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The synthesis and complexation study of some novel 3-methoxyphenyl chromenone crown ethers using conductometry

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Abstract

7,8-Dihydroxy-3-(3,4-dimethoxyphenyl)-2*H*-chromenones, 7,8-dihydroxy-3-(3,5-dimethoxyphenyl)-2*H*-chromenones and 7,8-dihydroxy-3-(3,4,5-trimethoxyphenyl)-2*H*-chromenones, *o*-dihydroxy-3-methoxyphenylcoumarins, were prepared from 2,3,4-trihydroxybenzaldehyde and corresponding methoxyphenylacetic acid in NaOAc/Ac_2O, respectively. 3-Methoxyphenyl-7,8-dihydroxy-2*H*-chromenone reacted with the polyethylene glycol ditosylate or dichloride in CH_3CN/alkali carbonate to afford [12]crown-4, [15]crown-5 and [18]crown-6-chromonones.

The chromatographically purified novel chromenone crown ethers were identified with IR, ^1H NMR, ^{13}C NMR and low and high resolution mass spectroscopy and elemental analysis.

Stability constants for the 1:1 complexes of Na^+ and K^+ with different substituted methoxyphenyl derivatives of coumarino[12]crown-4, coumarino[15]crown-5 and coumarino[18]crown-6 (**5a–5i**) have been determined by conductometry at 25 °C in a binary solvent, dioxane/water. For all the coumarino crown ether derivatives, the stability constant decreases for K^+ ion compared to Na^+ ion.

The selectivity sequence of these crown ethers in dioxane/water has showed an irregular order with respect to their cavity size.

Keywords: 3-Aryl-chromenone crown ethers; Coumarino crown ethers; Synthesis; Complexation; Binary solvent; Conductometry

1. Introduction

The complexation selectivity of nonarmed crown ethers has often been explained in terms of the size-fit concept that the crown ether forms a more stable complex with the cation which is more suitable in size for the crown ether cavity.

From early investigation of crown ether–cation interactions it was determined that crown ethers can form 2:1 (crown:metal) "Sandwich" complexes with cations that are too large to fit into the macrocyclic cavity [1–5].

This led to the synthesis of new armed crown ethers which are attachment of functional side arm. Such derivatives bind alkaline cations in the macrocyclic cavity with the participation of the side arm donors, and they have been designated as lariat ethers [6,7]. We have recently synthesized various chromenone crown ethers with different chromophore moieties and reported their cationic interaction in acetonitrile. However, the oxygen

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atom which is contained in the phenyl moiety in coumarin arms can potentially participate along with the other oxygen atoms in the analog crown ether moiety to form 1:1 complex with a host ion [8–12].

We now report some new 3-methoxyphenyl chromenone crown ethers to provide a series of substituted coumarin compounds in which the ring size of the macrocyclic ring is systematically varied from [12]crown-4 to [18]crown-6. Metal ion complexation abilities of new coumarino crown ethers **5a–5i** were studied by conductometry.

2. Experimental

The starting chemicals **1**, **2a–2c** were purchased from Aldrich or Merck unless otherwise cited. Compounds **3a–3c** and chromenone crown ethers **5a–5i** have been newly prepared according to our early study [14]. IR spectra have taken as a KBr pellets with a JASCO FT-IR spectrometer, model 5300. High resolution EI mass spectra have been obtained with Fission Instruments, model UG-ZABSPEC. ^{1}H NMR spectra have been obtained with a BRUKER spectrometer, model AVANCE-400 Cpx and TMS was the initial standard. Melting points have been obtained on a Gallenkamp apparatus uncorrectedly. Combustion analyses have been acquired with an LECO-932 CHN analyser.

3. Complexation studies and the determination of the stability constants (K_e)

NaCl and KCl (Merck) were recrystallised three times from a conductivity water–ethanol mixture, and the salts were then heated to below their decomposition temperature at reduced pressure. Stability constants were measured by means of a conductometric method. The water used in the conductometric studies was redistilled from alkaline potassium permanganate. Dioxane was dried over sodium metal, and anhydrous methanol was used without further purification (Merck: H_2O content less than 0.01%). The solutions were prepared at constant 1:1 ratio of metal salt to ligand L in 80% dioxane/water mixture. All solutions were prepared in a dry box and transferred to dry conductivity cell. The conductances were measured at 25 ± 0.05 °C. The measuring equipment consisted of a glass vessel (type Ingold) with an external jacket. At the same time, the system was connected to a thermostatted water-bath (25 ± 0.05 °C) and a conductivity cell (Cole Parmer 19050-66) with a conductometer (Suntex SC-170 Model). The cell constant was determined as 0.769 cm^{-1} at 25 °C, measuring the conductivity of aqueous potassium chloride solutions of various concentrations [13]. Log K_e and $-\Delta G^0$ values for the reaction of the ligand with the cations were determined by a conductometric procedure outlined previously. Results are reported as the average and standard deviation from the average of four–six independent experimental determinations.

