Platelet Aggregation Inhibiting and Anticoagulant Effects of Oligoamines, XVIII:

Oligoamines with Fluorescent Properties, Part B: Fluorophores in the Molecular Periphery

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Seventeen *N,N'*-benzene-1,3-dimethane and nine *N,N',N''*-benzene-1,3,5-trimethane derivatives with fluorescent properties have been synthesized. Three of them show antiplatelet activities (inducer collagen, IC50 *Born*-test) in concentrations < 10 µmol/L. They are suitable for interaction studies with biological macromolecules and synthetical and biological membranes. Structure activity relationships demonstrate that heteropolycyclic fluorophores *i.e.* quinoline, dibenzofurane, or carbazole are favorable substituents for this purpose.

Antiaggregatorische und anticoagulante Eigenschaften von Oligoaminen, 18. Mitt.: Fluoreszierende Oligoamine, Teil B: Fluorophore in der Molekülperipherie

Siebzehn *N,N'*-Benzol-1,3-dimethanamine und neun *N,N',N''*-Benzol-1,3,5-trimethanamine mit fluoreszierenden Eigenschaften wurden dargestellt. Hiervon hemmten drei Verbindungen die Thrombocytenaggregation in Konzentration < 10 µmol/L halbmaximal (*Born*-Test, Aggregationsauslöser Collagen). Sie sind damit für Interaktionsstudien an biologischen Makromolekülen sowie an synthetischen und natürlichen Membranen geeignet. Die Untersuchungen ergaben, daß mehrkernige Heterocyclen wie Chinolin, Dibenzofuran oder Carbazol besonders geeignete fluorophore Substituenten sind.

Recently we reported on oligoamines with fluorescent bridged nitrogen functions[1]. These compounds were designed to investigate their interactions with membranes and synthetic vesicles from phospholipids of diverse structure. Unfortunately a decrease in antiplatelet activity was observed with these compounds therefore suggesting a decreased potential of interaction with phospholipids of the platelet membrane. We tried to overcome this difficulty by placing the fluorophore in peripheric parts of the oligoamine. This means its use as a substituent of the nitrogen functions. The compounds which were synthesized in order to obtain more active fluorescent amines are compiled in table 1 and table 2.

Compound **1** was synthesized from 3-(2-fluorenyl)-propanecarboxamide[2], reduction with $LiAlH_4$, reaction with isophthalic acid dichloride and repeated reaction with $LiAlH_4$. - **2** was obtained by condensation of 4-(1-pyrenyl)-butanoic acid and benzene-1,3-dimethanamine using *Staab's* method[3] followed by reduction with $LiAlH_4$. - The synthesis of **3** and **27** has been reported[4,5]. - Compounds **15** and **16** were synthesized from known[6,7] compounds, **4**, **17**, and **26** from commercially available amines and isophthaldehyde or benzene-1,3,5-trialdehyde[8] as usual[1]. All other compounds (**5-14** and **18-25**) were prepared according to Scheme 1 using the methods of *Bayer*[9] and *Okano*[10].

The results obtained with **1-27** concerning their antiplatelet (*Born*-test, IC_{50}) and anticoagulant activities (Quick-test) are summarized in Tables 1 and 2. Obviously three compounds (**7**, **14**, **15**) develop antiplatelet activities (IC_{50}) in concentrations < 10 µmol/L. This suggests a strong interaction with platelets. Therefore, these compounds seem to be the most suitable candidates for membrane and vesicle studies. A closer inspection of the structure activity relationship delivers the following results:

Comparison of compounds **1-3** show that the antiplatelet activity is decreased by bulky hydrocarbons (naphthyl > fluorenyl > pyrenyl) while the anticoagulant effects are markedly improved (naphthyl < fluorenyl < pyrenyl). Compounds **4-6** surprisingly show that the substituent tolerates an (weakly basic) amino group and that a rather short carbon chain to the basic nitrogens of the molecule yields a remarkable antiplatelet effect (**4**). These findings encouraged us to synthesize further compounds (**5-15**) with aromatic amino groups in the molecular periphery. Now rather strong antiplatelet and/or anticoagulant activities were obtained with bulky aromatic systems provided a heteroatom like nitrogen or oxygen was involved. These effects were unexpected with respect to the rather poor activities seen earlier[11] in pyrrolyl-, pyridyl- and indolyl-derivatives. So the quinoline derivative **15** was more active than the naphthylamino compounds **4-6**. Even more surprising were the antiplatelet effects of the carbazolyl compounds **10** and **11**. In the same order of magnitude was the corresponding oxygen containing dibenzofuryl derivative **7** which additionally shows a pronounced inhibition of the fibrin formation from fibrinogen. Comparison of **10** and **11** with the corresponding ring open compounds **13** and **14** shows a remarkable variability concerning steric requirements. In this series the most powerful anticoagulant effect was found in compounds with short aliphatic chains in the substituent

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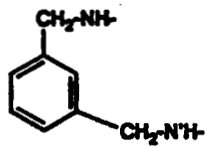
Table 1: Antiplatelet and anticoagulant activities of benzene-1,3-dimethanamine-N,N'-derivatives

Compound	N,N'-substituent of 	Quick c[µmol/L]/Δt[s]	IC_{50} [µmol/L]
1	4-(2-fluorenyl)-butyl	200/7	22
2	4-(1-pyrenyl)-butyl	100/11	36
3[4]	4-(1-naphthyl)-butyl	400/14	15
4	2-(1-naphthylamino)-ethyl	400/3	13
5	3-(1-naphthylamino)-propyl	400/3	22
6	4-(1-naphthylamino)-butyl	400/0	28
7	2-(2-methoxy-3-dibenzofuranylamino)-ethyl	100/9	8
8	3-(2-methoxy-3-dibenzofuranylamino)-propyl	400/5	22
9	4-(2-methoxy-3-dibenzofuranylamino)-butyl	40070	23
10	3-(9-ethyl-3-carbazolylamino)-propyl	400/9	12
11	4-(9-ethyl-3-carbazolylamino)-butyl	400/0	11
12	2-(4-phenylaminophenylamino)-ethyl	100/9	15
13	3-(4-phenylaminophenylamino)-propyl	400/6	13
14	4-(4-phenylaminophenylamino)-butyl	400/9	6
15	4-(6-methoxy-8-quinolinylamino)-pentyl	400/16	9
16	4-(2-naphthylsulfonylamino)-butyl	400/0	35
17	5-(5-dimethylamino-1-naphthylsulfonylamino)-pentyl	400/0	22

e.g. **7** and **12**. The introduction of a sulfonamide group (**16**, **17**) was without advantage.

