Efficient synthesis of naphthalene-fused dilactam crown ethers

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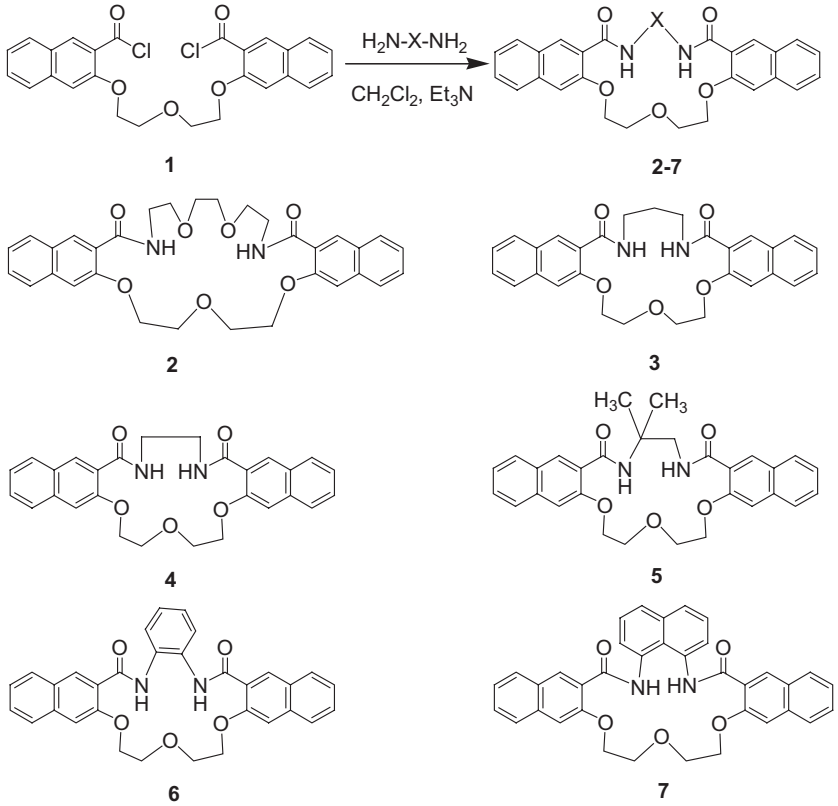
The novel macrocyclic dilactams that structurally fuse to naphthalene chromophore were synthesised. These compounds were obtained in the macrocyclisation step by fast addition methods and the results were compared with solvent-free conditions.

Keywords: solvent free conditions, macrocyclisation, fluorescence, dilactam, fast addition

Recently, much attention has been paid to the fluorometric sensing of a specific molecule based on the host–guest interaction.[1] Light emitting fragments such as naphthalene,[2] anthracene,[3] pyrene,[4] isoquinoline *N*-oxide,[5] flavone,[6] and binaphthyl[7] groups have often been used as an excellent fluorescence probe on account of their high sensitivity for detector. We decided to synthesise novel macrocyclic systems of which fluorophores are the constructing part of the macrocycles rings (Scheme 1). In these compounds, naphthalene rings were used as the constructing and signalling part of the systems which already have been used as side-arms in lariat ethers.[2,3]

One of the most common and conventional methods of constructing macrocyclic lactams is to utilise the reaction of dicarboxylic acid chlorides with diamines. This route is indeed effective, especially with simple acyl chlorides that are readily purified and in cases of less reactive diamines. Adverse factors, however, arise in the generally low yields and difficulty in purifying larger acyl chlorides. Furthermore, high-dilution techniques[8,9] are necessary in most cases to perform such reactions, in order to obtain reasonable yields because of a tendency to form linear polyamides. Moreover, besides the desired one-to-one adduct, two-to-two cyclisation products were sometimes obtained,[10] which increased the problems of purification. Recently, we have reported that the high dilution technique is not required for the reaction of diacid chloride with diamines to form macrocyclic dilactams.[11,12] On the other hand, some of these products were shown to be selective for complexation as well as selective electrodes formation.[13,14] Recently, Sharghi[15] and coworkers were showed that these compounds efficiently catalysed the regioselective ring opening of epoxides with elemental halogens or ammonium thiocyanate.

In this paper, we report the synthesis of novel macrocyclic dilactams (**2–7**) with 17–23 membered rings (Scheme 1). The target macrocycles were intended to evaluate the range of applicability of our fast addition method as well as their effect on metal-ion complexing behaviour related to the above discussion.