4. General procedure for the synthesis of 7,8-dihydroxy-3-(methoxyphenyl)chromenones (3a–3c)

In a typical reaction, a mixture of 20 mmol 2,3,4-trihydroxybenzaldehyde, 20 mmol of methoxyphenylacetic acid, 50 mmol of sodium acetate in 40 mL acetic anhydride was heated with stirring at 160 °C under N_2 for 6 h. After removal of acetic acid by distillation, the resulting mixture was treated with $MeOH/H_3O^+$, and the precipitates were collected by filtration. The dried product was purified by recrystallisation from ethanol.

*4.1. 7,8-Dihydroxy-3-(3,4-dimethoxyphenyl)-2H-chromen-2-one (**3a**: $C_{17}H_{14}O_6$)*

A mixture of compound **1** (3.08 g, 20 mmol), 3,4-dimethoxyphenylacetic acid (**2a**) (3.92 g, 20 mmol), NaOAc (4.10 g, 50 mmol) in acetic anhydride (40 mL) was treated as described above to afford **3a**, 5.14 g (82%); mp: 220 °C (ethanol); IR (KBr) 3400 (OH), 2950–2853 (C–H, alkyl), 1700 (C=O, lactone), 1620 (C=C, aromatic), 1190 (C–O) cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz): δ 3.76 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 6.71 (d, $J = 8.5$ Hz, 1H, H-5′), 6.88 (d, $J = 8.5$ Hz, 1H, H-6), 6.94 (d, $J = 8.5$ Hz, 1H, H-5), 7.15 (dd, $J = 8.5$ Hz and 2 Hz, 1H, H-6′), 7.22 (d, $J = 2$ Hz, 1H, H-2′), 7.80 (s, 1H, H-4).

Anal. calcd for $C_{17}H_{14}O_6$: C, 64.97%; H, 4.49%. Found: C, 64.82%; H, 4.12%.

*4.2. 7,8-Dihydroxy-3-(3,5-dimethoxyphenyl)-2H-chromen-2-one (**3b**: $C_{17}H_{14}O_6$)*

Compound **1** (3.08 g, 20 mmol), **2a** (3.92 g, 20 mmol), NaOAc (4.10 g, 50 mmol) in acetic anhydride (40 mL) was treated as described above to give **3b**, 4.60 g (73%); mp: 128–130 °C (ethanol); IR (KBr) 3361–3438 (OH), 3060 (C–H, aromatic), 2850–2978 (C–H, alkyl), 1720 (C=O, lactone), 1625 (C=C, aromatic), 1200 (C–O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.82 (s, 6H, OCH_3), 5.81 (s, 1H, OH), 6.08 (s, 1H, OH), 6.45 (br s, 1H, H-4′), 6.81 (br s, 2H, H-2′ and H-6′), 6.92 (d, $J = 8$ Hz, 1H, H-6), 7.05 (d, $J = 8$ Hz, 1H, H-5), 7.76 (s, 1H, H-4).

Anal. calcd for $C_{17}H_{14}O_6$: C, 64.97%; H, 4.49%. Found: C, 64.75%; H, 4.23%.

*4.3. 7,8-Dihydroxy-3-(3,4,5-trimethoxyphenyl)-2H-chromen-2-one (**3c**: $C_{18}H_{16}O_7$)*

Compound **1** (3.08 g, 20 mmol), **2c** (4.52 g, 20 mmol), NaOAc (4.10 g, 50 mmol) in acetic anhydride (40 mL) was treated as described above to give **3c**, 6.33 g (92%); mp: 238–239 °C (ethanol); IR (KBr) 3361–3463 (OH), 3055 (C–H, aromatic), 2851–2953 (C–H, alkyl), 1727 (C=O, lactone), 1625 (C=C, aromatic), 1242 (C–O) cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz): δ 3.69 (s, 3H, OCH_3), 3.78 (s, 6H, OCH_3), 6.72 (d, $J = 8.5$ Hz, 1H, H-6), 6.90 (br s, 2H, H-2′ and H-6′), 6.96 (d, $J = 8.5$ Hz, 1H, H-5), 7.88 (s, 1H, H-4).

Anal. calcd for $C_{18}H_{16}O_7$: C, 62.79%; H, 4.68%. Found: C, 61.60%; H, 4.50%.