As we had recognized that oligoamines with three basic nitrogen functions normally were more active than the corresponding diamines[5] we synthesized and tested compound **18-26**. In general the results were surprisingly disappointing. In no case an improvement could be obtained (see pairs **4/18**, **5/19**, **8/22**, **9/23**, **10/24**, **13/25**, and **15/26**). No compound was able to approach the activities of the lead **27**.

Experimental part

The apparatus used and the pharmacologic tests were identical with those of the previous communication[1]. The same is true for the preparation of amides from carboxylic acids and their reduction to amines with $LiAlH_4$.- Temp. in °C.

N,N'-Bis-[4-(2-fluorenyl)-butyl]-benzene-1,3-dimethanamine-dihydrochloride (**1**)

Yellow crystals (ethanol), mp. 274° (degr.). Yield 40%.- $C_{42}H_{44}N_2 \cdot 2$ HCl (649.7) Calcd. C 77.6 H 7.14 N 4.3 Found C 77.4 H 7.07 N 4.1.- IR (KBr): 3420; 2932; 2857; 2774; 1632; 1585; 1536; 1454; 829; 762; 736 cm^{-1}.- ^{1}H-NMR/250 MHz ([D_6]DMSO): δ (ppm) = 9.46 (bs, 4H, NH_2^+, D_2O exchange), 7.86-7.20 (m, 18H aromat.), 4.11 (bs, 4H, Ar-CH_2-NH_2^+), 3.87 (s, 4H, 9-H-fluo.), 2.90 (m, 4H, NH_2^+-CH_2-CH_2), 2.66 (m, 4H, CH_2-CH_2-Ar), 1.68 (m, 8H, CH_2-(CH_2)$_2$-CH_2).- MS (80°): m/z = 576 (3%, $M^{+\cdot}$), 369 (12), 287 (30), 193 (11), 179 (73), 165 (51), 105 (70), 38 (100).

N,N'-Bis-[4-(1-pyrenyl)-butyl]-benzene-1,3-dimethanamine-dihydrochloride (**2**)

Light brown crystals (methanol/ethanol), mp. 205° (degr.). Yield 20%.- $C_{48}H_{44}N_2 \cdot 2$ HCl (721.8) Calcd. C 77.9 H 6.42 N 3.9 Found C 79.8 H 6.32 N 3.7.- IR (KBr): 3416; 2934; 2784; 1602; 1456; 1182; 845; 755; 705 cm^{-1}.- ^{1}H-NMR/250 MHz ([D_6]DMSO): δ (ppm) = 9.54 (bs, 4H, NH_2^+, D_2O exchange), 8.35-7.90 (m, 18H, H-pyrene), 7.73 (s, 1H, 2-H), 7.62 (d, J = 7 Hz, 4-H, 6-H), 7.47 (t, J = 7 Hz, 1H, 5-H), 4.10 (bs, 4H, Ar-CH_2-NH_2^+), 3.37 (t, J = 7 Hz, 4H, CH_2-pyrene), 2.94 (m, 4H, NH_2^+-CH_2-CH_2), 1.88-1.75 (m, 8H, CH_2-(CH_2)$_2$-CH_2).- MS (190°): m/z = 648 (3%, $M^{+\cdot}$), 273 (57), 215 (100), 201 (23).

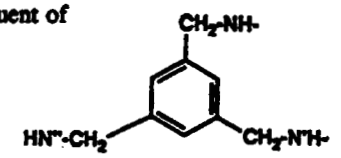
N,N'-Bis-[2-(1-naphthylamino)-ethyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**4**)

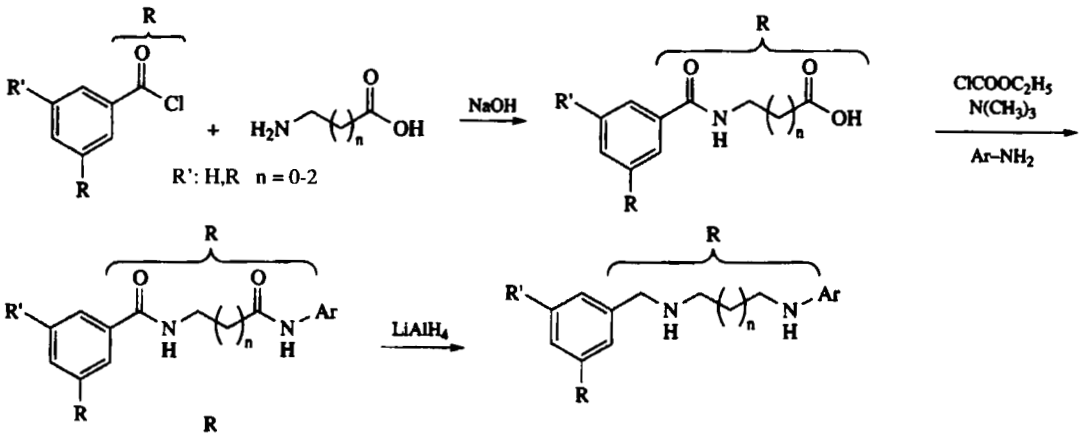
Crystals (H_2O/DMSO), mp. 209°. Yield 60%.- $C_{32}H_{34}N_4 \cdot 2\ C_2H_2O_4$ (654.7) Calcd. C 66.0 H 5.85 N 8.6 Found C 66.0 H 5.85 N 8.4.- IR (KBr): 3383; 3040; 1840; 1721; 1633; 1579; 1529; 1457; 1408; 1281; 1216; 1132; 787; 769; 704 cm^{-1}.- ^{1}H-NMR/250 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 8.13 (dd, J = 7/1 Hz, 2H, 8'-H-napht.), 7.79 (d, J = 7 Hz, 2H, 5'-H-napht.), 7.59 (m, 4H, 7'-H, 6'-H-napht.), 7.33 (dd, J = 7.7/7.7 Hz, 2H, 3'-H-napht.), 7.20 (d, J = 7.9 Hz, 2H, 4'-H-napht.), 6.62 (d, J = 7.2 Hz, 2H, 2'-H-napht.), 4.29 (bs, 4H, Ar-CH_2-NH_2^+), 3.59 (m, 4H, Ar-NH-CH_2), 3.29 (m, 4H, Ar-NH-CH_2-CH_2).- MS (170°): m/z = 474 (18%, $M^{+\cdot}$), 318 (49), 288 (33), 170 (12), 157 (77), 156 (52), 105 (33), 104 (31), 44 (100).

