Efficient Synthesis of Some Novel Macrocyclic Diamides Using Fast Addition Method

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Abstract: Synthesis of some new macrocyclic diamides based on catechol scaffold by cyclization reactions between various diamines and 2-[2-(2-chloro-2-oxoethoxy)phenoxy]ethanoyl chloride using fast addition method has been described. The reactions were carried out in short reaction times and the expected macrocycles were obtained in good to high yields.

Key words: macrocyclic diamide, fast addition, catechol, diamine, dicarboxylic acid dichloride, cyclization

Macrocyclic compounds with amide units in the macro ring are of interest because they have important applications in selective noble metal complexing agents and metal ion-selective electrodes.[1] For example, some of these compounds were shown to be selective for the complexation with Hg^{2+},[1a] Zn^{2+},[1b] Cu^{2+},[1c] and Sr^{2+} ions.[1d] Furthermore, recently we have shown that these macrocycles can efficiently catalyze the regioselective ring opening of epoxides with elemental halogen[2a,b] or ammonium thiocyanate.[2c] Interestingly, some macrocyclic amides are receptors for anions such as OAc^-, $H_2PO_4^-$, F^- and Cl^-.[3] In this case, the electronegative atom from anions (oxygen, fluorine or chlorine) interact with NH groups of macrocycles.[3] Lactams also have been used as starting materials for the preparation of polyaza-crowns and related compounds such as cryptands.[4] Although macrocyclic diamides have many applications, only a few methods have been developed for their preparation. In these methods, carboxylic acid derivatives such as dicarboxylic acid diesters,[5] labile dicarboxylic acid dichlorides[6] or bis(α-chloroamide) compounds[4a] were allowed to react with diamines under different conditions. The more common methods involve high dilution,[7] template effect,[8] high pressure approach,[9] ESI-MS[10] and 'Crab-like'[4d] techniques. Most of these methods are associated with several drawbacks such as long reaction times, low yields of products, harsh reaction conditions and difficulty in separation and purification.

Recently, we provided a synthetic route toward dilactam derivatives.[11] In this method, the cyclization reaction does not require high dilution techniques or template effect. The advantages of this method (fast addition) are high yield, short reaction time, ease of purification, low volume of solvent, no side reactions and synthetic versatility (this method allows to provide various even or odd membered dilactams). In fact, because of high significance of these compounds and also in extension of the applicability of fast addition method, herein, we would like to report an efficient synthesis of some new macrocyclic diamides based on catechol structure using this method (Scheme 1).

Catechol was reacted with 2-chloroacetic acid in water in the presence of sodium hydroxide to give 2-[2-(2-hydroxy-2-oxoethoxy)phenoxy]acetic acid (**1**) as a white solid in 91% yield (Scheme 1). Treatment of **1** with thionyl chloride gave 85% yield of 2-[2-(2-chloro-2-oxoethoxy)phenoxy]ethanoyl chloride (**2**) (Scheme 1). The cyclization reactions between dicarboxylic acid dichloride **2** and different diamines were performed by fast addition procedure without high dilution technique. This step was carried out by fast addition of diamines in anhydrous solvent into a solution of dicarboxylic acid dichloride **2** in anhydrous solvent over a few seconds with vigorous stirring at room temperature.

Macrocycles **3a** and **3b** were synthesized to study the effect of alkyl chain length of aliphatic diamines on results of cyclization reactions. As shown in Table 1, 1,6-diaminohexane gave higher yield than 1,3-diaminopropane (Table 1, entries 1 and 2). This aspect indicates the dependency of macrocyclization yield to the ring size of the macrocycle. We have also extended the cyclization reaction to aromatic diamines. As Table 1 indicates, when aromatic diamines were used instead of aliphatic diamines, the reaction yields were higher. Moreover, the presence of CO_2R as functional group on the ring of aromatic diamines afforded the macrocyclic diamides in higher yields as well as shorter reaction times in comparison to the NO_2 (Table 1, entries 5, 6, 8 and 10). In the synthesis of compounds **3f–h**, two-to-two cyclization products **4f–h** were also obtained in low yields, and were easily separated from one-to-one adducts (Table 1, entries 7, 9 and 11).

