Supporting Information

Synthesis of Ultra-Short-Acting Neuromuscular Blocker GW 0430: A Remarkably Stereo- and Regioselective Synthesis of Mixed-Tetrahydroisoquinolinium Chlorofumarates

Vicente Samano,* John A. Ray, James B. Thompson, Robert A. Mook, Jr., David K. Jung, Cecilia S. Koble, Michael T. Martin, Eric C. Bigham, Craig S. Regitz, Paul L. Feldman, Eric E. Boros*

General Experimental. All reagent chemicals were used without purification. Analytical HPLC analyses were performed on 4 × 250 mm 5μ Si60 LiChrosorb columns (E. Merck, Darmstad, Germany) at a flow rate of 1.6 mL/min. Preparative HPLC separations were performed on twin Porasil (15-20μ) cartridges (Waters/Millipore, Milford, MA, USA) at a flow rate of 60 mL/min. The mobile phase for analytical and preparative HPLC separations consisted of 0-25% MeOH/CH_2Cl_2 mixtures containing 0.25 mL methanesulfonic acid/L. Elemental analyses were performed by Atlantic Microlabs, Norcross, Georgia. All ^{1}H NMR spectra were recorded at 300, 400 or 500 MHz and coupling constants are in Hz. Chemical shifts are reported in ppm relative to the residual protonated solvent resonance of DMSO-d_6 (δ2.50). Positive ion flow injection electrospray mass spectra (MS) are reported in the form *m/z* (doubly charged positive ion, relative intensity). The 2'- and 6'-protons on the trimethoxyphenyl substituent of quaternary head groups **4a**, **4b**, and **12** are nonequivalent by ^{1}H NMR (DMSO-d_6) appearing as broadened signals. Heating the ^{1}H NMR samples produces coalescence of these peaks. This slow exchange process presumably results from hindered rotation of the trimethoxyphenyl substituent.

(1*S*)-6,7-Dimethoxy-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydroisoquinolinium formate (2a)

To a solution of triethylamine (6.8 g, 67.1 mmol) in acetonitrile (90 mL) was slowly added formic acid (7.73 g, 168 mmol) followed by a mixture of 3,4-dihydroisoquinoline **8**[9] (12.0 g, 33.6 mmol), RuCl[(1*R*,2*R*)-1-naphthyl-$SO_2NCH(C_6H_5)CH(C_6H_5)NH_2$]($\eta^6$-benzene)[10] (0.13 g, 0.21 mmol), and acetonitrile (18

mL). The reaction mixture was stirred overnight at ambient temperature and analyzed by chiral HPLC (83% ee, Chiralpak AS, 20% IPA/hexanes/0.1% TEA). The resulting slurry was cooled in an ice bath for 30 min, filtered, and rinsed with acetonitrile (20 mL) to yield the formic acid salt of **2a** (10.4 g, 76% yield) as a white solid: Chiral HPLC (99% ee, Chiralpak AS, 20% IPA/hexanes/0.1% TEA); ^{1}H NMR (DMSO-d_6): δ 2.65-2.75 (m, 1H), 2.80-2.85 (m, 1H), 2.90-3.00 (m, 1H), 3.05-3.15 (m, 1H), 3.57 (s, 3H), 3.65 (s, 3H), 3.67 (s, 3H), 3.72 (s, 3H), 3.78 (s, 3H), 4.60-5.00 (br s, 2H), 5.05 (s, 1H), 6.30 (s, 1H), 6.60 (s, 2H), 6.75 (s, 1H), 8.30 (s, 1H). Anal. Calcd. for $C_{20}H_{25}NO_5$·HCOOH·H2O: C, 59.57; H, 6.90; N, 3.31. Found: C, 59.57; H, 6.88; N, 3.30.

(*S*)-(+)-Cryptostyline III [(1*S*)-6,7-Dimethoxy-2-methyl-1-(2,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydroisoquinoline] (2b)

A mixture of the formic acid salt of **2a** (108 g, 0.26 mol), 37% formalin (450 mL) and 97% formic acid (225 ml) were heated at 100°C for 2h and allowed to cool to ambient temperature. The solution was cooled in a MeOH/ice bath and made basic with aqueous NaOH solution. The resulting mixture was extracted with CH_2Cl_2 and the organic layer was washed with water and brine, dried (Na_2SO_4) and concentrated. Crystallization from MeOH provided **2b** (95.5 g, 96% yield) as a white solid: Chiral HPLC (99% ee, Daicel Chiralcel OD-H, 30% IPA/hexanes/0.1% TEA); ^{1}H NMR (DMSO-d_6): δ 2.20 (s, 3H), 2.45-2.55 (m, 1H), 2.65-2.70 (m, 1H), 3.00-3.15 (m, 2H), 3.55 (s, 3H), 3.70 (s, 3H), 3.78 (s, 9H), 4.18 (br s, 1H), 6.25 (s, 1H), 6.65 (s, 2H), 6.80 (s, 1H).