5. General procedure for the synthesis of 3-methoxyphenyl chromenone crown ethers (5a–5i)

The typical procedure for the cyclisation reaction leading to macrocycle ethers (**5a–5i**) is as follows. A mixture of *o*-dihydroxycoumarins **3a–3c** (5 mmol), polyethylene glycol ditosylate or polyethylene glycol dichloride (5 mmol) and 10 mmol alkali metal carbonate was dissolved in 60 mL of CH_3CN in a 250-mL reaction flask. The mixture was heated for 35–40 h at 80–85 °C. The solvent was evaporated in vacuo. Diluted HCl was added to the residue and the mixture was extracted with $CHCl_3$ (4 × 30 mL). The combined organic extracts were washed with water, dried over $CaCl_2$ and evaporated in vacuo. Chromatography of the crude products (silica gel 60, Merck) with chloroform gave pure chromenone crown ethers (**5a–5i**).

5.1. 14-(3,4-Dimethoxyphenyl)-2,3,5,6,8,9-hexahydro-13H-[1,4,7,19]-tetraoxacyclododecino[2,3-h]chromen-13-one (5a: $C_{23}H_{24}O_8$)

Compound **3a** (1.57 g, 5 mmol), Na_2CO_3 (1.06 g, 10 mmol), **4a** (2.30 g, 5 mmol) in CH_3CN (60 mL) reacted as described above to afford **5a**, 0.43 g (20%); mp: 169–171 °C; IR (KBr) 3100 (C–H, aromatic), 2830–2910 (C–H, alkyl), 1710 (C=O, lactone), 1220 (C–O, aryl), 1140 (C–O, alkyl) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): 3.90 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 3.94 (t, $J = 4$ Hz, 4H), 4.20 (t, $J = 4$ Hz, 4H), 4.39 (t, $J = 4$ Hz, 4H), 6.84 (d, $J = 8.5$ Hz, 1H, H-5′), 6.90 (d, $J = 8.5$ Hz, 1H, H-6), 7.18 (d, $J = 8.5$ Hz, 1H, H-5), 7.23 (dd, $J = 8.5$ Hz and 2 Hz, 1H, H-6′), 7.27 (d, $J = 2$ Hz, 1H, H-2′), 7.68 (s, 1H, H-4); MS: *m/z* 428 (M^+), 400 ($M^+ - 28$), 384 (400 – 16).

Anal. calcd for $C_{23}H_{24}O_8$: C, 64.48%; H, 5.65%. Found: C, 64.35%; H, 5.27%.

5.2. 17-(3,4-Dimethoxyphenyl)-2,3,5,6,8,9,11,12-octahydro-15H-[1,4,7,10,13]pentaoxacyclopentadecino[2,3-h]chromen-15-one (5b: $C_{25}H_{28}O_9$)

A mixture of compound **3a** (1.57 g, 5 mmol), Na_2CO_3 (1.06 g, 10 mmol), and **4b** (1.16 g, 5 mmol) and CH_3CN (60 mL) was stirred and heated and then worked up as described above to afford **5b**, 0.73 g (31%); mp: 148 °C; IR (KBr) 3100 (C–H, aromatic), 2876–2927 (C–H, alkyl), 1727 (C=O, lactone), 1625 (C=C, aromatic), 1370 (C–O, aryl), 1089 (C–O, alkyl) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): 3.76 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.83 (t, $J = 5$ Hz, 8H), 4.08 (t, $J = 5$ Hz, 4H), 4.24 (t, $J = 5$ Hz, 4H), 6.70 (d, $J = 9$ Hz, 1H, H-5′), 6.77 (d, $J = 8.5$ Hz, 1H, H-6), 7.03 (d, $J = 8.5$ Hz, 1H, H-5), 7.09 (dd, $J = 9$ Hz and 2 Hz, 1H, H-6′), 7.14 (d, $J = 2$ Hz, 1H, H-2′), 7.55 (s, 1H, H-4); ^{13}C NMR ($CDCl_3$): 56.3 (OCH_3), 56.4 (OCH_3), 69.3, 69.7, 70.6, 70.7, 70.8, 71.3, 71.4, 74.0, 110.1, 111.6, 112.4, 115.1, 121.4, 122.9, 125.2, 128.2, 135.7, 139.5, 147.9, 149.2, 149.9, 155.1, 160.1; MS: *m/z* 472 (M^+), 384 ($M^+ - 88$), 340 (384 – 44).

Anal. calcd for $C_{25}H_{28}O_9$: C, 63.55%; H, 5.97%. Found: C, 63.07%; H, 5.51%.