N,N'-Bis-[3-(1-naphthylamino)-propyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**5**)

Crystals (H_2O/DMSO), mp. 204°. Yield 40%.- $C_{34}H_{38}N_4 \cdot 2\ C_2H_2O_4$ (682.8) Calcd. C 66.8 H 6.20 N 8.1 Found C 66.8 H 6.17 N 8.1.- IR (KBr):

Table 2: Antiplatelet and anticoagulant activities of benzene-1,3,5-methanamine-*N,N',N''*-derivatives

Compound	N,N'N''-substituent of 	Quick c[µmol/L]/Δt[s]	IC_{50} [µmol/L]
18	3-(1-naphthylamino)-propyl	400/8	14
19	4-(1-naphthylamino)-butyl	400/2	17
20	3-(2-fluorenylamino)-propyl	400/0	28
21	4-(2-fluorenylamino)-butyl	400/8	80
22	3-(2-methoxy-3-dibenzofuranylamino)-propyl	400/4	35
23	4-(2-methoxy-3-dibenzofuranylamino)-butyl	400/4	25
24	3-(9-ethyl-3-carbazolylamino)-propyl	400/7	17
25	3-(4-phenylaminophenylamino)-propyl	400/7	22
26	4-(6-methoxy-8-quinolinylamino)-pentyl	400/1	18
27	4-(phenylbutyl)	50/12	3



Scheme 1: Synthesis of the fluorescent arylaminoalkyl derivatives **5-14** and **18-25**
Ar = napthyl (**5, 6, 18, 19**), 2-methoxydibenzofurane (**7-9, 22, 33**), 9-ethylcarbazole (**10, 11, 24**), diphenylamine (**12, 14, 25**), fluorene (**20, 21**).

3392; 3041; 2928; 1715; 1639; 1577; 1529; 1453; 1408; 1247; 1209; 770; 703 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 8.17 (dd, J = 7/2 Hz, 2H, 8'-H-napht.), 7.89 (dd, J = 7/2 Hz, 2H, 5'-H-napht.), 7.56-7.41 (m, 12H aromat.), 6.97 (d, J = 7.2 Hz, 2H, 2'-H-napht.), 4.17 (s, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.43 (t, J = 7 Hz, 4H, Ar-NH-C$\underline{H}_2$), 3.09 (t, J = 7 Hz, 4H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 2.10 (tt, J = 7/7 Hz, 4H, CH_2-C$\underline{H}_2$-CH_2).- MS (40°): m/z = 502 (8%, $M^{+\cdot}$), 180 (52), 170 (35), 156 (32), 143 (68), 127 (43), 115 (35), 69 (66), 18 (100).

N,N'-Bis-[4-(1-naphthylamino)-butyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**6**)

Crystals (ethanol/DMSO), mp. 211°. Yield 45%.- $C_{36}H_{42}N_4 \cdot 2\ C_2H_2O_4$ (710.8) Calcd. C 67.6 H 6.52 N 7.9 Found C 67.3 H 6.65 N 7.8.- IR (KBr): 3392; 3038; 2938; 2845; 1715; 1577; 1520; 1473; 1408; 1279; 1218; 1126; 785; 706 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 8.18 (dd, J = 7/1 Hz, 2H, 8'-H-napht.), 7.94 (dd, J = 7/2 Hz, 2H, 5'-H-napht.), 7.71-7.45 (m, 12H aromat.), 7.13 (d, J = 7.4 Hz, 2H, 2'-H-napht.), 4.14 (bs, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.22 (t, J = 7 Hz, 4H, Ar-NH-C$\underline{H}_2$), 2.97 (t, J = 7 Hz, 4H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 1.75 (m, 8H, CH_2-(CH_2)$_2$-CH_2).- MS (160°): m/z = 530 (6%, $M^{+\cdot}$), 317 (16), 198 (17), 195 (40), 156 (31), 143 (78), 127 (44), 115 (53), 105 (41), 95 (40), 69 (88), 55 (100).

N,N'-Bis-[2-(2-methoxy-3-dibenzofuranylamino)-ethyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**7**)

Crystals (H_2O/DMSO), mp. 197°. Yield 25%.- $C_{38}H_{38}N_4O_4 \cdot 2\ C_2H_2O_4$ (794.8) Calcd. C 63.5 H 5.33 N 7.1 Found C 63.9 H 5.38 N 7.2.- IR (KBr): 3410; 2949; 1634; 1511; 1482; 1353; 1298; 1220; 1162; 1027; 860; 811; 747; 705 cm^{-1}.- ^{1}H-NMR/250 MHz ([D_6]DMSO): δ (ppm) = 7.89 (dd, J = 8/3 Hz, 2H, 9'-H-dibenz.), 7.53 (m, 8H aromat.), 7.28 (m, 4H, 7'-H, 8-H-dibenz.), 6.91 (s, 2H, 4'-H-dibenz.), 6.1-5.2 (bs, NH_2^+, NH, COOH D_2O exchange), 4.21 (bs, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.90 (s, 6H, CH_3), 3.54 (m, 4H, Ar-NH-C$\underline{H}_2$).- MS (110°): m/z = 614 (23%, $M^{+\cdot}$), 388 (31), 358 (20), 240 (14), 227 (77), 226 (76), 213 (43), 212 (27), 211 (59), 198 (50), 131 (49), 119 (43), 69 (88), 45 (100).