Procedure A. (1*R*,2*S*)- and (1*R*,2*R*)-6,7-Dimethoxy-2-(3-hydroxypropyl)-2-methyl-1-[(3,4,5-trimethoxyphenyl)methyl]-1,2,3,4-tetrahydroisoquinolinium chloride (3a and 3b)

A mixture of (*R*)-(-)-5'-methoxylaudanosine[4] (**1**, 23.5 g, 61.0 mmol), NaI (18.3 g, 122.0 mmol), Na_2CO_3 (1.6 g, 15.2 mmol), 3-chloro-1-propanol (11.5 g, 122.0 mmol) and 2-butanone (245 mL) was heated to reflux for 18 h under nitrogen atmosphere. Solvent was evaporated and the residue was dissolved in water and washed EtOAc. The aqueous phase was stirred with Dowex 1×8-50 (400 mL), filtered, and the filtrate was saturated with NaCl. The mixture was extracted with $CHCl_3$ and the combined organic layers were dried (Na_2SO_4) and concentrated to provide a ~3:1 mixture of **3a** and **3b** (31.5 g, 99% yield) as a yellow solid. Preparative HPLC (Silica gel, 12% MeOH/CH_2Cl_2, 0.25 mL methane sulfonic acid/L) provided **3a** (10.4 g, 35% yield) as a yellow hygroscopic solid: ^{1}H NMR (DMSO-d_6): δ 1.95-2.05 (m, 2H), 2.94 (t, 1H), 3.08 (br s, 2H), 3.36 (s, 3H), 3.38 (s, 3H), 3.40-3.50 (m, 3H), 3.41 (s, 3H), 3.55-3.65 (m, 3H), 3.68 (s, 3H), 3.72 (s, 3H), 3.79 (s, 3H), 3.85-3.90 (m, 1H), 4.80 (t, 1H), 4.85 (s, 1H), 5.79 (s, 1H), 6.46 (s, 2H), 6.92 (s, 1H); MS (*m/z*): 446 (M^+, 100).

(1*S*,2*R*)- and (1*S*,2*S*)-6,7-Dimethoxy-2-(3-hydroxypropyl)-2-methyl-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydroisoquinolinium chloride (4a and 4b)

(*S*)-(+)-Cryptostyline III[5] (**2b**, 56.0 g, 150 mmol) was subjected to procedure A to provide a ~3:1 mixture of **4a** and **4b** (69.5 g, 99% yield) as a white solid: ^{1}H NMR (DMSO-d_6) showed two sets of signals for **4a** and **4b**; MS (*m/z*): 432 (M^+, 9). Anal. Calcd. for $C_{24}H_{34}ClNO_6 \cdot 0.89\ CHCl_3 \cdot 0.75$ H2O: C, 50.86; H, 6.24; N, 2.38. Found: C, 50.86; H, 6.24; N, 2.22.

(*Z*)-2-Chloro-4-{3-[(1*S*,2*R*)-6,7-dimethoxy-2-methyl-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydro-2-isoquinolinio]propyl}-1-{3-{(1*R*,2*S*)-6,7-dimethoxy-2-methyl-1-[(3,4,5-trimethoxyphenyl)methyl]-1,2,3,4-tetrahydro-2-isoquinolinio}propyl}-2-butenedioate dichloride and (*Z*)-2-Chloro-1-{3-{(1*S*,2*R*)-6,7-dimethoxy-2-methyl-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydro-2-isoquinolinio}propyl}-4-{3-{(1*R*,2*S*)-6,7-dimethoxy-2-methyl-1-[(3,4,5-trimethoxyphenyl)methyl]-1,2,3,4-tetrahydro-2-isoquinolinio}propyl}-2-butenedioate dichloride (1:1) (5ab)