5.3. 20-(3,4-Dimethoxyphenyl)-2,3,5,6,8,9,11,12,14,15-decahydro-18H-[1,4,7,10,13,16]hexaoxacyclooctadecino[2,3-h]chromen-18-one (5c: $C_{27}H_{32}O_{10}$)

A mixture of compound **3a** (1.57 g, 5 mmol), K_2CO_3 (1.38 g, 10 mmol), and **4c** (2.73 g, 5 mmol) and CH_3CN (60 mL) was treated as described above to give **5c**, 0.44 g (17%); mp.: 130–131 °C; IR (KBr) 3000 (C–H, aromatic), 2810–2930 (C–H, alkyl), 1710 (C=O, lactone), 1620 (C=C, aromatic), 1230 (C–O, aryl), 1160 (C–O, alkyl) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): 3.90 (t, $J = 5$ Hz, 4H), 4.08 (t, $J = 5$ Hz, 4H), 4.05 (s, 3H, OCH_3), 4.07 (s, 3H, OCH_3), 4.15 (t, $J = 5$ Hz, 4H), 4.39 (t, $J = 5$ Hz, 4H), 4.50 (t, $J = 5$ Hz, 4H), 7.01 (d, $J = 8$ Hz, 1H, H-5′), 7.06 (d, $J = 8.5$ Hz, 1H, H-6), 7.32 (d, $J = 8.5$ Hz, 1H, H-5), 7.37 (dd, $J = 8$ Hz and 2 Hz, 1H, H-6′), 7.41 (d, $J = 2$ Hz, 1H, H-2′), 7.82 (s, 1H, H-4); ^{13}C NMR ($CDCl_3$): 56.3 (OCH_3), 56.4 (OCH_3), 69.6, 70.0, 70.5, 70.9, 71.2, 71.3, 71.4, 71.6, 73.5, 77.6, 110.7, 111.6, 112.4, 115.3, 121.4, 122.9, 125.3, 128.2, 135.8, 139.4, 147.9, 149.2, 149.9, 154.9, 160.8; MS: *m/z* 516 (M^+), 460, 416 (460 – 44), 372 (416 – 44), 328 (372 – 44).

Anal. calcd for $C_{27}H_{32}O_{10}$: C, 62.78%; H, 6.24%. Found: C, 62.23%; H, 6.55%.

5.4. 14-(3,5-Dimethoxyphenyl)-2,3,5,6,8,9-hexahydro-13H-[1,4,7,10]-tetraoxacyclooctadecino[2,3-h]chromen-13-one (5d: $C_{23}H_{24}O_8$)

Compound **3b** (1.57 g, 5 mmol), Na_2CO_3 (1.06 g, 10 mmol), **4a** (2.30 g, 5 mmol) in CH_3CN (60 mL) reacted as described to give **5d**, 0.49 g (23%); mp: 170–172 °C; IR (KBr) 3100 (C–H, aromatic), 2876–2927 (C–H, alkyl), 1727 (C=O, lactone), 1625 (C=C, aromatic), 1370 (C–O, aryl), 1089 (C–O, alkyl) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.75 (s, 6H, OCH_3), 3.90 (t, $J = 4$ Hz, 4H), 4.16 (t, $J = 4$ Hz, 4H), 4.33 (t, $J = 4$ Hz, 4H), 6.41 (t, $J = 2$ Hz, 1H, H-4′), 6.74 (d, $J = 2$ Hz, 2H, H-2′ and H-6′), 6.78 (d, $J = 8$ Hz, 1H, H-6), 7.12 (d, $J = 8$ Hz, 1H, H-5), 7.65 (s, 1H, H-4); MS: m/z 428 (M^+), 384 ($M^+ - 44$), 340 (384 – 44).

Anal. calcd for $C_{23}H_{24}O_8$: C, 64.48%; H, 5.65%; Found: C, 64.75%; H, 5.57%.

*5.5. 17-(3,5-Dimethoxyphenyl)-2,3,5,6,8,9,11,12-octahydro-15H-[1,4,7,10,13]pentaoxacyclopentadecino[2,3-h]chromen-15-one (**5e**: $C_{25}H_{28}O_9$)*

A mixture of compound **3b** (1.57 g, 5 mmol), Na_2CO_3 (1.06 g, 10 mmol), and **4b** (1.16 g, 5 mmol) and CH_3CN (60 mL) was stirred and heated and then worked up as described above to give **5e**, 0.49 g (21%); mp.: 139–141 °C; IR (KBr) 3100 (C–H, aromatic), 2830–2890 (C–H, alkyl), 1710 (C=O, lactone), 1600 (C=C, aromatic), 1220 (C–O, aryl), 1160 (C–O, alkyl) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.75 (s, 6H, OCH_3), 3.88 (t, $J = 4$ Hz, 8H), 4.16 (t, $J = 4$ Hz, 4H), 4.30 (t, $J = 4$ Hz, 4H), 6.41 (t, $J = 2$ Hz, 1H, H-4′), 6.74 (d, $J = 2$ Hz, 2H, H-2′ and H-6′), 6.77 (d, $J = 9$ Hz, 1H, H-6), 7.10 (d, $J = 9$ Hz, 1H, H-5), 7.63 (s, 1H, H-4); MS: m/z 472 (M^+), 384 ($M^+ - 88$), 340 (384 – 44), 296 (340 – 44).