We have also studied the effect of alkyl chain length of ester moiety (CO_2R) present on aromatic diamines on the yields and the solubility of products in organic solvents. The results have illustrated that increment of the length of alkyl chain decreased the yields of diamides and increased the yields of tetraamides (Table 1, entries 6–11). This aspect enhanced the solubility of dilactams and tetralactams in organic solvents. The useful solvents for synthesis of macrocycles **3a–h** and **4f–h** were ethyl acetate, dichlo-

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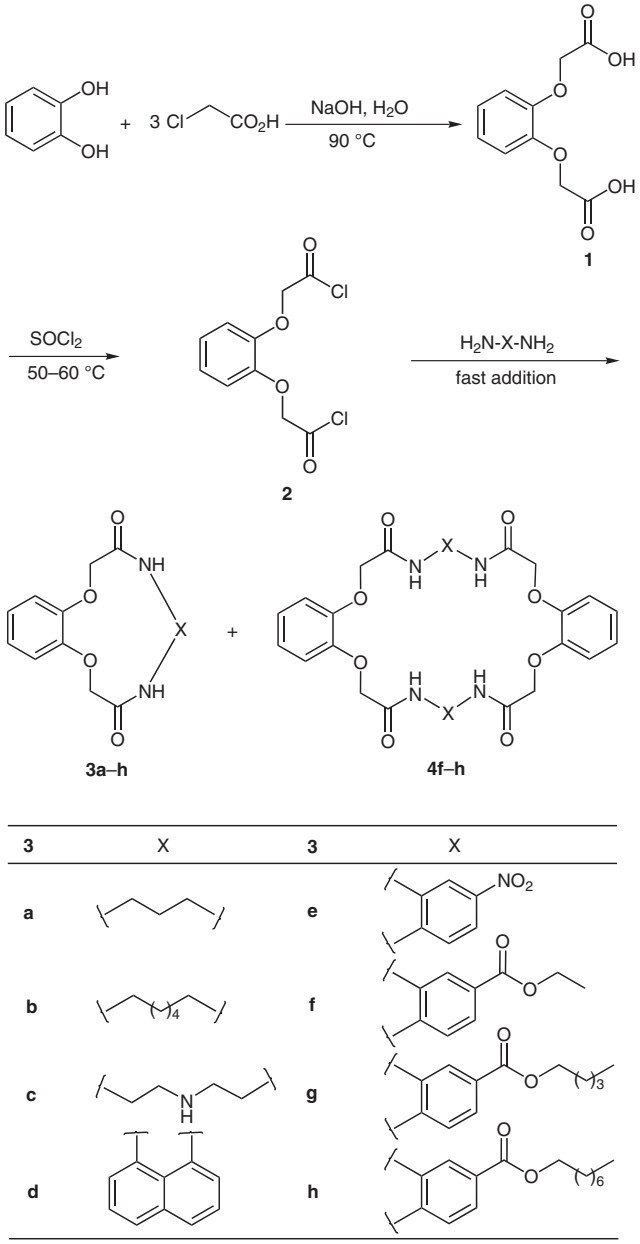


Scheme 1

romethane, acetone, acetonitrile, THF, diethyl ether and ethyl acetate–dichloromethane (1:1). In all reactions, chloroform, DMSO and DMF were found to be unsuitable as solvents.

In conclusion, we have prepared some novel macrocyclic dilactams and tetralactams by cyclization reactions between dicarboxylic acid dichloride and different diamines (aliphatic and aromatic) using fast addition technique. Furthermore, these macrocycles with different ring sizes were obtained in high yields and short reaction times. The applications of these compounds in organic and analytical chemistry are currently under investigation.

All chemicals were obtained from Merck or Fluka. Solvents were purified and dried according to reported methods and stored over molecular sieves.[12] The progress of reactions was followed with TLC using silica gel SILG/UV 254 plates. Chromatography was carried out on a column over silica gel 60, 0.063–0.200 mm (70–230 mesh ASTM). IR spectra were run on a Shimadzu FTIR-8300 spectrophotometer. The ^{1}H (250 MHz) and ^{13}C NMR (62.5 MHz) were run on a Bruker Avance DPX-250, FT-NMR spectrometer (δ in ppm, *J* in Hz). Mass spectra were recorded on a Shimadzu GC MS-QP 1000 EX apparatus. Microanalyses were performed on a Perkin-Elmer 240-B microanalyzer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes and are uncorrected.