To a solution of **3a** (2.34 g, 4.2 mmol) and a ~3:1 mixture of **4a** and **4b** (2.4 g, 4.2 mmol) in 1,2-dichloroethane (DCE, 30 mL) was added chlorofumaryl chloride[7] (0.83 g, 4.4 mmol) and the solution was stirred at ambient temperature under nitrogen atmosphere for 18 h. Solvent was evaporated and the residue was purified by preparative HPLC (Silica gel, 5-20% MeOH/CH_2Cl_2, 0.25 mL methane sulfonic acid/L). The appropriate fractions were combined and most of the MeOH was removed by coevaporation with $CHCl_3$. The remaining $CHCl_3$ solution was washed with 1:1 brine/water, dried (Na_2SO_4), and concentrated. Lyophilization from water provided **5ab** (0.70 g, 14% yield) as a white solid: ^{1}H NMR (DMSO-d_6): δ 2.22-2.30 (m, 8H), 2.88 (br s, 6H), 2.75-2.89 (m, 2H), 3.27 (s, 6H), 3.37 (s, 6H), 3.57 (s, 6H), 3.61 (s, 6H), 3.64 (s, 12H), 3.695 (s, 6H), 3.70 (s, 3H), 3.71 (s, 3H), 3.77 (s, 3H), 3.78 (s, 3H), 3.04-4.03 (br m, 38H), 4.20-4.30 (m, 8H), 4.70-4.80 (m, 2H), 5.70 (s, 2H), 5.84 (s, 1H), 5.88 (s, 1H), 6.14(br, 2H), 6.25-6.45 (s, 6H), 6.84 (s, 2H), 6.94 (s 2H), 7.12 (s, 1H), 7.16 (s, 1H), 7.24 (br, 2H); MS (*m/z*): 496 (M^{2+}, 100). Anal. Calcd. for $C_{53}H_{69}Cl_3N_2O_{14}\cdot 4.0\ H_2O$: C, 56.01; H, 6.83; N, 2.46; Cl, 9.36. Found: C, 55.84; H, 6.71; N, 2.40; Cl, 9.60.

1,3-Dioxa-2-thiane 2,2-dioxide[13] (10)

To a solution of 1,3-propanediol (50.0 g, 0.65 mol) in CCl_4 (650 mL) was added thionyl chloride (57.5 mL, 93.7 g, 0.79 mol) and the mixture was heated to reflux for 1.5 h. The solution was cooled to 0°C and diluted with acetonitrile (650 mL) followed by sequential addition of $RuCl_3 \cdot H_2O$ (81 mg, 0.39 mmol), $NaIO_4$ (210.0 g, 0.98 mol), and H_2O (980 mL). The resulting orange mixture was stirred at ambient temperature for 1.5 h and then diluted with Et_2O (6 L). The separated organic phase was washed with water, satd. $NaHCO_3$ and brine. The Et_2O layer was dried and filtered through a bed of silica gel. The filtrated was concentrated and the resulting oil was treated with Et_2O (50 mL) and hexanes (100 mL) and stored at 5°C for 18 h. Filtration of the resulting precipitate afforded the title compound as an off-white solid (79.0 g, 87% yield): mp 54-56°C.

Procedure B. 3-{(1*R*,2*S*)-6,7-Dimethoxy-2-methyl-1-[(3,4,5-trimethoxyphenyl) methyl]-1,2,3,4-tetrahydro-2-isoquinolinio}propyl-1-sulfate (11)

A mixture of (*R*)-(-)-5'-methoxylaudanosine[4] (**1**, 52.6 g, 0.13 mol) and **10** (30.3 g, o.22 mol) in acetone (450 mL) was heated to 65°C for 5 h. The mixture was cooled to ambient temperature and the resulting precipitate was filtered and triturated with acetone to yield **11** (49.3 g, 69% yield) as an off-white powder: mp 191-193ºC; HPLC (98% *de*, silica gel, 15% MeOH/CH_2Cl_2, 0.25 mL methane sulfonic acid/L); ^{1}H NMR (DMSO-d_6): δ 2.05-2.15 (m, 2H), 2.85 (br t, 1H), 3.05-3.10 (m, 2H), 3.29 (s, 6H), 3.61 (s, 3H), 3.64 (s, 6H), 3.30-3.70 (m, 6H), 3.72 (s, 3H), 3.80-3.87 (m, 1H), 4.71 (dd, 1H), 5.74 (s, 1H), 6.36 (s, 2H), 6.83 (s, 1H); MS (*m/z*): 548 ($M+Na^+$, 40), 526 (M+1, 7), 446 (100); Anal. Calcd for $C_{25}H_{35}NO_9S \cdot 0.5\ H_2O$: C, 56.17; H, 6.79; N, 2.62; S, 6.00. Found: C, 56.05; H, 6.58; N, 2.61; S, 5.92.