Anal. calcd for $C_{25}H_{28}O_9$: C, 63.55%; H, 5.97%. Found: C, 62.95%; H, 5.37%.

*5.6. 20-(3,5-Dimethoxyphenyl)-2,3,5,6,8,9,11,12,14,15-decahydro-18H-[1,4,7,10,13,16]hexaoxacyclooctadecino[2,3-h]chromen-18-one (**5f**: $C_{27}H_{32}O_{10}$)*

Compound **3b** (1.57 g, 5 mmol), K_2CO_3 (1.38 g, 10 mmol) and **4c** (2.73 g, 5 mmol) in CH_3CN (70 mL) reacted as described above to give **5f**, 0.31 g (12%); mp.: 108–110 °C; IR (KBr) 2850–2920 (C–H, alkyl), 1727 (C=O, lactone), 1625 (C=C, aromatic), 1370 (C–O, aromatic), 1089 (C–O, alkyl) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.83 (s, 6H, OCH_3), 3.94 (t, $J = 5$ Hz, 4H), 4.02 (t, $J = 5$ Hz, 4H), 4.26 (t, $J = 5$ Hz, 4H), 4.36 (t, $J = 5$ Hz, 4H), 4.49 (t, $J = 5$ Hz, 4H), 6.45 (t, $J = 2$ Hz, 1H, H-4′), 6.82 (d, $J = 2$ Hz, 2H, H-2′ and H-6′), 6.87 (d, $J = 8.5$ Hz, 1H, H-6), 7.18 (d, $J = 8.5$ Hz, 1H, H-5), 7.72 (s, 1H, H-4); MS: m/z 516 (M^+), 472 ($M^+ - 44$), 428 (472 – 44), 384 (428 – 44), 340 (384 – 44).

Anal. calcd for $C_{27}H_{32}O_{10}$: C, 62.78%; H, 6.24%. Found: C, 62.55%; H, 5.67%.

*5.7. 14-(3,4,5-Trimethoxyphenyl)-2,3,5,6,8,9-hexahydro-13H-[1,4,7,10]-tetraoxacyclodecino[2,3-h]chromen-13-one (**5g**: $C_{24}H_{26}O_9$)*

Compound **3c** (0.70 g, 2.04 mmol), Na_2CO_3 (0.50 g, 5 mmol), **4a** (0.94 g, 2.04 mmol) in CH_3CN (50 mL) reacted as described to give **5g**, 0.20 g (22%); mp: 175–176 °C; IR (KBr) 3055 (C–H, aromatic), 2851–2920 (C–H, alkyl), 1727 (C=O, lactone), 1523 (C=C, aromatic), 1242 (C–O, aromatic), 1100 (C–O, alkyl) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.80 (s, 3H, OCH_3), 3.85 (s, 6H, OCH_3), 4.00 (t, $J = 5$ Hz, 4H), 4.21 (t, $J = 5$ Hz, 4H), 4.43 (t, $J = 5$ Hz, 4H), 6.82 (d, $J = 8$ Hz, 1H, H-6), 6.85 (d, $J = 2$ Hz, 2H, H-2′ and H-6′), 7.22 (d, $J = 8$ Hz, 1H, H-5), 7.70 (s, 1H, H-4); MS: m/z 458 (M^+), 459 $(M + 1)^+$, 460 $(M + 2)^+$, 398 ($M^+ - 60$), 354 (398 – 44).

Anal. calcd for $C_{24}H_{26}O_9$: C, 62.88%; H, 5.72%. Found: C, 61.90%; H, 5.38%.

*5.8. 17-(3,4,5-Trimethoxyphenyl)-2,3,5,6,8,9,11,12-octahydro-15H-[1,4,7,10,13]-pentaoxacyclopentadecino[2,3-h]chromen-15-one (**5h**: $C_{26}H_{30}O_{10}$)*