2-[2-(2-Hydroxy-2-oxoethoxy)phenoxy]acetic Acid (1)

To a mixture of catechol (11.01 g, 100 mmol) and 2-chloroacetic acid (28.35 g, 300 mmol) at 90 °C on a water-bath, was added dropwise a solution of aq 33% (w/v) NaOH solution (48.02 g in 97.5 mL H_2O). The mixture was stirred at 90 °C for 2 h and after cooling to r.t., the solution was kept in ice bath. Then, concentrated HCl was added dropwise to the solution with stirring. The mixture was allowed to warm to r.t. and the solution was filtered and the white precipitate was washed with cold H_2O. Crystallization of the residue from hot water afforded **1** as white crystals; yield: 20.58 g (91%); mp 176–177 °C (Lit.[13] mp 177–178 °C).

2-[2-(2-Chloro-2-oxoethoxy)phenoxy]ethanoyl Chloride (2)

The acid **1** (5.65 g, 25 mmol) was heated in $SOCl_2$ (50 mL) for 4 h at 50–60 °C. The $SOCl_2$ was evaporated under vacuo at low temperature (40 °C) and the residue was crystallized from petroleum ether (bp 60–80 °C) to give **2** as white crystals; yield: 5.58 g (85%); mp 48–49 °C.

IR (KBr): 3075, 2977, 1805 (s), 1501 cm^{-1}.

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 4.96 (s, 4 H), 6.78–6.88 (complex, 4 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 73.3, 116.7, 123.5, 146.5, 170.6.

Ethyl, Pentyl and Octyl 3,4-Diaminobenzoate; General Procedure

The appropriate alcohol (2.0 mmol) and carboxylic acid (2.0 mmol) were added to a stirred mixture of Al_2O_3 (acidic type 540 C, 0.31 g, 3.0 mmol) and $MeSO_3H$ (1 mL). The mixture was allowed to stir in an oil bath at 80 °C for 2–3 h, then poured into H_2O (20 mL), and extracted with $CHCl_3$ (50 mL). The organic layer was washed with sat. aq solution of $NaHCO_3$ (2 × 20 mL), dried ($CaCl_2$), and evaporated to give the corresponding ester.[14]

Ethyl 3,4-Diaminobenzoate

Pale yellow solid; yield: 0.32 g (89%); mp 79–80 °C.

IR (KBr): 3327, 3188, 3048, 2959, 1686 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.25 (t, 3 H, *J* = 6.9 Hz), 3.52 (s, 4 H), 4.24 (q, 2 H, *J* = 6.9 Hz), 6.60 (d, 1 H, *J* = 8.1 Hz), 7.33–7.41 (complex, 2 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 14.8, 60.8, 115.2, 118.6, 121.7, 123.5, 133.5, 140.7, 167.3.

MS: *m*/*z* (%) = 181 (M^+ + 1, 18.6), 180 (M^+, 97.1), 152 (57.0), 151 (6.4), 135 (100), 107 (45.5), 75 (1.4), 73 (1.7), 45 (5.6), 43 (51.2).

Pentyl 3,4-Diaminobenzoate

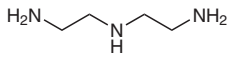
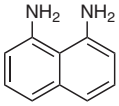
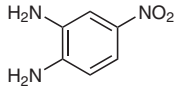
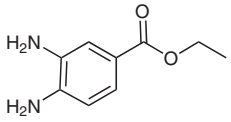
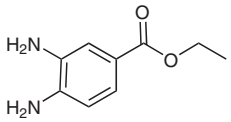
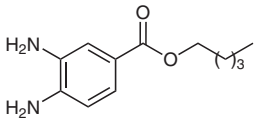
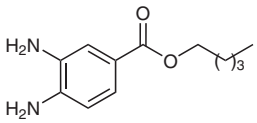
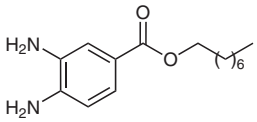
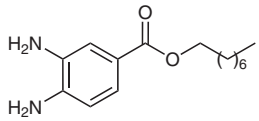
Pale yellow solid; yield: 0.38 (85%); mp 65–67 °C.

