (6H, *m*-H, *p*-H), 7.55 d (1H, 5-H, *J* = 9.8), 8.16 s (1H, 4-H), 11.05 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 40.89 t ($C^{2'}$), 51.89 t ($C^{5'}$), 55.65 q (OCH_3), 62.06 d ($C^{4'}$), 101.51 d (C^9), 112.83 d (C^6), 113.66 s (C^{4a}), 115.48 s (C^{3a}), 123.50 d (C^4), 126.16 s ($C^{1'}$), 126.72 d (C^p), 128.44 d (C^m), 129.14 d (C^o), 137.01 s (C^i), 143.13 d (C^5), 144.72 s (C^2), 158.83 s (C^{8a}), 161.95 s (C^{9a}), 168.82 s (C^7), 175.23 s ($COOCH_3$), 189.99 s (C^3). Found, %: C 68.26; H 6.61; N 4.32. $C_{34}H_{32}N_2O_8$. Calculated, %: C 68.45; H 5.41; N 4.70.

***N*,*N*′-[2-(3,7-Dioxo-2*H*-furo[3,2-*g*]chromen-2-ylidene)propane-1,3-diyl]bis[2-aminobutanoic acid] (VII)** was synthesized from 300 mg (0.75 mmol) of compound **II** and 150 mg (1.5 mmol) of 2-aminobutanoic acid in 5 ml of anhydrous DMF in the presence of 3.2 mg (2 mol %) of $Pd(OAc)_2$, 34 mg

(8 mol %) of (*o*-$MeC_6H_4)_3P$, and 0.07 ml (1.3 equiv) of Et_3N (*iv*). Yield 160 mg (48%), mp 138–139°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3600, 3330, 3250, 3057, 2967, 2916, 2542, 1737, 1702, 1653, 1620, 1586, 1517, 1354, 1141, 1115, 1067, 980, 900, 806, 763, 698, 664. UV spectrum, λ_{max}, nm (logε): 224 (3.93), 228 (3.94), 241 (4.02), 278 (4.0), 306 (4.09), 335 (3.74). ^1H NMR spectrum, δ, ppm (*J*, Hz): 0.97 t (6H, $C^{6'}H_3$, *J* = 7.0), 1.54 m and 1.70 m (2H each, 5′-H), 3.19 d and 3.33 d (2H each, 2′-H, *J* = 11.8), 3.36 d.d.d (2H, 4′-H, *J* = 6.6, 3.2, 1.2), 4.25 br.s (4H, NH, OH), 6.24 d (1H, 6-H, *J* = 9.8), 6.97 s (1H, 9-H), 7.54 d (1H, 5-H, *J* = 9.8), 7.94 s (1H, 4-H), 11.05 br.s (2H). ^{13}C NMR spectrum, δ_C, ppm: 10.73 q ($C^{6'}$), 21.89 t ($C^{5'}$), 43.47 t ($C^{2'}$), 63.26 d ($C^{4'}$), 98.23 d (C^9), 113.02 d (C^6), 113.71 s (C^{4a}), 116.63 s (C^{3a}), 120.06 s ($C^{1'}$), 123.52 d (C^4), 144.41 d (C^5), 145.01 s (C^2), 158.05 s (C^{9a}), 162.04 s (C^{8a}), 171.83 s (C^7), 173.01 s (COOH), 193.22 s (C^3). Found, %: C 59.16; H 5.53; N 6.22. $C_{22}H_{24}N_2O_8$. Calculated, %: C 59.45; H 5.44; N 6.30.

2-[1,3-Bis(4-fluorophenylamino)propan-2-ylidene]-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (IXa) was synthesized from 300 mg (0.75 mmol) of compound **II** and 168 mg (1.5 mmol) of 4-fluoroaniline in the presence of 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et_3N in 4 ml of anhydrous DMF (*v*). Yield 179 mg (52%), mp 113–114°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3413, 3023, 2778, 2439, 1737, 1704, 1615, 1587, 1508, 1392, 1350, 1223, 1155, 1140, 1098, 1024, 836, 720, 616. UV spectrum, λ_{max}, nm (logε): 235 (4.10), 301 (3.93), 328 (3.98), 440 (2.62). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.93 br.s (4H, 2′-H), 6.26 d (1H, 6-H, *J* = 10.2), 6.98 s (1H, 9-H), 7.02 d and 7.04 d (2H each, *m*-H, *J* = 8.3), 7.38 d and 7.39 d (2H each, *o*-H, *J* = 8.3), 7.54 d (1H, 5-H, *J* = 10.2), 7.94 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 42.26 t ($C^{2'}$), 97.86 d (C^9), 112.77 d (C^6), 113.02 s (C^{4a}), 113.67 s (C^{3a}), 115.55 d (C^m), 118.38 s ($C^{1'}$), 119.29 d (C^o), 122.24 d (C^4), 144.16 d (C^5), 144.97 s (C^i), 147.33 s (C^2), 157.12 d (C^p, J_{CF} = 251.2 Hz), 160.02 s (C^{9a}), 161.49 s (C^{8a}), 172.21 s (C^7), 192.58 s (C^3). ^{19}F NMR spectrum: δ_F 83.34 ppm (relative to C_6F_6 as reference). Found, %: C 68.08; H 3.25; F 8.02; N 6.26. $C_{26}H_{18}F_2N_2O_4$. Calculated, %: C 67.82; H 3.94; F 8.29; N 6.08.