Scheme 1

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Results and discussion

The cyclisation was carried out with fast addition of a mixture of the diamines (2 mmol) and triethylamine (4 mmol) in CH_2Cl_2 (20 ml) into a solution of dicarboxylic acid dichloride **1** (2 mmol) in CH_2Cl_2 (20 ml) over 5 s with vigorous stirring at 0°C. The mixture was then stirred at room temperature for 20 min to give dilactam crown ethers **2–7** in 60–90% yields (Scheme 1).

A low reaction time was observed for this macrocyclisation reaction. Our previous study[11,12] showed that CH_2Cl_2 is a properly selected solvent for this type of macrocyclisation reaction. The structures proposed for the macrocyclic compounds are consistent with data derived from IR, ^{1}H NMR and ^{13}C NMR in addition to satisfactory combustion analysis and molecular weights that are determined by mass spectrometric analysis. Several types of aromatic and aliphatic, solid or liquid, rigid or fully flexible diamines reacted with different dicarboxylic acid dichlorides by this procedure. The size of these macrocycles varied between 17 and 23 membered rings that with our earlier reports[11,12] well improved the versatility of the fast addition method.

In conclusion, the current method provides a very simple and convenient procedure for the high-yield synthesis of macrocyclic dilactams without additional external cyclisation factors such as high dilution approach, template effect or nitrogen protection. Moreover, synthetic versatility, no side reactions, ease of workup, and short reaction time can be considered as the advantages of this method. The fluorescence behaviour of these novel compounds is in progress in our laboratories.

Experimental

All materials and solvents were obtained from Merck chemical company (Germany) and Fluka (Switzerland). Melting points were determined in open capillary tubes in an Electrothermal IA 9000 melting point apparatus. IR spectra were recorded on a Shimadzu - IR 470 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-500 MHz and Bruker-100 MHz instruments using tetramethylsilane (TMS) as an internal standard. Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX instrument at 70 eV. Elemental analyses were performed at the Research Institute of Petroleum Industry of Iran. Columns chromatography was carried out on short columns of silica gel 60 (230–400 mesh) in glass columns (2–3 cm diameter) using 15–30 g of silica gel per 1 g of crude mixture. Compound **1** is known compound and was prepared as previously described.[12b]

General procedure for the synthesis of dilactam crown ethers (**2–7**)
A solution of diamine (2 mmol) and triethylamine (0.41 g, 4 mmol) in CH_2Cl_2 (40 ml) was added quickly (5 s) to a vigorously stirred solution of diacid chloride (**1**) (2 mmol) in CH_2Cl_2 (40 ml) at 0°C. The reaction mixture was stirred at room temperature for 30 min. The precipitate was filtered off and the filtrate washed with water (2 × 50 ml) and 10% aqueous sodium hydroxide solution (50 ml) and then with water (100 ml). The organic layer was dried with anhydrous magnesium sulfate and the solvent was evaporated to give a solid (or oily) product. The crude product was purified by either recrystallisation from methylene chloride and *n*-hexane or column chromatography using petroleum ether (b.p. = 60–80°C)-ethyl acetate as eluent.

8,9,11,12,15,16,25,26,28,29-Decahydrodinaphtho[2,3-h: 2,3-v][1,4,7,14,17,11,20] pentaoxadiazacyclotricosine-6,17(7H,14H)-dione (**2**)**:** Obtained from 1,8-diamino-3,6-dioxaoctane (0.30 g, 2 mmol) in 95% yield; white solids; m.p. = 151–152°C; IR (KBr) 720 (s), 840 (m), 1105 (s), 1125 (s), 1180 (s), 1250 (s), 1328 (s), 1350 (s), 144(s)6, 1507 (s), 1593 (s), 1622 (s), 1660 (s), 2870 (s), 3090 (w), 3300 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.78 (s, 2H), 8.66 (br s, 2H, NH), 7.89 (d, 2H, *J* = 8.1 Hz), 7.70 (d, 2H, *J* = 8.2 Hz), 7.50 (t, 2H, *J* = 7.5 Hz), 7.38 (t, 2H, *J* = 7.2 Hz), 7.18 (s, 2H), 4.36 (t, 4 H, *J* = 4.5 Hz), 4.18 (t, 4 H, *J* = 5 Hz), 3.74 (t, 4 H, *J* = 4.5 Hz), 3.70 (s, 4H), 3.67 (t, 4 H, *J* = 4.5 Hz); ^{13}C NMR: 165.09, 153.94, 135.61, 133.84, 129.16, 128.42, 128.29, 126.25, 124.70, 122.50, 107.52, 70.42, 70.16, 69.31, 68.44, 39.82; MS *m/z* 558 (M^+, 5), 556 (M-2, 20), 530 (7), 515 (10), 502 (15), 326 (10), 261 (45), 216 (25), 187 (30), 162 (95), 144 (54), 135 (90), 119 (base peak), 85 (98), 64 (65). Anal. Calcd. for $C_{32}H_{34}N_2O_7$: C, 68.80; H, 6.13; N, 5.01 Found: C, 68.95; H, 6.05; N, 5.35.