N,N'-Bis-[3-(2-methoxy-3-dibenzofuranylamino)-propyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**8**)

Crystals (ethanol/H_2O), mp. 207°. Yield 25%.- $C_{40}H_{42}N_4O_4 \cdot 2\ C_2H_2O_4$ (822.8) Calcd. C 64.2 H 5.64 N 6.8 Found C 64.0 H 5.60 N 6.7.- IR (KBr): 3420; 2949; 1719; 1631; 1511; 1482; 1405; 1298; 1279; 1219; 1162; 1028; 747; 720 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 7.93 (d, J = 8.5 Hz, 2H, 9'-H-dibenz.), 7.56 (m, 8H), 7.31 (m, 4H, 7'-H,

8'-H dibenz.), 6.98 (s, 2H, 4'-H-dibenz.), 4.19 (bs, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.94 (s, 6H, CH_3), 3.32 (t, J = 7 Hz, 4H, Ar-NH-C$\underline{H}_2$), 3.07 (t, J = 7 Hz, 4H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 2.00 (tt, J = 7/7 Hz, 4H, CH_2-C$\underline{H}_2$-CH_2).- MS (380°): m/z = 642 (16%, $M^{+\cdot}$), 372 (10), 270 (41), 240 (60), 226 (65), 213 (100), 198 (90), 170 (63), 133 (39), 105 (38), 91 (44), 55 (18).

N,N'-Bis-[4-(2-methoxy-3-dibenzofuranylamino)-butyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**9**)

Crystals (ethanol/H_2O), mp. 185°. Yield 20%.- $C_{42}H_{46}N_4O_4 \cdot 2\ C_2H_2O_4$ (850.9) Calcd. C 64.9 H 5.92 N 6.6 Found C 64.7 H 5.81 N 6.5.- IR (KBr): 3418; 2935; 2775; 1719; 1631; 1477; 1403; 1278; 1225; 1194; 1169; 1109; 1024; 861; 750; 720; 705 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO): δ (ppm) = 7.87 (d, J = 8 Hz, 2H, 9'-H-dibenz.), 7.49 (m, 8H aromat.), 7.26 (m, 4H, 7'-H, 8'-H-dibenz.), 6.78 (s, 2H, 4'-H-dibenz.), 5.6-4.8 (bs, NH_2^+, NH, COOH, D_2O exchange), 4.14 (bs, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.90 (s, 6H, CH_3), 3.18 (m, 4H, Ar-NH-C$\underline{H}_2$), 2.97 (m, 4H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 1.66 (m, 8H, CH_2-(C$\underline{H}_2$)$_2$-CH_2).- MS (40°): m/z = 670 (1%, $M^{+\cdot}$), 213 (10), 198 (10), 148 (10), 137 (16), 109 (10), 95 (17), 81 (47), 69 (100), 55 (35).

N,N'-Bis-[3-(9-ethyl-3-carbazolylamino)-propyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**10**)

Crystals (ethanol/DMSO), mp. 176°, (degr.). Yield 30%.- $C_{42}H_{48}N_6 \cdot 2\ C_2H_2O_4$ (816.9) Calcd. C 67.6 H 6.42 N 10.3 Found C 67.5 H 6.47 N 10.0.- IR (KBr): 3404; 2967; 2797; 1717; 1700; 1605; 1490; 1470; 1403; 1308; 1277; 1229; 1152; 802; 765; 747 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 8.32 (s, 2H, 4'-H-carbaz.), 8.18 (d, J = 7.5 Hz, 2H, 5'-H-carbaz.), 7.83 (d, J = 8.5 Hz, 2H, 1'-H-carbaz.), 7.70 (d, J = 8.3 Hz, 2H, 8'-H-carbaz.), 7.56 (m, 8H aromat.), 7.31 (dd, J = 7.5/7.5 Hz, 2H, 6'-H-carbaz.), 4.51 (q, J = 7 Hz, 4H, C$\underline{H}_2$-CH_3), 4.16 (s, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.55 (m, 4H, Ar-NH-C$\underline{H}_2$), 3.09 (m, 4H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 2.08 (m, 4H, CH_2-C$\underline{H}_2$-CH_2), 1.35 (t, J = 7 Hz, 6H, CH_3).- MS (60°): m/z = 636 (4%, $M^{+\cdot}$), 237 (27), 223 (31), 210 (22), 194 (44), 181 (32), 165 (21), 110 (42), 78 (45), 69 (63), 63 (100), 55 (94).

N,N'-Bis-[4-(9-ethyl-3-carbazolylamino)-butyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**11**)

Light brown crystals (ethanol/DMSO), mp. 211° (degr.). Yield 60%.- $C_{44}H_{52}N_6 \cdot 2\ C_2H_2O_4$ (845.0) Calcd. C 68.2 H 6.68 N 9.9 Found C 68.0 H 6.49 N 10.0.- IR (KBr): 3406; 2968; 2782; 1717; 1629; 1469; 1403; 1344; 1277; 1232; 1151; 798; 747; 720 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 8.34 (s, 2H, 4'-H-carbaz.), 8.20 (d, J = 7.6 Hz, 2H, 5'-H-carbaz.), 7.81 (d, J = 8.5 Hz, 2H, 1'-H-carbaz.), 7.70 (d, J = 8.2 Hz, 2H, 8'-H-carbaz.), 7.55 (m, 8H aromat.), 7.35 (dd, J = 7.5/7.5 Hz, 2H, 6'-H-carbaz.), 4.51 (q, J = 7 Hz, 4H, C$\underline{H}_2$-CH_3), 4.15 (s, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.48 (m, 4H, Ar-NH-CH_2), 3.00 (m, 4H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 1.74 (m, 8H, CH_2-(C$\underline{H}_2$)$_2$-CH_2), 1.35 (t, J = 7 Hz, 6H, CH_3).- MS (120°): m/z = 664 (8%, $M^{+\cdot}$), 210 (17), 194 (19), 181 (12), 91 (18), 78 (40), 69 (10), 63 (78), 45 (100).