2-[1,3-Bis(2-piperidinophenylamino)propan-2-ylidene]-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (IXb) was synthesized from 300 mg (0.75 mmol) of compound **II** and 265 mg (1.5 mmol) of 2-piperidinoaniline in the presence of 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et_3N in 4 ml of anhydrous DMF (*v*). Yield 212 mg (48%), mp 183–184°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3432, 3068, 2839, 1737, 1704, 1657, 1620, 1600, 1507, 1139, 1124, 1003, 908, 888, 829, 764, 750, 686. UV spectrum, λ_{max}, nm (logε): 224 (4.48), 261 (4.19), 277 (4.16), 308 (4.10), 350 sh (3.77). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.57 m and 1.61 m [6H each, $(CH_2)_3$], 3.18 m and 3.32 m (4H each, CH_2NCH_2), 3.99 br.s (4H, 2′-H), 6.03 d (2H, 6″-H, *J* = 8.8), 6.25 d (1H, 6-H, *J* = 10.1), 6.58 d (2H, 3″-H, *J* = 8.6), 6.78 d.d (2H, 4″-H, *J* = 8.0, 8.6), 6.82 d.d (2H, 5″-H, *J* = 8.0. 8.8), 6.97 s (1H, 9-H), 7.56 d (1H, 5-H, *J* = 10.1), 7.94 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 24.19 t ($C^{4'''}$), 26.19 t ($C^{3'''}$, $C^{5'''}$), 42.60 t ($C^{2'}$), 51.30 t ($C^{2'''}$, $C^{6'''}$), 99.73 d (C^9), 113.02 d (C^6), 113.71 s (C^{4a}), 114.03 d ($C^{3''}$), 116.63 s (C^{3a}), 118.24 d ($C^{6''}$), 119.55 s ($C^{1'}$), 120.10 d ($C^{4''}$), 123.52 d (C^4), 133.48 s ($C^{5''}$), 140.61 s ($C^{2''}$), 144.11 s ($C^{1''}$), 144.41 d (C^5), 147.27 s (C^2), 157.64 s (C^{9a}), 161.56 s (C^{8a}), 171.56 s (C^7), 192.15 s (C^3). Found, %: C 73.56; H 6.21; N 9.68. $C_{36}H_{38}N_4O_4$. Calculated, %: C 73.20; H 6.48; N 9.48.

2-[1,3-Bis(3,4,5-trimethoxyphenylamino)propan-2-ylidene]-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (IXc) was synthesized from 300 mg (0.75 mmol) of compound **II** and 295 mg (1.5 mmol) of 3,4,5-trimethoxyaniline in the presence of 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et_3N in 4 ml of anhydrous DMF (*v*). Yield 244 mg (54%), mp 192–193°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3437, 3080, 3043, 2839, 1737, 1704, 1657, 1620, 1600, 1507, 1139, 1124, 1004, 909, 888, 829, 764, 750, 688, 674. UV spectrum, λ_{max}, nm (logε): 231 (4.27), 276 (4.41), 305 (4.54), 365 sh (3.82). ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.64 s (6H, 4″-OCH_3), 3.82 br.s (12H, 3″-OCH_3, 5″-OCH_3), 4.04 s (4H, 2′-H), 5.67 s (4H, 2″-H, 6″-H), 6.36 d (1H, 6-H, *J* = 9.8), 7.08 s (1H, 9-H), 7.67 d (1H, 5-H, *J* = 9.8), 8.05 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 42.59 t ($C^{2'}$), 55.80 q (3″-OCH_3, 5″-OCH_3), 60.15 q (4″-OCH_3), 98.08 d (C^9), 98.38 d ($C^{2''}$, $C^{6''}$), 113.03 s (C^{4a}), 113.68 d (C^6), 114.95 s (C^{3a}), 116.12 s ($C^{1'}$), 123.49 d (C^4), 133.62 s ($C^{4''}$), 135.11 s ($C^{1''}$), 141.94 d (C^5), 147.24 s (C^2), 152.85 d ($C^{3''}$, $C^{5''}$), 157.61 s (C^{9a}), 161.53 s (C^{8a}), 172.85 s (C^7), 193.22 s (C^3). Found, %: C 63.08; H 5.12; N 4.22. $C_{32}H_{32}N_2O_{10}$. Calculated, %: C 63.57; H 5.33; N 4.63.