7,8,10,11,21,22,23,24-Octahydro-19H-dinaphtho[2,3-h: 2,3-q][1,4,7,11,15] trioxadiazacyclooctadecine-19,25(20H)-dione **(3):** Obtained from 1,3-diaminopropane (0.15 g, 2 mmol) in 80% yield; white solids; m.p. = 272–273°C; IR (KBr) 720 (s), 830 (s), 860 (s), 930 (s), 950 (s), 1080 (s), 1130 (s), 1180 (s), 1220 (s), 1240 (s), 1350 (s), 1410 (s), 1537 (s), 1640 (s), 3360 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.33 (s, 2H), 8.33 (br, 2H, NH), 7.2–8.0 (complex, 10H), 4.0–4.4 (m, 8H), 3.34 (m, 4H), 1.8 (m, 2H); ^{13}C NMR: 164.79, 153.09, 134.90, 134.83, 132.05, 128.23, 127.59, 125.77, 124.06, 122.50, 107.41, 68.56, 68.09, 42.50, 32.24; MS *m/z* 484 (M^+, 3), 482 (M-2, 40), 439 (3), 361 (18), 329 (12), 304 (11), 186 (35), 161 (70), 143 (55), 135 (20), 118 (base peak), 102 (25), 90 (55), 63 (55). Anal. Calcd. for $C_{29}H_{28}N_2O_5$: C, 71.89; H, 5.82; N, 5.78. Found: C, 71.24; H, 5.45; N, 5.92.

7,8,10,11,20,21,22,23-Octahydrodinaphtho[2,3-h: 2,3-p][1,4,7,11,14]trioxadiazacycloheptadecine-19,24-dione **(4):** Obtained in 60% yield; yellow solids; m.p. = 180–181°C; IR (KBr) 741 (s), 1096 (s), 1129 (s), 1223 (s), 1354 (s), 1444 (s), 1498 (s), 1537 (s), 1594 (s), 1643 (s), 2925 (s), 3056 (w), 3270 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.30 (br s, 2H, NH), 8.42 (s, 2H), 7.75 (d, 2H, *J* = 8.2 Hz), 7.63 (d, 2H, *J* = 8.3 Hz), 7.45 (t, 2H, *J* = 7.5 Hz), 7.28 (t, 2H, *J* = 7.8 Hz), 7.26 (s, 2H), 3.78 (t, 4H, *J* = 6.2 Hz), 3.45 (t, 4H, *J* = 6.2 Hz); ^{13}C NMR: 170.09, 156.16, 137.74, 132.31, 129.13, 129.08, 126.88, 126.14, 123.85, 114.04, 111.47, 71.12, 70.38. MS *m/z* 470 (M^+, 12), 468 (M-2, 25), 414 (31), 399 (10), 253 (3), 237 (5), 210 (12), 166 (4), 165 (38), 147 (36), 121 (base peak), 119 (40), 105 (22), 92 (30), 91 (38), 76 (18). Anal. Calcd. for $C_{28}H_{26}N_2O_5$: C, 71.48; H, 5.57; N, 5.95. Found: C, 71.65; H, 5.45; N, 6.05.