N,N'-Bis-[2-[4-(phenylamino)-phenylamino]-ethyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**12**)

Brown crystals (ethanol/H_2O), mp. 188°. Yield 40%.- $C_{36}H_{40}N_6 \cdot 2\ C_2H_2O_4$ (736.8) Calcd. C 65.2 H 6.02 N 11.4 Found C 65.5 H 5.84 N 11.6.- IR (KBr): 3391; 2919; 1718; 1597; 1514; 1407; 1313; 1279; 1214; 905; 826; 748; 719; 696 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]-DMSO/CF_3COOD): δ (ppm) = 7.60 (m, 4H, aromat.), 7.26-7.07 (m, 16H aromat.), 6.88 (dd, J = 7/7 Hz, 2H, 4''-H), 4.28 (bs, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.58 (m, 4H, Ar-NH-C$\underline{H}_2$), 3.30 (m, 4H, Ar-NH-CH_2-C$\underline{H}_2$).- MS (180°): m/z = 556 (28%, $M^{+\cdot}$), 359 (10), 227 (15), 197 (100), 168 (19), 105 (17), 44 (31).

N,N'-Bis-[3-[4-(phenylamino)-phenylamino]-propyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**13**)

Light brown crystals (ethanol/DMSO), mp. 177°. Yield 30%.- $C_{38}H_{44}N_6 \cdot 2\ C_2H_2O_4$ (764.9) Calcd. C 65.9 H 6.38 N 11.0 Found C 65.5 H 6.38 N 11.2.- IR (KBr): 3382; 3304; 3016; 2949; 2783; 1717; 1700; 1632; 1595; 1572; 1493; 1402; 1303; 1229; 1180; 1108; 750; 721; 695 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 7.55 (m, 4H aromat.), 7.32 (m, 8H aromat.), 7.15 (m, 8H aromat.), 6.97 (dd, J = 7/7 Hz, 2H, 4''-H), 4.17 (s, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.37 (m, 4H, Ar-NH-C$\underline{H}_2$), 3.09 (m, 4H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 2.04 (m, 4H, CH_2-C$\underline{H}_2$-CH_2).- MS (40°): m/z = 584 (2%, $M^{+\cdot}$), 222 (23), 211 (16), 197 (30), 184 (35), 183 (18), 168 (15), 167 (44), 91 (20), 78 (50), 69 (55), 63 (100), 55 (78).

N,N'-Bis-[4-[4-(phenylamino)-phenylamino]-butyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**14**)

Grey crystals (ethanol/H_2O), mp. 203°. Yield 45%.- $C_{40}H_{48}N_6 \cdot 2\ C_2H_2O_4$ (792.9) Calcd. C 66.6 H 6.61 N 10.6 Found C 66.5 H 6.50 N 10.4.- IR (KBr): 3413; 2943; 2782; 1717; 1700; 1595; 1512; 1492; 1403; 1313; 1278; 1218; 1108; 832; 749; 720; 697 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 7.56 (m, 4H aromat.), 7.31 (m, 8H aromat.), 7.15 (m, 8H aromat.), 6.93 (dd, J = 7/7 Hz, 2H, 4''-H), 4.15 (s, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.29 (m, 4H, Ar-NH-C$\underline{H}_2$), 2.99 (m, 4H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 1.69 (m, 8H, CH_2-(C$\underline{H}_2$)$_2$-CH_2).- MS (50°): m/z = 612 (20%, $M^{+\cdot}$), 239 (11), 238 (26), 197 (20), 184 (100), 183 (19), 167 (21), 143 (21), 105 (16), 57 (11), 45 (20).

N,N'-Bis-[4-(6-methoxy-8-quinolylamino)-pentyl]-benzene-1,3-dimethanamine-dihydrogenoxalate (**15**)

Yellow green crystals (ethanol), mp. 186°. Yield 40%.- $C_{38}H_{48}N_6O_2 \cdot 2\ C_2H_2O_4 \cdot 1\ 1/2\ H_2O$ (827.9) Calcd. C 60.9 H 6.45 N 10.2 Found C 60.7 H 6.37 N 9.9.- IR (KBr): 3383; 2956; 1722; 1614; 1576; 1517; 1454; 1422; 1386; 1218; 1197; 1163; 1049; 1028; 824; 791; 704 cm^{-1}.- ^{1}H-NMR/250 MHz ([D_6]DMSO): δ (ppm) = 8.54 (dd, J = 4.1/1.4 Hz, 2H, 2'-H-quinol.), 8.10 (dd, J = 8.3/1.3 Hz, 2H, 4'-H-quinol.), 7.55-7.41 (m, 6H aromat.), 6.49 (d, J = 2.2 Hz, 2H, 5'-H-quinol.), 6.27 (d, J = 2.2 Hz, 2H, 7'-H-quinol.), 5.3-4.4 (bs, NH_2^+, NH, COOH, D_2O exchange), 4.16 (bs, 4H, Ar-C$\underline{H}_2$-NH_2^+), 3.87 (s, 6H, OCH_3), 3.63 (m, 2H, CH), 2.94 (m, 4H, NH_2^+-C$\underline{H}_2$-CH_2), 1.81-1.58 (m, 8H, CH-(C$\underline{H}_2$)$_2$-CH_2), 1.19 (d, J = 6 Hz, 6H, CH-C$\underline{H}_3$).- MS (150°): m/z = 620 (12%, $M^{+\cdot}$), 445 (69), 379 (13), 361 (25), 243 (37), 241 (100), 201 (87), 187 (51), 175 (44), 159 (16), 105 (23), 44 (55).