2-(1,3-Dimorpholinopropan-2-ylidene)-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (XIIa) was synthe-

sized from 300 mg (0.75 mmol) of compound **II** and 0.13 ml (1.5 mmol) of morpholine in the presence of 3.2 mg (2 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of $(o\text{-}MeC_6H_4)_3P$, and 0.07 ml (1.3 equiv) of Et_3N in 5 ml of anhydrous DMF (*iv*). Yield 68 mg (22%), mp 165–166°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3414, 3054, 2780, 2449, 1733, 1623, 1582, 1479, 1353, 1140, 1110, 1102, 1085, 1043, 994, 929, 900, 871, 826, 810, 750, 725, 683. UV spectrum, λ_{max}, nm (logε): 263 (4.25), 299 (4.04), 349 (3.61). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.33–2.41 m and 2.43–2.50 m (4H each, CH_2NCH_2), 3.03 br.s (4H, 2′-H), 3.42–3.51 m and 3.54–3.60 m (4H each, CH_2OCH_2), 6.25 d (1H, 6-H, *J* = 9.8), 6.97 s (1H, 9-H), 7.55 d (1H, 5-H, *J* = 9.8), 7.94 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 53.13 t (CH_2NCH_2), 57.45 t ($C^{2'}$), 66.75 t (CH_2OCH_2), 101.78 d (C^9), 112.87 s (C^{4a}), 113.56 d (C^6), 116.42 s (C^{3a}), 119.18 s ($C^{1'}$), 126.48 d (C^4), 144.67 d (C^5), 144.86 s (C^2), 157.55 s (C^{9a}), 161.96 s (C^{8a}), 172.85 s (C^7), 193.22 s (C^3). Found, %: C 57.30; H 5.24; N 5.89. $C_{22}H_{24}N_2O_6 \cdot 1/2CHCl_3$. Calculated, %: C 57.20; H 5.08; N 5.93.

2-[1,3-Bis(4-methylpiperazin-1-yl)propan-2-ylidene]-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (XIIb) was synthesized from 300 mg (0.75 mmol) of compound **II** and 150 mg (1.5 mmol) of *N*-methylpiperazine in the presence of 3.2 mg (2 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of $(o\text{-}MeC_6H_4)_3P$, and 0.07 ml (1.3 equiv) of Et_3N in 5 ml of anhydrous DMF (*iv*). Yield 111 mg (34%), mp 132–133°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3417, 3026, 2469, 1722, 1624, 1574, 1500, 1354, 1292, 1215, 1142, 1050, 920, 900, 826. UV spectrum, λ_{max}, nm (logε): 202 (4.37), 257 (4.27), 320 (4.04), 345 (3.56). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.25 s (6H, NCH_3), 2.26 m and 2.35 m (4H each, 2″-H, 6″-H), 2.54 m and 2.63 m (4H each, 3″-H, 5″-H), 3.04 br.s (4H, 2′-H), 6.25 d (1H, 6-H, *J* = 9.8), 6.98 s (1H, 9-H), 7.55 d (1H, 5-H, *J* = 9.8), 7.94 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 42.69 q (NCH_3), 45.66 t ($C^{2'}$), 50.50 t ($C^{2''}$, $C^{6''}$), 56.17 t ($C^{3''}$, $C^{5''}$), 99.30 d (C^9), 112.91 d (C^6), 113.60 s (C^{4a}), 116.52 s (C^{3a}), 118.17 s ($C^{1'}$), 124.39 d (C^4), 143.11 d (C^5), 144.90 s (C^2), 157.53 s (C^{9a}), 161.94 s (C^{8a}), 172.20 s (C^7), 192.36 s (C^3). Found, %: C 58.73; H 6.24; N 11.55. $C_{24}H_{30}N_4O_4 \cdot 1/2CHCl_3$. Calculated, %: C 59.03; H 6.22; N 11.24.