IR (KBr): 3331, 3190, 3050, 2950, 1685 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.94–1.02 (complex, 5 H), 1.54–1.72 (complex, 4 H), 3.63 (s, 4 H), 4.28 (t, 2 H, *J* = 7.0 Hz), 6.66 (d, 1 H, *J* = 8.2 Hz), 7.40–7.47 (complex, 2 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 16.9, 26.6, 30.1, 37.9, 63.5, 115.3, 118.7, 121.7, 123.6, 133.3, 140.8, 167.4.

Table 1 Macrocyclization Reactions between Dicarboxylic Acid Dichloride **2** and Various Diamines Using Fast Addition Method

Entry	Diamine	Product	Reaction time (min)	Solvent	Yield (%)[a]
1		**3a**	10	acetone	31
2		**3b**	5	acetone	70
3		**3c**	5	EtOAc	45
4		**3d**	3	EtOAc	75
5		**3e**	5	CH_2Cl_2	69
6		**3f**	3	CH_2Cl_2	89
7		**4f**	3	CH_2Cl_2	7
8		**3g**	3	CH_2Cl_2	82
9		**4g**	3	CH_2Cl_2	11
10		**3h**	3	CH_2Cl_2	74
11		**4h**	3	CH_2Cl_2	16

[a] Isolated yields.

MS: *m*/*z* (%) = 223 (M^+ + 1, 15.2), 222 (M^+, 41.5), 194 (28.3), 166 (14.1), 151 (2.5), 135 (100), 107 (25.6), 71 (4.9), 57 (38.5), 43 (46.1).

Octyl 3,4-Diaminobenzoate

Pale yellow solid; yield: 0.44 g (83%); mp 56–58 °C.

IR (KBr): 3329, 3191, 3054, 2955, 1685 cm^{-1} (s).

^1H NMR ($CDCl_3$, 250 MHz): δ = 0.88 (t, 3 H, *J* = 6.8 Hz), 1.25–1.34 (complex, 10 H), 1.70 (m, 2 H), 3.59 (s, 4 H), 4.24 (t, 2 H, *J* = 7.0 Hz), 6.68 (d, 1 H, *J* = 8.3 Hz), 7.44–7.51 (complex, 2 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 14.5, 23.0, 26.5, 29.2, 29.6, 29.7, 32.2, 65.1, 115.3, 118.8, 121.8, 123.7, 133.3, 140.7, 167.3.

MS: *m*/*z* (%) = 265 (M^+ + 1, 6.7), 264 (M^+, 31.6), 165 (1.3), 151 (3.3), 135 (40.6), 107 (19.0), 84 (19.7), 70 (31.8), 56 (60.0), 43 (78.3), 41 (100).

Dilactams 3a–h and 4f–h; General Procedure

A solution of diamine (2.0 mmol) in anhyd solvent (50 mL) was added quickly to a vigorous stirring solution of dicarboxylic acid dichloride (2.0 mmol) in anhyd solvent (50 mL) at r.t. The mixture was stirred for a further 3–10 min (see Table 1 for solvent used and time of reaction). The organic layer was washed first with aq $NaHCO_3$ solution (2 × 50 mL), then with H_2O (2 × 50 mL), and dried ($MgSO_4$). The crude product obtained by evaporation of the solvent was purified by column chromatography over silica gel using *n*-hexane–EtOAc as eluent (15:1 to 10:1).

5,6,7,8-Tetrahydro-2*H*-1,11,4,8-benzodioxadiazacyclotridecine-3,9(4*H*,10*H*)-dione (3a)

Colorless crystals; mp 178–179 °C.

IR (KBr): 3334, 3078, 2956, 1647 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.92 (t, 2 H, *J* = 5.9 Hz), 3.63 (t, 4 H, *J* = 5.9 Hz), 4.47 (s, 4 H), 6.98–7.09 (complex, 4 H), 7.41 (s, 2 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 28.1, 40.1, 71.4, 115.4, 124.5, 149.2, 168.5.