N,N''-m-Xylylene-bis-[N-(4-aminobutyl)-naphthalene-2-sulfonamide]-dihydrochloride (**16**)

Crystals (ethanol/ether), mp. 92°. Yield 35%.- $C_{36}H_{42}N_4O_4S_2 \cdot 2\ HCl \cdot H_2O$ (749.8) Calcd. C 57.7 H 6.18 N 7.5 Found C 57.9 H 6.17 N 7.2.- IR (KBr): 3386; 3134; 3053; 2940; 2867; 1649; 1588; 1429; 1319; 1153; 1073; 863; 818; 750; 657 cm^{-1}.- ^{1}H-NMR/250 MHz ([D_6]DMSO): δ (ppm) = 9.38 (bs, 4H, NH_2^+, D_2O exchange), 8.45 (s, 2H, 1-H-napht.), 8.16 (m, 4H, 3-H-napht., 4-H-napht.), 8.06 (dd, J = 7/2 Hz, 2H, 8-H-napht.), 7.84 (m, 4H, 5-H-napht., SO_2-NH, D_2O exchange), 7.75 (m, 5H aromat.), 7.64 (d, J = 7 Hz, 2H, 4-H, 6-H), 7.52 (t, J = 7 Hz, 1H, 5-H), 4.07 (s, 4H, Ar-C$\underline{H}_2$-NH_2^+), 2.79 (m, 8H, NH-C$\underline{H}_2$-CH_2), 1.65, 1.44 (2m, 8H, NH-CH_2-C$\underline{H}_2$).- MS (380°): m/z = 658 (1%, $M^{+\cdot}$), 261 (12), 191 (23), 127 (100), 70 (97).

N,N''-m-Xylylene-bis-[N-(5-aminopentyl)-5-dimethylaminonaphthalene-1-sulfonamide]-tetrahydrogenoxalate (**17**)

Crystals (ethanol/H_2O), mp. 121°. Yield 25%.- $C_{42}H_{56}N_6O_4S_2 \cdot 4\ C_2H_2O_4 \cdot 2\ H_2O$ (1169.2) Calcd. C 51.4 H 5.86 N 7.2 Found C 51.4 H 5.79

N 6.9.- IR (KBr): 3422; 2939; 2863; 1724; 1636; 1512; 1463; 1317; 1203; 1142; 1093; 794; 704 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO): δ (ppm) = 8.45 (d, J = 8.2 Hz, 2H, 2-H-napht.), 8.29 (d, J = 8.4 Hz, 2H, 8-H-napht.), 8.08 (d, J = 7.1 Hz, 2H, 4-H-napht.), 7.92 (bs, 2H, SO_2-NH, D_2O exchange), 7.62-7.50 (m, 8H aromat.), 7.25 (d, J = 7.5 Hz, 2H, 6-H-napht.), 6.4-5.8 (bs, NH_2^+, COOH, D_2O exchange), 4.09 (bs, 4H, Ar-C$\underline{H}_2$-NH_2^+), 2.82 (s, 12H, CH_3), 2.76 (m, 8H, NH-C$\underline{H}_2$-CH_2), 1.50, 1.33 (2m, 8H, NH-CH_2-C$\underline{H}_2$), 1.20 (m, 4H $(CH_2)_2$-C$\underline{H}_2$-$(CH_2)_2$).- MS (280°): m/z = 772 (1%, $M^{+\cdot}$), 250 (51), 169 (39), 154 (17), 127 (17), 105 (15), 84 (21), 44 (100).

N,N',N''-Tris-[3-(1-naphthylamino)-propyl]-benzene-1,3,5-trimethanamine-trihydrogenoxalate (**18**)

Crystals (ethanol/H_2O), mp. 201°. Yield 35%.- $C_{48}H_{54}N_6 \cdot 3\ C_2H_2O_4$ (985.1) Calcd. C 65.8 H 6.14 N 8.5 Found C 65.5 H 6.07 N 8.4.- IR (KBr): 3396; 2950; 2848; 1718; 1642; 1579; 1527; 1479; 1409; 1279; 1227; 1129; 787; 769; 719 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 8.16 (dd, J = 7/1 Hz, 3H, 8'-H-napht.), 7.90 (dd, J = 7/1 Hz, 3H, 5'-H-napht.), 7.63 (s, 3H aromat.), 7.55 (m, 9H, 4'-H, 6'-H, 7'-H-napht.), 7.44 (dd, J = 7.8/7.8 Hz, 3H, 3'-H-napht.), 7.03 (d, J = 7.8 Hz, 3H, 2'-H-napht.), 4.16 (s, 6H, Ar-C$\underline{H}_2$-NH_2^+), 3.44 (t, J = 7 Hz, 6H, Ar-NH-C$\underline{H}_2$), 3.11 (t, J = 7 Hz, 6H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 2.11 (m, 6H, CH_2-C$\underline{H}_2$-CH_2).- MS (170°): m/z = 714 (1%, $M^{+\cdot}$), 180 (48), 169 (20), 156 (20), 143 (100), 127 (38), 115 (41), 104 (30), 91 (13), 45 (63).

N,N',N''-Tris-[4-(1-naphthylamino)-butyl]-benzene-1,3,5-trimethanamine-trihydrogenoxalate (**19**)

Crystals (ethanol/H_2O), mp. 200°. Yield 70%.- $C_{51}H_{60}N_6 \cdot 3\ C_2H_2O_4$ (1027.1) Calcd. C 66.7 H 6.48 N 8.2 Found C 66.5 H 6.62 N 7.9.- IR (KBr): 3407; 2925; 2851; 1718; 1646; 1579; 1528; 1476; 1407; 1342; 1278; 1217; 1127; 770; 719 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]-DMSO/CF_3COOD): δ (ppm) = 8.19 (d, J = 7 Hz, 3H, 8'-H-napht.), 7.99 (d, J = 7 Hz, 3H, 5'-H-napht.), 7.78 (s, 3H aromat.), 7.63 (m, 9H, 4'-H, 6'-H, 7'-H-napht.), 7.54 (dd, J = 7/7 Hz, 3H, 3'-H-napht.), 7.36 (d, J = 7 Hz, 3H, 2'-H-napht.), 4.16 (s, 6H, Ar-C$\underline{H}_2$-NH_2^+), 3.45 (m, 6H, Ar-NH-C$\underline{H}_2$), 3.00 (m, 6H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 1.79 (m, 6H, CH_2-$(C\underline{H}_2)_2$-CH_2).- MS (340°): m/z = 756 (10%, $M^{+\cdot}$), 185 (73), 170 (31), 156 (12), 142 (24), 137 (26), 127 (11), 112 (30), 97 (21), 81 (46), 69 (100), 57 (52).