2-[1,3-Bis(2-hydroxyethylamino)propan-2-ylidene]-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (XIVa) was synthesized from 300 mg (0.75 mmol) of compound **II** and 91 mg (1.5 mmol) of 2-aminoethanol in the presence of 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et_3N in 4 ml of anhydrous DMF (*v*). Yield 97 mg (36%), mp 112–113°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3344, 3300, 3003, 2550, 1731, 1663, 1640, 1571, 1315, 1155, 1071, 1026, 860, 820, 703. UV spectrum, λ_{max}, nm (logε): 239 (2.95), 272 (2.96), 319 (3.87), 350 (2.82), 360 sh (2.80). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.15 br.s (4H, NH, OH), 2.83 m (4H, 4′-H), 3.23 m (4H, 2′-H), 3.66 m (4H, 5′-H), 6.26 d (1H, 6-H, *J* = 9.8), 6.99 s (1H, 9-H), 7.57 d (1H, 5-H, *J* = 9.8), 7.95 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 45.59 t ($C^{2'}$), 51.40 t ($C^{4'}$, 59.83 t ($C^{5'}$), 99.00 d (C^9), 112.97 d (C^6), 113.66 s (C^{4a}), 116.70 s (C^{3a}), 119.73 s ($C^{1'}$), 123.47 d (C^4), 144.44 d (C^5), 144.96 s (C^2), 157.59 s (C^{9a}), 161.51 s (C^{8a}), 172.51 s (C^7), 192.12 s (C^3). Found, %: C 59.72; H 5.76; N 8.09. $C_{18}H_{20}N_2O_6$. Calculated, %: C 59.99; H 5.59; N 7.77.

2-[1,3-Bis(3-hydroxypropylamino)propan-2-ylidene]-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (XIVb) was synthesized from 300 mg (0.75 mmol) of compound **II** and 112 mg (1.5 mmol) of amine **XIIIb** in the presence of 3.2 mg of $Pd(OAc)_2$, 34 mg of $(o\text{-}MeC_6H_4)_3P$, and 0.07 ml (1.3 equiv) of Et_3N in 5 ml of anhydrous DMF (*v*). Yield 122 mg (42%), mp 97–99°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3338, 3290, 3083, 2500, 1727, 1670, 1563, 1311, 1148, 1064, 960, 911, 820, 770, 700. UV spectrum, λ_{max}, nm (logε): 236 (3.98), 276 (3.92), 350 (3.23). ^1H NMR spectrum, δ, ppm (*J*, Hz): 1.75 m (4H, 5′-H), 2.78 m (4H, 4′-H), 2.95 br.s (4H, NH, OH), 3.20 m (4H, 2′-H), 3.81 m (4H, 6′-H), 6.25 d (1H, 6-H, *J* = 9.8), 6.98 s (1H, 9-H), 7.55 d (1H, 5-H, *J* = 9.8), 7.94 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 31.21 t ($C^{5'}$), 45.60 t ($C^{2'}$), 46.75 t ($C^{4'}$), 62.59 t ($C^{6'}$), 98.39 d (C^9), 112.48 d (C^6), 112.98 s (C^{4a}), 116.38 s (C^{3a}), 120.12 s ($C^{1'}$), 123.46 d (C^4), 144.35 d (C^5), 144.95 s (C^2), 157.58 s (C^{9a}), 161.70 s (C^{8a}), 173.07 s (C^7), 192.93 s (C^3). Found, %: C 61.72; H 6.01; N 7.63. $C_{20}H_{24}N_2O_6$. Calculated, %: C 61.84; H 6.23; N 7.21.

2-[1,3-Bis(2-aminoethylamino)propan-2-ylidene]-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (XIVc) was synthesized from 300 mg (0.75 mmol) of compound **II** and 90 mg (1.5 mmol) of ethylenediamine in the presence of 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et_3N in 4 ml of anhydrous DMF (*v*). Yield 102 mg (38%), mp 132–133°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3260, 3160, 3048, 2883, 2800, 2678, 1657, 1537, 1459, 1392, 1322, 1258, 1228,