3-[(1*S*,2*R*)-6,7-Dimethoxy-2-methyl-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydro-2-isoquinolinio]propyl-1-sulfate (12)

(*S*)-(+)-Cryptostyline III[5] (**2b**, 36.8 g, 98.6 mmol) was subjected to procedure B and the resulting precipitate was filtered and triturated with acetonitrile to afford **12** (30.0 g, 60% yield) as an off-white powder: mp 207-209ºC; HPLC (98% *de*, silica gel, 15% MeOH/CH_2Cl_2, 0.25 mL methane sulfonic acid/L); ^{1}H NMR (DMSO-d_6): δ 2.10-2.20 (m, 2H), 2.79 (s, 3H), 3.15-3.25 (m, 2H), 3.43 (br t, 2H), 3.57 (s, 3H), 3.69 (s, 3H), 3.78 (s, 3H), 3.4-4.0 (m, 10H), 5.75 (s, 1H), 6.07 (br, 1H), 6.36 (s, 1H), 6.94 (s, 1H), 7.20 (br, 1H); MS (*m/z*): 534 (M+23, 60), 512 (M+1, 30), 432 (M-SO_3, 100). Anal. Calcd for $C_{24}H_{33}NO_9S \cdot 0.4\ H_2O \cdot 0.4$ MeCN: C, 55.72; H, 6.61; N, 4.35. Found: C, 55.70; H, 6.54; N, 4.33.

Procedure C. (1*R*,2*S*)-6,7-Dimethoxy-2-(3-hydroxypropyl)-2-methyl-1-[(3,4,5-trimethoxyphenyl)methyl]-1,2,3,4-tetrahydroisoquinolinium chloride (3a)

Acetyl chloride (71.1 mL, 78.5 g, 1.0 mol) was added dropwise to ice-cold MeOH (700 mL) and the resulting solution was stirred for 10 min. Compound **11** (54.5 g, 0.10 mol) was added and the reaction mixture was stirred at ambient temperature for 6 h. The solution was neutralized by careful addition of excess $NaHCO_3$ and the solid was filtered through a pad of celite. The filtrate was evaporated and the residue was dissolved in $CHCl_3$. The resulting solid was filtered through a pad of celite and washed with $CHCl_3$. The filtrate was evaporated, the remaining residue was dissolved in H_2O, and the aqueous solution was saturated with NaCl. The aqueous phase was extracted with $CHCl_3$ and the organic layers were dried and concentrated to give **3a** (50.7 g, 100% yield) as a hygroscopic white solid with spectral properties identical to those given above.

(1*S*,2*R*)-6,7-Dimethoxy-2-(3-hydroxypropyl)-2-methyl-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydroisoquinolinium chloride (4a)

Compound **12** (28.1 g, 0.05 mol) was subjected to procedure C to give **4a** (25.0 g, 98% yield) as a hygroscopic white solid: ^{1}H NMR (DMSO-d_6): δ 2.0-2.1 (m, 2H), 2.86 (s, 3H), 3.1-3.4 (m, 3H), 3.41 (s, 3H), 3.42-4.00 (m, 5H), 3.66 (s, 3H), 3.75 (s, 3H), 3.85 (s, 6H), 4.9 (t, 1H), 5.8 (s, 1H), 6.2 (br, 1H), 6.4 (s, 1H), 7.0 (s, 1H), 7.2 (br, 1H); MS (*m/z*) 432 (M^+, 100). Anal. Calcd for $C_{24}H_{34}ClNO_6 \cdot 1.86\ H_2O \cdot 0.74\ CHCl_3$: C, 50.38; H, 6.57; Cl, 19.35; N, 2.37. Found: C, 50.38; H, 6.26; Cl, 19.35; N, 2.31.