MS: *m*/*z* (%) = 265 (M^+ + 1, 11.7), 264 (M^+, 11.9), 150 (9.9), 142 (3.9), 122 (12.5), 114 (4.6), 100 (3.7), 99 (8.9), 92 (8.4), 76 (7.2), 70 (9.1), 57 (17.3), 52 (45.5), 42 (100).

Anal. Calcd for $C_{13}H_{16}N_2O_4$ (264.28): C, 59.08; H, 6.10; N, 10.60. Found: C, 59.01; H, 6.19; N, 10.51.

4,5,6,7,8,9,10,11-Octahydro-1,14,4,11-benzodioxadiazacyclohexadecine-3,12(2*H*,13*H*)-dione (3b)
Colorless crystals; mp 199–201 °C.

IR (KBr): 3342, 3069, 2948, 1649 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.52–1.69 (complex, 8 H), 3.49 (t, 4 H, *J* = 5.7 Hz), 4.52 (s, 4 H), 6.86–7.04 (complex, 4 H), 7.54 (s, 2 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 24.5, 30.1, 41.0, 70.7, 118.2, 124.6, 149.3, 168.8.

MS: *m*/*z* (%) = 307 (M^+ + 1, 7.0), 306 (M^+, 30.3), 248 (5.5), 236 (4.3), 184 (4.2), 150 (9.3), 137(44.8), 121 (45.7), 114 (15.8), 107 (15.9), 97 (38.6), 43 (100).

Anal. Calcd for $C_{16}H_{22}N_2O_4$ (306.36): C, 62.73; H, 7.24; N, 9.14. Found: C, 62.66; H, 7.19; N, 9.02.

5,6,7,8,9,10-Hexahydro-2*H*-1,13,4,7,10-benzodioxatriazacyclopentadecine-3,11(4*H*,12*H*)-dione (3c)
Colorless crystals; mp 230 °C (dec.).

IR (KBr): 3360, 3244, 3080, 2979, 1676 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.75 (s, 1 H), 2.94 (t, 4 H, *J* = 5.3 Hz), 3.48 (t, 4 H, *J* = 5.3 Hz), 4.48 (s, 4 H), 6.87–6.98 (complex, 4 H), 7.81 (s, 2 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 38.5, 47.8, 67.2, 112.6, 122.4, 146.5, 167.5.

MS: *m*/*z* (%) = 294 (M^+ + 1, 73.3), 293 (M^+, 12.0), 278 (1.1), 250 (3.7), 192 (1.3), 150 (4.1), 121 (19.8), 108 (1.2), 100 (8.2), 99 (14.1), 92 (5.1), 86 (8.9), 85 (32.0), 71 (20.3), 57 (29.5), 52 (19.9), 44 (85.5), 43 (100), 42 (84.4).

Anal. Calcd for $C_{14}H_{19}N_3O_4$ (293.32): C, 57.33; H, 6.53; N, 14.33. Found: C, 57.42, H, 6.69; N, 14.41.

7*H*,16*H*-Naphtho[1,8-*ef*][1,11,4,8]benzodioxadiazacyclotridecine-8,17(9*H*,18*H*)-dione (3d)
Colorless crystals; mp 276 °C (dec.).

IR (KBr): 3294, 3053, 2922, 1661 cm^{-1} (s).

^{1}H NMR (250 MHz, DMSO-d_6): δ = 4.68 (s, 4 H), 7.12 (d, 2 H, *J* = 7.5 Hz), 7.21 (dd, 2 H, *J* = 5.7, 7.5 Hz), 7.58 (dd, 2 H, *J* = 6.8, 7.9 Hz), 7.86 (d, 2 H, *J* = 6.8 Hz), 7.98 (d, 2 H, *J* = 7.9 Hz), 11.06 (s, 2 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 70.5, 118.2, 122.1, 123.0, 123.5, 125.7, 126.8, 132.4, 135.5, 148.4, 167.9.