N,N',N''-Tris-[3-(2-fluorenylamino)-propyl]-benzene-1,3,5-trimethanamine-trihydrochloride (**20**)

Light yellow crystals (ethanol/H_2O), mp. 185°. Yield 45%.- $C_{57}H_{60}N_6 \cdot 6$ HCl (1047.9) Calcd. C 65.0 H 6.35 N 8.0 Found C 65.0 H 6.14 N 8.3.- IR (KBr): 3413; 2921; 2749; 1615; 1575; 1455; 1401; 1308; 765; 733 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 8.04 (d, J = 8.1 Hz, 3H, 4'-H-fluoren.), 7.96 (d, J = 7.4 Hz, 3H, 5'-H-fluoren.), 7.89 (s, 3H aromat.), 7.81 (d, 3H, 1'-H-fluoren.), 7.63 (m, 6H, 3'-H, 8'-H-fluoren.), 7.41 (m, 6H, 6'-H, 7'-H-fluoren., 4.04 (s, 6H, Ar-C$\underline{H}_2$-NH_2^+), 3.99 (s, 6H, 9'-H-fluoren.), 3.41 (m, 6H, Ar-NH_2^+-C$\underline{H}_2$), 3.17 (m, 6H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 2.21 (m, 6H, CH_2-C$\underline{H}_2$-CH_2).- MS (+FAB/DMSO/*m*-nitrobenzylalcohol): m/z = 829 (1%, $[M+H]^+$), 239 (15), 194 (10), 165 (15), 107 (67), 90 (69), 76 (74).

N,N',N''-Tris-[4-(2-fluorenylamino)-butyl]-benzene-1,3,5-trimethanamine-hexahydrochloride (**21**)

Light yellow crystals (ethanol/H_2O), mp. 276° (degr.). Yield 25%.- $C_{60}H_{66}N_6 \cdot 6$ HCl (1090.0) Calcd. C 66.1 H 6.66 N 7.7 Found C 66.2 H 6.60 N 7.4.- IR (KBr): 3414; 2930; 2764; 2436; 1576; 1455; 1400; 1306; 1193; 953; 831; 765; 733 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]-DMSO/CF_3COOD): δ (ppm) = 8.07 (d, J = 8.2 Hz, 3H, 4'-H-fluoren.), 7.95 (d, J = 7 Hz, 3H, 5'-H-fluoren.), 7.79 (s, 3H aromat.), 7.75 (s, 3H, 1'-H-fluoren.), 7.61 (m, 6H, 3'-H, 8'-H-fluoren.), 7.41 (m, 6H, 6'-H, 7'-H-fluoren.), 4.03 (s, 6H, Ar-C$\underline{H}_2$-NH_2^+), 4.01 (s, 6H, 9'-H-fluoren.), 3.44 (m, 6H, Ar-NH_2^+-C$\underline{H}_2$), 3.03 (m, 6H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 1.79 (m, 12H, CH_2-$(C\underline{H}_2)_2$-CH_2).- MS (+FAB/DMSO/glycerol): m/z = 871 (2%, $[M+H]^+$), 252 (13), 236 (41), 234 (57), 208 (11), 207 (21), 194 (100), 181 (46), 180 (38), 165 (62), 119 (35), 71 (50).

N,N',N''-Tris-[3-(2-methoxy-3-dibenzofuranylamino)-propyl]-benzene-1,3,5-trimethanamine-trihydrogenoxalate (**22**)

Crystals (ethanol/H_2O), mp. 182° (degr.). Yield 20%.- $C_{57}H_{60}N_6O_6 \cdot 3\ C_2H_2O_4$ (1195.2) Calcd. C 63.3 H 5.57 N 7.0 Found C 63.1 H 5.48 N 7.1.- IR (KBr): 3411; 2944; 1719; 1632; 1511; 1483; 1298; 1281; 1220; 1163; 1029; 746; 721 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 7.91 (d, J = 7.5 Hz, 3H, 9'-H-dibenz.), 7.64 (s, 3H aromat.), 7.58 (s, 3H, 1'-H-dibenz.), 7.53 (d, J = 7.5 Hz, 3H, 6'-H-dibenz.), 7.28 (m, 6H, 7'-H, 8'-H-dibenz.), 6.91 (s, 3H, 4'-H-dibenz.), 4.19 (s, 6H, Ar-C$\underline{H}_2$-NH_2^+), 3.92 (s, 9H, CH_3), 3.30 (m, 6H, Ar-NH-C$\underline{H}_2$), 3.06 (m, 6H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 1.99 (m, 6H, CH_2-C$\underline{H}_2$-CH_2).- MS (+FAB/DMSO/glycerol): m/z = 925 (1%, $[M+H]^+$), 226 (10), 171 (12), 74 (55).