1119, 982, 842, 752, 709. UV spectrum, λ_{max}, nm (logε): 227 (3.03), 231 (3.04), 241 (3.38), 282 (2.56), 331 (2.08), 363 (1.48). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.65–2.72 m (8H, 4′-H, 5′-H), 3.23 br.s (4H, 2′-H), 4.54 br.s (6H, NH_2, NH), 6.25 d (1H, 6-H, *J* = 9.8), 6.98 s (1H, 9-H), 7.55 d (1H, 5-H, *J* = 9.8), 7.94 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 41.12 t ($C^{5'}$), 45.45 t ($C^{2'}$), 51.90 t ($C^{4'}$), 99.73 d (C^9), 112.89 d (C^6), 113.57 s (C^{4a}), 116.88 s (C^{3a}), 119.07 s ($C^{1'}$), 123.39 d (C^4), 144.28 d (C^5), 144.88 s (C^2), 157.51 s (C^{9a}), 161.00 s (C^{8a}), 171.54 s (C^7), 192.15 s (C^3). Found, %: C 60.05; H 6.43; N 15.90. $[M]^+$ 358. $C_{18}H_{22}N_4O_4$. Calculated, %: C 60.32; H 6.19; N 15.63. *M* 358.16.

2-(1,5-Diazacycloundecan-3-ylidene)-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (XVI). Yield 26 (*i*), 56 (*v*), 14% (*vii*), mp 186–188°C (from hexane). IR spectrum, ν, cm^{-1}: 3282, 3035, 2854, 1649, 1633, 1531, 1387, 1239, 1213, 1171, 1120, 1090, 1082, 1035, 779, 750, 715. UV spectrum, λ_{max}, nm (logε): 225 (3.51), 255 (3.40), 297 (3.31), 346 (3.13). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.75 m (4H, 8′-H, 9′-H), 1.63 m (4H, 7′-H, 10′-H), 2.39 m (4H, 6′-H, 11′-H), 2.84 br.s (4H, 2′-H, 4′-H), 6.26 d (1H, 6-H, *J* = 9.8), 6.98 s (1H, 9-H), 7.56 d (1H, 5-H, *J* = 9.8), 7.95 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 27.04 t ($C^{8'}$, $C^{9'}$), 29.78 t ($C^{7'}$, $C^{10'}$), 48.88 t ($C^{2'}$, $C^{4'}$), 51.92 t ($C^{6'}$, $C^{11'}$), 98.66 d (C^9), 112.91 d (C^6), 113.60 s (C^{4a}), 115.60 s (C^{3a}), 123.31 d (C^4), 126.75 s ($C^{3'}$), 144.30 d (C^5), 144.90 s (C^2), 157.53 s (C^{8a}), 161.93 s (C^{9a}), 171.78 s (C^7), 193.86 s (C^3). Found, %: C 67.25; H 6.34; N 8.01. $[M]^+$ 354. $C_{20}H_{22}N_2O_4$. Calculated, %: C 67.78; H 6.26; N 7.90. *M* 354.16.

(*E*)- and (*Z*)-2-(1,5,9-Triazacyclotridecan-3-ylidene)-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-diones (XIXa/XIXb) were synthesized from 300 mg (0.75 mmol) of compound **II** and 210 mg (1.5 mmol) of spermidine in the presence of 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et_3N in 4 ml of anhydrous DMF (*v*). Yield 158 mg (55%), mp 187–189°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3424, 3300, 3069, 2782, 1725, 1637, 1615, 1578, 1520, 1364, 1305, 1284, 1216, 1142, 1121, 1039, 980, 956, 877, 847, 823, 757. UV spectrum, λ_{max}, nm (logε): 201 (4.25), 217 (4.14), 257 (4.30), 297 (3.98), 336 (3.65). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.30 m and 1.47 m (1H each, 12′-H), 1.88 m (4H, 11′-H), 1.98 m (4H, 7′-H), 2.40 m (4H, 13′-H), 2.53 m and 2.55 m (4H each, 6′-H, 10′-H), 2.68 br.s and 2.79 br.s (4H each, 2′-H, 4′-H in *E* and *Z* isomers), 3.46 m (4H, 8′-H), 3.60 br.s (3H, NH), 6.22 d (1H, 6-H, *J* = 9.8), 6.93 s (1H, 9-H), 7.51 d (1H, 5-H, *J* = 9.8), 7.90 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 20.47 t ($C^{12'}$), 21.42 t ($C^{11'}$), 26.18 t ($C^{7'}$), 46.39 t ($C^{6'}$), 47.38 t ($C^{13'}$), 48.12 t ($C^{8'}$), 49.36 t ($C^{10'}$), 50.13 t ($C^{2'}$, $C^{4'}$), 99.03 d (C^9), 113.76 s (C^{4a}), 115.10 d (C^6), 117.41 d (C^4), 118.64 s (C^{3a}), 123.07 s ($C^{3'}$), 144.61 s (C^2), 146.07 d (C^5), 153.04 s (C^{8a}), 160.07 s (C^{9a}), 171.17 s (C^7), 191.71 s (C^3). Found, %: C 65.48; H 6.25; N 10.39. $[M]^+$ 383. $C_{21}H_{25}N_3O_4$. Calculated, %: C 65.78; H 6.57; N 10.96. *M* 383.14.