MS: *m*/*z* (%) = 349 (M^+ + 1, 25.3), 348 (M^+, 100), 272 (2.6), 198 (13.7), 184 (60.5), 169 (58.2), 154 (8.9), 141 (4.5), 122 (8.9), 108 (1.9), 92 (6.9), 76 (15.4), 52 (54.9).

Anal. Calcd for $C_{20}H_{16}N_2O_4$ (348.35): C, 68.96; H, 4.63; N, 8.04 Found: C, 68.82; H, 4.50; N, 7.93.

10-Nitro-8,13-dihydrodibenzo[*b*,*h*][1,4,7,10]dioxadiazacyclododecine-7,14(6*H*,15*H*)-dione (3e)
Colorless crystals; mp 252–253 °C (dec.).

IR (KBr): 3348, 3122, 3063, 2960, 1697 (s), 1676 cm^{-1} (s).

^{1}H NMR (DMSO-d_6, 250 MHz): δ = 4.82 (s, 2 H), 4.88 (s, 2 H), 7.04 (d, 2 H, *J* = 7.7 Hz), 7.32 (dd, 2 H, *J* = 6.1, 7.7 Hz), 8.10–8.18 (complex, 2 H), 8.35 (s, 1 H), 9.92 (s, 1 H), 10.17 (s, 1 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 70.9, 71.9, 117.3, 118.0, 120.4, 121.0, 122.1, 122.4, 123.3, 129.0, 137.2, 143.7, 148.4, 148.6, 167.3, 167.6.

MS: *m*/*z* (%) = 344 (M^+ + 1, 11.8), 343 (M^+, 25.8), 193 (5.3), 192 (14.0), 179 (8.0), 164 (100), 149 (8.4), 122 (26.4), 121 (55.8), 108 (7.0), 92 (11.4), 76 (14.1), 52 (55.2.

Anal. Calcd for $C_{16}H_{13}N_3O_6$ (343.29): C, 55.98; H, 3.82; N, 12.24. Found: C, 56.11; H, 3.76; N, 12.33.

Ethyl 7,14-Dioxo-6,7,8,13,14,15-hexahydrodibenzo[*b*,*h*][1,4,7,10]dioxadiazacyclododecine-10-carboxylate (3f)
Colorless crystals; mp 186–187 °C.

IR (KBr): 3364, 3242, 3050, 2980, 1721 (s), 1699 (s), 1653 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 1.35 (t, 3 H, *J* = 7.0 Hz), 4.36 (q, 2 H, *J* = 7.0 Hz), 4.60 (s, 2 H), 4.65 (s, 2 H), 6.90–7.00 (complex, 4 H), 7.79–7.99 (complex, 3 H), 8.26 (s, 1 H), 9.18 (s, 1 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 14.7, 61.6, 71.9, 73.6, 117.5, 118.3, 122.1, 124.3, 124.5, 127.2, 127.4, 127.8, 128.4, 129.9, 149.3, 149.6, 165.8, 167.5, 168.6.

MS: *m*/*z* (%) = 371 (M^+ + 1, 20.3), 370 (M^+, 22.7), 325 (17.2), 248 (8.4), 207 (19.7), 206 (100), 192 (12.4), 178 (39.8), 163 (39.8), 136 (10.3), 122 (10.5), 108 (6.3), 92 (10.2), 52 (24.8).

Anal. Calcd for $C_{19}H_{18}N_2O_6$ (370.36): C, 61.62; H, 4.90; N, 7.56. Found: C, 61.52; H, 4.77; N, 7.39.

Diethyl 7,14,23,30-Tetraoxo-6,7,8,13,14,15,22,23,24,29,30,31-dodecahydrotetrabenzo[*b*,*h*,*n*,*t*][1,4,13,16,7,10,19,22]tetraoxatetraazacyclotetracosine-10,27-dicarboxylate (4f)
Colorless crystals; mp 242–244 °C.

IR (KBr): 3356, 3269, 3070, 2953, 1720 (s), 1693 (s), 1657 cm^{-1} (s).

^{1}H NMR (DMSO-d_6, 250 MHz): δ = 1.34 (t, 6 H, *J* = 6.9 Hz), 4.38 (q, 4 H, *J* = 6.9 Hz), 4.68–4.79 (complex, 8 H), 7.03–7.11 (complex, 8 H), 7.78–7.88 (complex, 6 H), 8.15 (s, 2 H), 9.31 (s, 2 H).