A mixture of compound **3c** (1.50 g, 4.36 mmol), Na_2CO_3 (1.06 g, 10 mmol), **4b** (1.01 g, 4.35 mmol) and CH_3CN (60 mL) was stirred and heated after cooling the residue worked up as described above to give **5h**, 0.91 g (42%); mp:147–148 °C; IR (KBr) 3050 (C–H, aromatic), 2870–2924 (C–H, alkyl), 1702 (C=O, lactone), 1610 (C=C, aromatic), 1320 (C–O, aromatic), 1100 (C–O, alkyl) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.80 (s, 3H, OCH_3), 3.85 (s, 6H, OCH_3), 4.00 (t, $J = 5$ Hz, 8H), 4.21 (t, $J = 5$ Hz, 4H), 4.40 (t, $J = 5$ Hz, 4H), 6.82 (d, $J = 8$ Hz, 1H, H-6), 6.85 (d, $J = 2$ Hz, 2H, H-2′ and H-6′), 7.20 (d, $J = 8$ Hz, 1H, H-5), 7.70 (s, 1H, H-4); MS: m/z 502 (M^+), 503 $(M + 1)^+$, 504 $(M + 2)^+$, 414 ($M^+ - 88$), 370 (414 – 44), 326 (370 – 44).

Anal. calcd for $C_{26}H_{30}O_{10}$: C, 62.14%; H, 6.02%. Found: C, 61.98%; H, 5.80%.

*5.9. 20-(3,4,5-Trimethoxyphenyl)-2,3,5,6,8,9,11,12,14,15-decahydro-18H-[1,4,7,10,13,16]hexacyclooctadecino[2,3-h]chromen-18-one (**5i**: $C_{28}H_{34}O_{11}$)*

Compound **3c** (0.90 g, 2.62 mmol), K_2CO_3 (0.73 g, 5.29 mmol) and **4c** (1.43 g, 2.62 mmol) in CH_3CN (75 mL) reacted as described above to give **5i**, 0.20 g (14%); mp: 101–103 °C; IR (KBr) 3080 (C–H, aromatic), 2850–2927 (C–H, alkyl), 1727 (C=O, lactone), 1600 (C=C, aromatic), 1242 (C–O, aromatic), 1114 (C–O, alkyl) cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.63 (s, 3H,

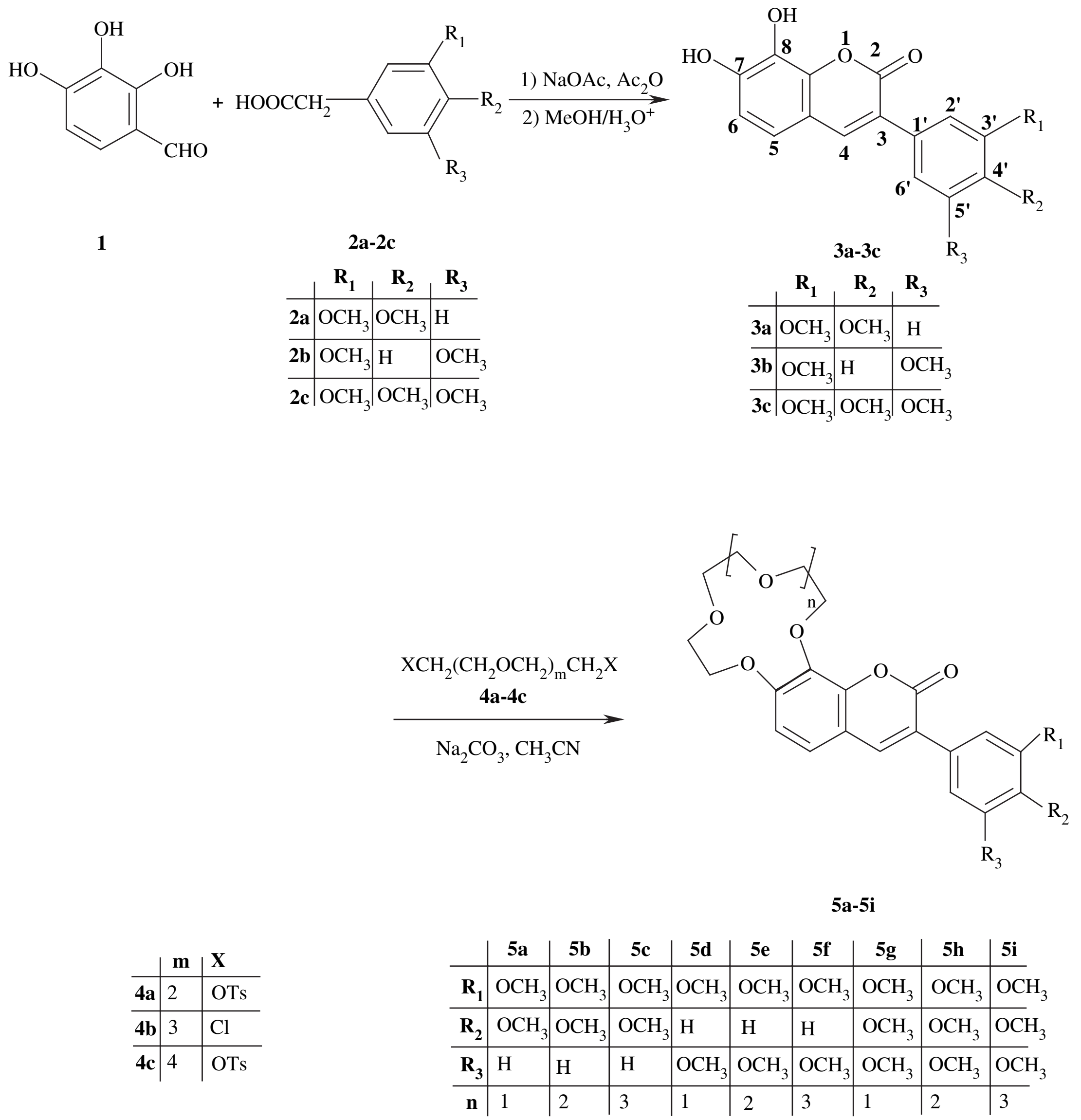
OCH_3), 3.82 (s, 6H, OCH_3), 3.85 (t, $J = 5$ Hz, 4H), 3.95 (t, $J = 5$ Hz, 4H), 4.00 (t, $J = 5$ Hz, 4H), 4.20 (t, $J = 5$ Hz, 4H), 4.23 (t, $J = 5$ Hz, 4H), 6.82 (d, $J = 8$ Hz, 1H, H-6), 6.85 (d, $J = 2$ Hz, 2H, H-2′ and H-6′), 7.20 (d, $J = 8$ Hz, 1H, H-5), 7.70 (s, 1H, H-4); MS: m/z 546 (M^+), 547 $(M + 1)^+$, 548 $(M + 2)^+$, 502 ($M^+ - 44$), 458 (502 − 44), 414 (458 − 44).