2-(1,5,9,13-Tetraazacycloheptadecan-7-ylidene)-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (XX). Yield 35 (*iv*), 60% (*v)*; mp 201–203°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3437, 3061, 2975, 2934, 2853, 2676, 2592, 2452, 1727, 1624, 1482, 1393, 1350, 1289, 1193, 1138, 1023, 909, 829, 741. UV spectrum, λ_{max}, nm (logε): 202 (4.83), 223 (4.7), 255 (4.96), 299 (4.73), 348 (4.56). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.93 m (4H, 15′-H, 16′-H), 2.02 m (4H, 3′-H, 11′-H), 2.57 m (4H, 14′-H, 17′-H), 2.70 m (4H, 2′-H, 12′-H), 2.72 s (4H, 6′-H, 8′-H), 3.50 m (4H, 4′-H, 10′-H), 6.24 d (1H, 6-H, *J* = 9.8), 6.98 s (1H, 9-H), 7.55 d (1H, 5-H, *J* = 9.8), 7.94 s (1H, 4-H), 8.92 br.s (4H, NH). ^{13}C NMR spectrum, δ_C, ppm: 27.54 t ($C^{15'}$, $C^{16'}$), 28.59 t ($C^{3'}$, $C^{11'}$), 45.88 t ($C^{4'}$, $C^{10'}$), 49.13 t ($C^{2'}$, $C^{12'}$), 49.84 t ($C^{14'}$, $C^{17'}$), 51.31 t ($C^{6'}$, $C^{8'}$), 99.65 d (C^9), 112.77 d (C^6), 113.46 s (C^{4a}), 116.38 s (C^{3a}), 123.23 d (C^4), 126.10 s ($C^{7'}$), 144.16 d (C^5), 144.76 s (C^2), 157.33 s (C^{8a}), 161.79 s (C^{9a}), 171.58 s (C^7), 192.36 s (C^3). Found, %: C 54.33; H 6.00; N 10.29. $[M]^+$ 443. $C_{24}H_{32}N_4O_4$. Calculated, %: C 53.71; H 5.90; N 10.01. *M* 442.23.

2-(1,4-Dithia-7,11-diazacyclotridecan-9-ylidene)-7*H*-furo[3,2-*g*]chromene-3,7(2*H*)-dione (XXII). Yield 28 (*i*), 44% (*v*); mp 101–103°C (from Et_2O). IR spectrum, ν, cm^{-1}: 3437, 3061, 2975, 2934, 2853, 2676, 2592, 2452, 1727, 1624, 1482, 1393, 1350, 1289, 1193, 1138, 1023, 909, 829, 741. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.86 m (8H, 5′-H, 8′-H, 10′-H, 13′-H), 2.92 m (4H, 6′-H, 12′-H), 2.98 m (4H, 2′-H, 3′-H), 6.24 d (1H, 6-H, *J* = 9.8), 6.97 s (1H, 9-H), 7.55 d (1H, 5-H, *J* = 9.8), 7.94 s (1H, 4-H), 8.60 br.s (2H, NH). ^{13}C NMR spectrum, δ_C, ppm: 28.76 t ($C^{5'}$, $C^{13'}$), 38.32 t ($C^{2'}$, $C^{3'}$), 50.63 t ($C^{8'}$, $C^{10'}$), 54.62 t ($C^{6'}$, $C^{12'}$), 103.81 d (C^9), 112.29 d (C^6), 113.46 s (C^{4a}), 116.13 s (C^{3a}), 123.08 d (C^4), 126.10 s ($C^{9'}$), 144.04 d (C^5), 145.00 s (C^2), 157.04 s (C^{8a}), 161.59 s (C^{9a}), 171.63 s (C^7), 192.69 s (C^3). Found, %: C 57.65; H 5.62; N 6.35; S 15.56. $[M]^+$ 418. $C_{20}H_{22}N_2O_4S_2$. Calculated, %: C 57.39; H 5.30; N 6.69; S 15.32. *M* 418.16.

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