21,21-Dimethyl-7,8,10,11,20,21,22,23-Octahydrodinaphtho[2,3-h: 2,3-p][1,4,7,11,14] trioxadiazacycloheptadecine-19,24-dione **(5):** Obtained from 1,2-diamino-2-methylpropane (0.17 g, 2 mmol) in 85% yield; white solids; m.p. = 200–201°C; IR (KBr) 730 (s), 1080 (s), 1130 (s), 1180(s), 1220 (s), 1355 (s), 1440 (s), 1540 (s), 1595 (s), 1655 (s), 2950 (s), 3390 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.58 (s,1H), 8.20–8.48 (br s, 2H, NH), 8.10 (s, 1H), 7.95 (d, 1H, *J* = 8.0 Hz), 7.89 (d, 1H, *J* = 8.0 Hz), 7.83 (d, 1H, *J* = 8.0 Hz), 7.80 (d, 1H, *J* = 8.0 Hz), 7.53 (t, 1H, *J* = 7.5 Hz), 7.48 (t, 1H, *J* = 7.5 Hz), 7.47 (s, 1H), 7.42 (s, 1H), 7.31–7.41 (complex, 2H), 4.14 (m, 2H), 4.33 (m, 2H), 3.97 (m, 2H), 3.94 (m, 2H), 3.81 (d, 2H), 1.50 (s, 6H); ^{13}C NMR: 165.26, 164.09, 154.05, 153.50, 135.58, 135.25, 133.83, 132.89, 129.22, 128.95, 128.81, 128.38, 128.32, 128.26, 127.88, 126.26, 126.06, 124.72, 124.64, 124.50, 107.27, 106.90, 69.14, 69.01, 68.09, 68.00, 53.94, 47.36, 25.69. MS *m/z* 498 (M^+, 10), 496 (M-2, 25), 442 (31), 353 (13), 337 (15), 210 (22), 166 (14), 165 (38), 147 (39), 122 (base peak), 119 (40), 105 (22), 92 (60), 91 (45), 76 (28). Anal. Calcd. for $C_{30}H_{30}N_2O_5$: C, 72.27; H, 6.06; N, 5.62. Found: C, 71.95; H, 5.98; N, 5.45.

5,14,15,17,18,27-Hexahydrodinaphtho[2,3-c: 2,3-l][5,8,11,1,15] benzotrioxadiazacycloheptadecine-6,26-dione **(6):** Obtained from 1,2-diaminobenzene (0.216 g, 2 mmol) in 65% yield; white solids; m.p. = 160&161°C; IR (KBr) 750 (s), 1105 (s), 1125 (s), 1221 (s), 1352 (s), 1446 (s), 1507 (s), 1593 (s), 1622 (s), 1670 (s), 2870 (s), 3300 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 80 MHz) δ 10.0 (br s, 2H, NH), 8.50 (s, 2H), 7.0–8.0 (complex, 10H), 4.2 (m, 4H), 3.90 (m, 4H); MS *m/z* 518 (M^+, 10), 516 (M-2, 15), 490 (31), 475 (10), 462 (3), 253 (25), 237 (5), 210 (12), 166 (4), 165 (38), 147 (36), 121 (base peak), 119 (40), 105 (22), 92 (30), 91 (38), 76 (18). Anal. Calcd. for $C_{32}H_{26}N_2O_5$: C, 74.12; H, 5.05; N, 5.40. Found: C, 74.65; H, 5.35; N, 5.05.

13,14,16,17-Tetrahydrotrinaphtho[2,3-h: 1,8-lm: 2,3-q][1,4,7,11,15]trioxadiazacyclooctadecine-5,25(4H,26H)-dione **(7):** Obtained from 1,8-diaminonaphthalene (0.316 g, 2 mmol) in 85% yield; white solids; m.p. = 300–301°C; IR (KBr) 750 (s), 1105 (s), 1125 (s), 1221 (s), 1352 (s), 1446 (s), 1507 (s), 1593 (s), 1622 (s), 1660 (s), 2870 (s), 3300 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.59 (br s, 2H, NH), 8.09 (s, 2H), 7.97 (d, 2H, *J* = 7.25 Hz), 7.77 (d, 2H, *J* = 8.1 Hz), 7.47 (t, 2H, *J* = 7.3 Hz), 7.27 (m, 4H), 7.14 (d, 2H, *J* = 7.95 Hz), 6.98 (t, 2H, *J* = 6.28 Hz), 6.60 (s, 2H), 4.11 (m, 4H), 3.85 (m, 4H); ^{13}C NMR: 164.96, 152.06, 136.02, 134.78, 133.11, 132.85, 128.41, 128.16, 127.74, 127.37, 125.75, 125.64, 124.64, 124.34, 124.27, 124.04, 108.09, 67.39, 66.60. MS *m/z* 568 (M^+, 4), 566 (M-2, 20), 540 (25), 525 (10), 353 (13), 287 (15), 237 (15), 210 (4), 168 (5), 165 (38), 147 (36), 121 (base peak), 119 (45), 105 (25). Anal. Calcd. for $C_{36}H_{28}N_2O_5$: C, 76.04; H, 4.96; N, 4.93. Found: C, 76.65; H, 5.05; N, 5.15.

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