N,N',N''-Tris-[4-(2-methoxy-3-dibenzofuranylamino)-butyl]-benzene-1,3,5-trimethanamine-trihydrogenoxalate (**23**)

Crystals (ethanol/H_2O), mp. 134° (degr.). Yield 20%.- $C_{60}H_{66}N_6O_6 \cdot 3\ C_2H_2O_4$ (1237.3) Calcd. C 64.1 H 5.87 N 6.8 Found C 63.9 H 6.24 N 6.5.- IR (KBr): 3413; 2942; 1718; 1631; 1475; 1401; 1306; 1275; 1226; 1191; 1113; 1021; 860; 813; 763; 749; 720; 704 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 7.98 (m, 3H, 9'-H-dibenz.), 7.69 (m, 6H aromat.), 7.57 (m, 3H, 6'-H-dibenz.), 7.35 (m, 6H, 7'-H, 8'-H-dibenz.), 7.14 (s, 3H, 4'-H-dibenz.), 3.98 (m, 15H, Ar-C$\underline{H}_2$-NH_2^+, CH_3), 3.28 (m, 6H, Ar-NH-C$\underline{H}_2$), 2.85 (m, 6H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 1.68 (m, 12H, CH_2-$(C\underline{H}_2)_2$-CH_2).- MS (+FAB/DMSO/glycerol): m/z = 967 (1%, $[M+H]^+$), 284 (39), 268 (60), 254 (15), 226 (67), 213 (41), 198 (49), 183 (38), 119 (100), 84 (47).

N,N',N''-Tris-[3-(9-ethyl-3-carbazolylamino)-propyl]-benzene-1,3,5-trimethanamine-trihydrogenoxalate (**24**)

Brown crystals (ethanol/H_2O), mp. 195° (degr.). Yield 30%.- $C_{60}H_{69}N_9 \cdot 3\ C_2H_2O_4$ (1186.3) Calcd. C 66.8 H 6.37 N 10.6 Found C 66.7 H 6.24 N 10.3.- IR (KBr): 3422; 2991; 1715; 1640; 1594; 1583; 1331; 1239; 1148; 805; 752; 722 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 8.33 (s, 3H, 4'-H-carbaz.), 8.21 (d, J = 7.5 Hz, 3H, 5'-H-carbaz.), 7.82 (d, J = 8.2 Hz, 3H, 1'-H-carbaz.), 7.69 (d, J = 8.1 Hz, 3H, 8'-H-carbaz.), 7.60 (m, 9H aromat.), 7.31 (m, 3H, 6'-H-carbaz.), 4.51 (q, J = 7 Hz, 6H, $C\underline{H}_2$-CH_3), 4.15 (s, 6H, Ar-C$\underline{H}_2$-NH_2^+), 3.56 (m, 6H, Ar-NH-C$\underline{H}_2$), 3.08 (m, 6H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 2.08 (m, 6H, CH_2-C$\underline{H}_2$-CH_2), 1.36 (t, J = 7 Hz, 9H, CH_3).- MS (+FAB/DMSO/glycerol): m/z = 916 (<1%, $[M+H]^+$), 278 (21), 267 (20), 251 (10), 237 (45), 223 (49), 209 (21), 195 (28), 194 (21), 180 (33), 167 (18), 119 (26), 76 44).

N,N',N''-Tris-[3-[4-(phenylamino)-phenylamino]-propyl]-benzene-1,3,5-trimethanamine-trihydrogenoxalate (**25**)

Crystals (ethanol/H_2O), mp. 193°. Yield 40%.- $C_{54}H_{63}N_9 \cdot 3\ C_2H_2O_4$ (1108.2) Calcd. C 65.0 H 6.27 N 11.4 Found C 64.6 H 6.21 N 11.1.- IR (KBr): 3394; 2950; 2787; 1720; 1595; 1512; 1493; 1458; 1316; 1225; 835; 749; 719 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 7.68 (m, 3H aromat.), 7.33 (m, 12H aromat.), 7.20 (m, 12H aromat.), 6.95 (dd, J = 7/7 Hz, 3H, 4''-H), 4.20 (s, 6H, Ar-C$\underline{H}_2$-NH_2^+), 3.40 (m, 6H, Ar-NH-C$\underline{H}_2$), 3.12 (m, 6H, Ar-CH_2-NH_2^+-C$\underline{H}_2$), 2.06 (m, 6H, CH_2-C$\underline{H}_2$-CH_2).- MS (+FAB/DMSO/glycerol): m/z = 838 (<1%, $[M+H]^+$), 78 (23), 74 (60).

N,N',N''-Tris-[4-(6-methoxy-8-quinolylamino)-pentyl]-benzene-1,3,5-trimethanamine-trihydrogenoxalate (**26**)

Yellow green crystals (ethanol/H_2O), mp. 155°. Yield 45%.- $C_{54}H_{69}N_9O_3 \cdot 2\ C_2H_2O_4$ (1162.3) Calcd. C 62.0 H 6.50 N 10.8 Found C 62.1 H 6.58 N 10.8.- IR (KBr): 3413; 2955; 1719; 1615; 1576; 1518; 1454; 1421; 1387; 1278; 1218; 1165; 824; 791; 721 cm^{-1}.- ^{1}H-NMR/300 MHz ([D_6]DMSO/CF_3COOD): δ (ppm) = 8.78 (dd, J = 4.2/1.5 Hz, 3H, 2'-H-quinol.), 8.51 (dd, J = 7.2/1.3 Hz, 3H, 4'-H-quinol.), 7.22 (dd, J = 8.2/5 Hz, 3H, 3'-H-quinol.), 7.61 (m, 3H aromat.), 6.80 (d, J = 2.4 Hz, 3H, 5'-H-quinol.), 6.57 (d, J = 2.4 Hz, 3H, 7'-H-quinol.), 4.15 (s, 6H, Ar-C$\underline{H}_2$-NH_2^+), 3.88 (s, 9H, OCH_3), 3.75 (m, 3H, CH), 2.98 (m, 6H, NH_2^+-C$\underline{H}_2$-CH_2), 1.8-1.6 (m, 12H, CH-(C$\underline{H}_2$)$_2$-CH_2), 1.25 (d, J = 6 Hz, 9H, CH-C$\underline{H}_3$).- MS (+FAB/DMSO/glycerol): m/z = 892 (2%, $[M+H]^+$), 243 (42), 241 (55), 201 (53), 187 (22), 175 (69), 159 (13), 117 (21), 74 (48).

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[Ph206]

Erratum

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