Anal. calcd for $C_{28}H_{34}O_{11}$: C, 61.53%; H, 6.27%. Found: C, 60.21%; H, 6.42%.

6. Results and discussion

3-Methoxyphenyl chromenone crown ether derivatives **5a–5i** were synthesized from the polyethylene glycol ditosylate or polyethylene glycol dichloride **4a–4c** and corresponding 7,8-dihydroxy-3-(methoxyphenyl)-coumarins **3a–3c** were prepared from 2,3,4-trihydroxybenzaldehyde and corresponding methoxyphenylacetic acid in $NaOAc/Ac_2O$ mixture (Scheme 1).

Compound **3a** was reacted with **4a**, **4b**, **4c** to give the crown ethers **5a**, **5b**, **5c**, respectively, in the presence of Na_2CO_3 in CH_3CN. **3b** was reacted with **4a**, **4b**, **4c** to afford the crown ethers **5d**, **5e**, **5f**, respectively. Compound **3c** was reacted with **4a**, **4b**, **4c** to give the crown ethers **5g**, **5h**, **5i**, respectively, in the presence of alkali metal in CH_3CN. The residue chromatographed over a silica gel column on eluting with $CHCl_3$ afforded the 3-methoxyphenyl chromenone crown ethers **5a–5i** in 12–42% yield. The novel compounds have been characterized by elemental analysis IR, ^1H NMR, ^{13}C NMR and MS spectroscopy.



	R_1	R_2	R_3
2a	OCH_3	OCH_3	H
2b	OCH_3	H	OCH_3
2c	OCH_3	OCH_3	OCH_3

	R_1	R_2	R_3
3a	OCH_3	OCH_3	H
3b	OCH_3	H	OCH_3
3c	OCH_3	OCH_3	OCH_3

	m	X
4a	2	OTs
4b	3	Cl
4c	4	OTs

	5a	5b	5c	5d	5e	5f	5g	5h	5i
R_1	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3
R_2	OCH_3	OCH_3	OCH_3	H	H	H	OCH_3	OCH_3	OCH_3
R_3	H	H	H	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3	OCH_3
n	1	2	3	1	2	3	1	2	3

Scheme 1.

The IR spectra of **5a–5i** showed two absorption band at ca. 2850 and 2940 cm^{-1} for their C–H stretching frequency. The characteristic absorption band of the carbonyl group (C=O) and benzene ring should appear in the region 1710–1727 cm^{-1} and 1523–1625 cm^{-1}, respectively. One absorption band in the range 1089–1160 cm^{-1} corresponding to C–O–C ether chain. The ^1H NMR spectra of **5a–5i** in $CDCl_3$ show the expected peak resonances and peak integrals due to the protons of 3-methoxyphenyl chromenone crown ether derivatives. The ^1H NMR spectra of **5a–5i** showed characteristic signals for etheral ($-O-CH_2-CH_2-O-$) protons at δ 3.83–4.50 ppm each a triplet. The peak at δ 3.63–4.07 ppm indicated the presence of $-OCH_3$ group. In addition the chemical shifts of the aromatic protons are observed at δ 6.41–7.82 ppm. ^{13}C NMR spectra of **5a–5i** showed expected signals for aromatic, etheral and $-OCH_3$ protons at δ 110.1–160.8, 69.3–77.6, 56.3–56.4 ppm, respectively. Also EI mass spectrum and elemental analysis confirmed the formation of 3-methoxyphenyl chromenone crown ether derivatives.