^{13}C NMR (DMSO-d_6, 62.5 MHz): δ = 14.5, 61.3, 71.8, 73.2, 117.9, 118.6, 122.5, 124.1, 124.9, 127.7, 127.9, 128.1, 128.5, 129.8, 149.8, 150.5, 167.0, 167.15, 168.4.

MS: *m*/*z* (%) = 576 (3.3), 476 (2.6), 434 (1.8), 373 (1.1), 389 (4.3), 370 (7.3), 354 (11.4), 326 (15.4), 312 (20.1), 297 (4.8), 267 (8.2), 239 (3.7), 222 (2.5), 206 (23.7), 178 (6.9), 150 (41.8), 134 (3.4), 121 (100), 106 (4.2), 92 (7.6), 76 (12.1), 52 (44.3).

Anal. Calcd for $C_{38}H_{36}N_4O_{12}$ (740.71): C, 61.62; H, 4.90; N, 7.56. Found: C, 61.75; H, 4.82; N, 7.67.

Pentyl 7,14-Dioxo-6,7,8,13,14,15-hexahydrodibenzo[*b*,*h*][1,4,7,10]dioxadiazacyclododecine-10-carboxylate (3g)
Colorless crystals; mp 148–151 °C.

IR (KBr): 3360, 3250, 3080, 2959, 1719 (s), 1695 (s), 1651 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.86–0.94 (complex, 5 H), 1.53–1.70 (complex, 4 H), 4.24 (t, 2 H, *J* = 6.8 Hz), 4.50 (s, 2 H), 4.55 (s, 2 H), 6.82–6.91 (complex, 4 H), 7.79–7.92 (complex, 3 H), 8.29 (s, 1 H), 9.11 (s, 1 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 16.9, 22.9, 26.5, 34.6, 64.3, 70.2, 71.9, 117.5, 118.4, 122.1, 124.3, 124.5, 127.3, 128.3, 129.8, 132.8, 136.2, 149.3, 149.6, 165.9, 167.5, 168.6.

MS: *m/z* (%) = 413 (M^+ + 1, 11.1), 412 (M^+, 14.9), 354 (1.1), 290 (11.8), 262 (12.7), 248 (35.4), 233 (24.7), 192 (8.4), 178 (100), 164 (18.8), 136 (10.6), 122 (9.0), 108 (5.5), 92 (9.0), 42 (11.4).

Anal. Calcd for $C_{22}H_{24}N_2O_6$ (412.44): C, 64.07; H, 5.87; N, 6.79. Found: C, 63.95; H, 5.96; N, 6.71.

Dipentyl 7,14,23,30-Tetraoxo-6,7,8,13,14,15,22,23,24,29,30,31-dodecahydrotetrabenzo[*b*,*h*,*n*,*t*][1,4,13,16,7,10,19,22]tetraoxotetraazacyclotetracosine-10,27-dicarboxylate (4g)
Colorless crystals; mp 218–220 °C.

IR (KBr): 3360, 3240, 2935, 3055, 2961, 1719 (s), 1680 (s), 1655 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.89–1.03 (complex, 10 H), 1.59–1.69 (complex, 8 H), 4.31 (t, 4 H, *J* = 7.0 Hz), 4.72 (s, 4 H), 4.77 (s, 4 H), 7.02–7.07 (complex, 8 H), 7.91–8.02 (complex, 6 H), 8.14 (s, 2 H), 9.21 (s, 2 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 16.7, 22.2, 27.1, 34.2, 63.4, 70.9, 72.4, 117.2, 119.1, 122.2, 124.8, 125.2, 127.7, 128.5, 130.1, 132.2, 135.6, 149.1, 149.8, 164.4, 167.9, 168.7.

MS: *m/z* (%) = 577 (2.1), 466 (1.4), 452 (2.3), 428 (5.9), 412 (7.1), 382 (2.1), 354 (3.4), 341 (5.4), 339 (3.9), 297 (2.4), 296 (4.9), 220 (3.3), 203 (100), 150 (2.5), 122 (6.9), 108 (2.5), 92 (2.9), 76 (7.2), 52 (17.1).