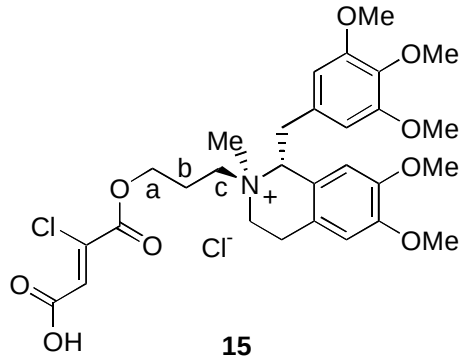
(±)-*trans*-2,3-Dichlorosuccinic anhydride[15] [(±)-13]

A solution of maleic anhydride (10.6 g, 108 mmol) and benzoyl peroxide (5 mg, 0.02 mmol) in $CHCl_3$ (250 mL) was saturated with chlorine gas and the resulting bright yellow solution was stirred for 5 h at ambient temperature. The solution was degassed with nitrogen and partially concentrated to provide **(±)-13** (11.9 g, 65% yield) as a white solid: mp 90-92ºC; ^{1}H NMR (Acetone-d_6): δ 5.68 (s, 2H). Anal. Calcd. for $C_4H_2O_3Cl_2$: C, 28.43; H, 1.19; Cl, 41.97. Found: C, 28.29; H, 1.32; Cl, 41.90.

Procedure D. (*Z*)-2-Chloro-1-{3-{(1*R*,2*S*)-6,7-dimethoxy-2-methyl-1-[(3,4,5-trimethoxyphenyl) methyl]-1,2,3,4-tetrahydro-2-isoquinolinio}propyl} hydrogen 2-butenedioate monochloride (15)

To a solution of **3a** (15.0 g, 31.1 mmol) in CH_2Cl_2 (50 mL) was added **(±)-13** (6.4 g, 37 mmol) and the mixture was stirred 18 h at ambient temperature. The mixture was diluted with CH_2Cl_2 (150 mL), cooled to –20ºC and triethylamine (18.2 mL, 130.4 mmol) was added dropwise. The mixture was warmed to 0ºC, diluted with $CHCl_3$ (200 mL), and washed with 2:1 brine/water containing methanesulfonic acid (4 mg/mL). The

organic layer was separated and the aqueous layer was saturated with NaCl, acidified with concentrated hydrochloric acid (9 mL) and extracted with $CHCl_3$. The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was triturated with Et_2O to provide **15** (16.3 g, 86% yield) as a tan solid: ^{1}H NMR (DMSO-d_6): δ 2.20-2.25(m, 2H), 2.87 (t, 1H), 3.0-3.1 (m, 2H), 3.27 (s, 3H), 3.32 (s, 3H), 3.35-3.45 (m, 2H), 3.55 (dd, 1H), 3.6 (s, 3H), 3.63 (s, 6H), 3.60-3.68 (m, 1H), 3.70 (s, 3H), 3.8-3.9 (m, 1H), 4.16-4.23 (m, 2H), 4.71 (dd, 1H), 5.70 (s, 1H), 6.35 (s, 2H), 6.83 (s, 1H), 7.15 (s, 1H); MS (*m/z*): 578 (M^+, 100). The stereochemistry and regiochemistry in the carbon-carbon double bond of compound **15** were determined using COSY and HMBC NMR experiments. Methylene protons **a** were identified in the COSY spectrum by their crosspeak to the upfield **b** methylene protons. In the HMBC spectrum, the crosspeak between these **a** protons and the carbonyl signal at 161.4 pm allowed assignment of this peak to the ester carbonyl carbon. The vinylic proton showed a weak two bond correlation to the acid carbonyl at 164.7 ppm and a much stronger 3-bond correlation to



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the ester carbonyl, confirming the regiochemistry of the chlorine in the double bond. Finally, the relatively small coupling constant between the vinylic proton and the ester carbonyl carbon ($^3J_{C,H}$=6 Hz) is consistent with the fumarate geometry (See: Vogeli, U.; Von Philipsborn, W. *Org. Magn. Reson.* **1975**, *7*, 617).