6.1. Complexation equilibria in 80% dioxane/water: conductometric measurements of Na^+ and K^+ complexations

Structures of the metal–ligand (M:L) complexes in dioxane/water mixture were estimated from the conductance parameters (κ and Λ) as well as the complex formation constant,

$$K_e = (\Lambda MA_m - \Lambda)/(\Lambda - \Lambda M_a L_b A_m)[L].$$

Molar conductivities, Λ ($S\,cm^2\,mol^{-1}$), were calculated from the infinite frequency electrolytic conductances, κ, after correcting for the pure solvent conductance, i.e. $\Lambda = 1000\kappa/C_{MX}$, where C_{MX} is the total concentration of the metal salt. The experimental molar conductance equations and all calculations for stability constants and Gibbs free enthalpy values have been published in our previous works [11,15]. All experimental studies have been made by the ratio 1:1 of the metal ion and the coumarino crown ethers.

All coumarino crown ethers **5a–5i** have di- or tri-substituted methoxyphenyl groups in the side arm with systematic variations in the ring size of the crown ether ring from [12]crown-4 to [15]crown-5 to [18]crown-6, respectively. Results for alkali metal complexation study by coumarino crown ether derivatives are presented in Table 1.

All the coumarino crown ether derivatives have shown high Na^+ selectivity over K^+ in dioxane/water. For the coumarino crown ethers with two metal ions examined, the variations in substitution of methoxy substituents to the phenyl group in the side arm did not show higher differences between complexation constants. Complexation efficiencies of these hosts for K^+ were uniformly low.

Table 1
The Log K_e and $-\Delta G^0$ (kcal/mol) values for the complexations of different coumarino crown ethers with Na^+ and K^+ ions in 80% dioxane/water at 25 °C by a conductometric study

Ion	Value	Coumarino crown ether								
		5a	**5b**	**5c**	**5d**	**5e**	**5f**	**5g**	**5h**	**5i**
Na^+	Log K_e	7.10 ± 0.19	7.34 ± 0.11	5.38 ± 0.21	7.24 ± 0.71	5.69 ± 0.28	5.99 ± 0.23	6.99 ± 0.22	6.26 ± 0.18	7.27 ± 0.16
	$-\Delta G^0$	9677.43 ± 0.28	10007.71 ± 0.15	7341.33 ± 0.22	9876.24 ± 0.38	7757.41 ± 0.06	8170.84 ± 0.98	9529.80 ± 0.55	8539.42 ± 0.68	9905.98 ± 0.21
K^+	Log K_e	4.20 ± 0.85	4.42 ± 0.70	5.02 ± 0.26	5.34 ± 0.68	4.30 ± 0.33	5.31 ± 0.55	4.40 ± 0.80	4.35 ± 0.49	4.88 ± 0.72
	$-\Delta G^0$	5736.40 ± 0.65	6032.21 ± 0.47	6847.26 ± 0.87	7286.64 ± 0.57	5863.81 ± 0.68	7236.31 ± 0.09	6000.72 ± 0.44	5932.00 ± 0.27	6657.44 ± 0.58

The higher complexation ability of Na^+ is more attributable to greater $\text{Log}\, K_e$ and $-\Delta G^{\theta}$ values compared with K^+.

The complexation selectivity order of 3,4-, 3,5- and 3,4,5-methoxy substituted coumarino crown ethers with Na^+ ion, were observed as follows:

5b > **5a** > **5c**; **5d** > **5f** > **5e**; **5i** > **5g** > **5h**

The complexation sequence for K^+ ion was obtained as follows:

5c > **5b** > **5a**; **5d** > **5f** > **5e**; **5i** > **5g** > **5h**

Thus, the highest association constant for complexation of sodium chloride was found for **5b** ligand.

As a result, differences in the nature of all coumarino crown ether derivatives, complexation with Na^+ versus K^+ may be due to easier formation of intermolecular complexes among the oxygen atoms in the mono crown ether molecule and oxygen atoms which is contained in the side arm of other coumarino crown ether analog, and so only interactions of complexed metal ion with a single crown ether cavity unit are evident.

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