Anal. Calcd for $C_{44}H_{48}N_4O_{12}$ (824.87): C, 64.07; H, 5.87; N, 6.79. Found: C, 64.15; H, 5.98; N, 6.65.

Octyl 7,14-Dioxo-6,7,8,13,14,15-hexahydrodibenzo[*b*,*h*][1,4,7,10]dioxadiazacyclododecine-10-carboxylate (3h)
Colorless crystals; mp 135–136 °C.

IR (KBr): 3355, 3240, 3060, 2924, 1721 (s), 1693 (s), 1657 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.92 (t, 3 H, *J* = 6.8 Hz), 1.26–1.37 (complex, 10 H), 1.76 (m, 2 H), 4.30 (t, 2 H, *J* = 7.1 Hz), 4.69 (s, 2 H), 4.74 (s, 2 H), 7.01–7.09 (complex, 4 H), 7.97 (d, 1 H, *J* = 7.8 Hz), 8.01–8.12 (complex, 3 H), 9.23 (s, 1 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 14.5, 23.1, 26.4, 29.1, 29.58, 29.6, 32.2, 65.8, 72.0, 73.6, 117.5, 118.4, 121.9, 124.5, 124.6, 127.9, 128.6, 130.1, 132.4, 137.2, 149.3, 149.6, 167.4, 168.6.

MS: *m/z* (%) = 455 (M^+ + 1, 13.7), 454 (M^+, 16.7), 332 (9.9), 325 (14.0), 290 (47.1), 275 (15.0), 192 (6.3), 179 (18.7), 178 (100), 164 (15.9), 136 (9.9), 122 (7.4), 108 (4.4), 92 (6.7), 52 (9.0).

Anal. Calcd for $C_{25}H_{30}N_2O_6$ (454.52): C, 66.06; H, 6.65; N, 6.16. Found: C, 66.21; H, 6.51; N, 6.03.

Dioctyl 7,14,23,30-Tetraoxo-6,7,8,13,14,15,22,23,24,29,30,31-dodecahydrotetrabenzo[*b*,*h*,*n*,*t*][1,4,13,16,7,10,19,22]tetraoxotetraazacyclotetracosine-10,27-dicarboxylate (4h)
Colorless crystals; mp 201–204 °C.

IR (KBr): 3362, 3244, 3070, 2926, 1715 (s), 1678 (s), 1661 cm^{-1} (s).

^{1}H NMR ($CDCl_3$, 250 MHz): δ = 0.89 (t, 6 H, *J* = 6.7 Hz), 1.24–1.35 (complex, 20 H), 1.72 (m, 4 H), 4.26 (t, 4 H, *J* = 7.1 Hz), 4.54 (s, 4 H), 4.65 (s, 4 H), 6.98–7.07 (complex, 8 H), 7.55 (d, 2 H, *J* = 7.9 Hz), 7.68–7.79 (complex, 4 H), 8.04 (s, 2 H), 9.05 (s, 2 H).

^{13}C NMR ($CDCl_3$, 62.5 MHz): δ = 14.2, 22.8, 26.1, 29.3, 29.9, 30.2, 32.4, 66.2, 71.4, 73.2, 117.1, 118.3, 122.2, 124.8, 125.1, 127.6, 129.2, 129.9, 133.1, 137.5, 149.8, 150.3, 166.5, 167.7, 168.3.

MS: *m/z* (%) = 576 (1.5), 454 (2.9), 439 (3.7), 438 (2.5), 424 (2.1), 411 (2.1), 397 (12.8), 396 (21.4), 381 (2.4), 378 (1.7), 348 (2.0), 332 (3.2), 290 (18.7), 275 (9.7), 192 (78.0), 178 (100), 164 (11.6), 150 (40.7), 129 (4.0), 122 (33.5), 108 (2.7), 92 (11.4), 52 (26.6).

Anal. Calcd for $C_{50}H_{60}N_4O_{12}$ (909.03): C, 66.06; H, 6.65; N, 6.16. Found: C, 65.94; H, 6.54; N, 5.98.

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