Procedure E. (*Z*)-2-Chloro-4-{3-[(1*S*,2*R*)-6,7-dimethoxy-2-methyl-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydro-2-isoquinolinio]propyl}-1-{3-{(1*R*,2*S*)-6,7-dimethoxy-2-methyl-1-[(3,4,5-trimethoxyphenyl)methyl]-1,2,3,4-tetrahydro-2-isoquinolinio}propyl}-2-butenedioate dichloride (5a)

To a solution of **15** (7.0 g, 11.4 mmol) in 1,2-dichloroethane (60 mL) was added 2M oxalyl chloride/CH_2Cl_2 (55 mL, 110 mmol) and the mixture was stirred at ambient temperature for 1 h and then heated to reflux for 5 min. Excess oxalyl chloride was removed *in vacuo* and the resulting residue was dissolved in 1,2-dichloroethane (35 mL). A solution of **4a** (6.62 g, 11.9 mmol) in 1,2-dichloroethane (10 mL) was added and the mixture was stirred for 18 h at ambient temperature. The mixture was diluted with CH_2Cl_2 (300 mL) and extracted with water three times. The aqueous layers were weighed and enough NaCl was added to prepare a 6.5 % (w/w) solution. The resulting aqueous layer was extracted with $CHCl_3$ three times. The combined organic layers were dried (Na_2SO_4), concentrated, and lyophilized from water to provide **5a** (10.1 g, 84% yield) as a white solid: HPLC (90 % pure, silica gel, 25% MeOH/CH_2Cl_2, 0.25 mL methanesulfonic acid/L). Alternatively, preparative HPLC (silica gel, 10-25% MeOH/CH_2Cl_2. 0.25 mL methanesulfonic acid/L) and lyophilization from water provided analytically pure **5a** (8.7 g, 72% yield) as white solid: ^{1}H NMR (DMSO-d_6): δ 2.2-2.3 (m, 4H), 2.85-2.89 (m, 1H), 2.88 (s, 3H), 3.08-3.10 (m, 2H), 3.11-3.15 (m, 1H), 3.26 (s, 3H),

3.40 (s, 3H), 3.56 (s, 3H), 3.60 (s, 3H), 3.63 (s, 3H), 3.68 (s, 3H), 3.69 (s, 3H), 3.77 (s, 3H), 3.20-3.95 (m, 19H), 4.18-4.28 (m, 4H), 4.80-4.87 (m, 1H), 5.70 (s, 1H), 5.90 (s, 1H), 6.10 (br 1H), 6.35 (s, 1H), 6.41 (s, 2H), 6.83 (s, 1H), 6.93 (s, 1H), 7.18 (s, 1H), 7.30 (br, 1H); MS (*m/z*): 496 (M^{2+}, 100). Anal. Cald. for $C_{53}H_{69}N_2O_{14}Cl_3 \cdot 4H_2O$: C, 56.01; H, 6.83; N, 2.46; Cl, 9.36. Found: C, 56.21; H, 6.80; N, 2.45; Cl, 9.50.

(*Z*)-2-Chloro-1-{3-{(1*S*,2*R*)-6,7-dimethoxy-2-methyl-1-(3,4,5-trimethoxyphenyl)-1,2,3,4-tetrahydro-2-isoquinolinio}propyl}-4-{3-{(1*R*,2*S*)-6,7-dimethoxy-2-methyl-1-[(3,4,5-trimethoxyphenyl)methyl]-1,2,3,4-tetrahydro-2-isoquinolinio}propyl}-2-butenedioate dichloride (5b)

The title compound was prepared through a sequence similar to that employed for **5a**. The sequence involved ring opening of **(±)-13** with **4a** and subsequent treatment with base (Procedure D), followed by acid chloride formation and coupling with **3a** (Procedure E) to provide **5b** as a white solid: ^{1}H NMR (DMSO-d_6): δ 2.25-2.31 (m, 4H), 2.88 (s, 1H), 2.86-3.02 (m, 1H), 3.28 (s, 3H), 3.39 (s, 3H), 3.58 (s, 3H), 3.61 (s, 3H), 3.64 (s, 6H), 3.70 (s, 3H), 3.72 (s, 3H), 3.78 (s, 3H), 3.04-4.00 (m, 21H), 4.20 (br t, 2H), 4.30 (br t, 2H), 4.78 (dd, 1H), 5.70 (s, 1H), 5.90 (s, 1H), 6.13 (br, 1H), 6.38 (s, 1H), 6.39 (s, 2H), 6.85 (s, 1H), 6.95 (s, 1H), 7.18 (s, 1H), 7.34 (br, 1H); MS (*m/z*): 496 (M^{2+}, 100). Anal. Cald. for $C_{53}H_{69}N_2O_{14}Cl_3 \cdot 4H_2O$: C, 56.01; H, 6.83; N, 2.46; Cl, 9.36. Found: C, 56.02; H, 6.82; N, 2.48; Cl, 9.45.