The synthesis and complexation study of some coumestan and coumestan analog derivatives of crown ethers using conductometry

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Abstract

8,9-Dihydroxycoumestans, the 8,9-dihydroxy-6H-benzofuro[3,2-c][1]-benzopyran-6-one, derivatives were prepared from corresponding 4-hydroxy-2H-[1]benzopyran-2-one and catechol in oxidizing mixture $KIO_3/CH_3COONa/H_2O$/acetone while for the oxidative coupling of cyclohexane-1,3-dione and catechol, $K_3[Fe(CN)_6]/CH_3COONa/H_2O$/acetone was used. The derivatives of 8,9-dihydroxycoumestan and 8,9-dihydroxy-1,4-dimethy-6H-benzofuro[3,2-c][1]-benzopyran-6-one and two coumestan analog compounds reacted with the bis-dihalides of polyglycols in CH_3CN/Me_2CO_3 to furnish coumestano-12-Crown-4, 15-Crown-5 and 18-Crown-6. The crude products were purified using silica gel chromatography with chloroform. The obtained novel pure crown ethers were identified with IR, ^1H NMR, ^{13}C NMR, mass spectroscopy and elemental analysis.

Formation constants for complexation between $NaClO_4$ and the various coumestano-crown ethers in the solvent acetonitrile at 25 °C were determined from conductance measurements. The method also permits accurate evaluation of association equilibrium constants between the complex species (M—Coumestano-crown ether)$^+$ and the anion. The magnitudes of these ion association constants are related to the nature of the solvation of the cation and of the complexed cation. Structures of crown compound—cation complexes in acetonitrile are estimated from the conductance parameters (κ, Λ and α) as well as complex formation constant $\{K_e = (\Lambda_{MAm} - \Lambda)/((\Lambda - \Lambda_{MLAm})[L])\}$.

The complexation study indicates 1:1 complex formation between the metal ion and the crown ether. All the experimental studies have been conducted using the ratio 1:1 of the metal ion and the crown ether.
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Keywords: Coumestano-crown ethers; Synthesis; Complexation; Conductometry

1. Introduction

Since the syntheses of crown ethers by Pedersen [1] and cryptands by Lehn [2], the application of macrocyclic ligand chemistry has taken many directions as shown in the review by Izatt and co-workers [3] which cites close to 1200 references up to early 1990.

The ability of macrocyclic polyethers (crown ethers) to form stable complexes with cations, mainly with alkali and alkaline earth cations, has spurred interest in these compounds [4]. Recently published studies include conductometric measurement of some electrolytes in non-aqueous solvents (tetrahydrofuran [5], tetrahydropyran [5], acetonitrile [6,7] and methanol [7]), in the presence of crown ethers. Studies carried out in

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solutions of alkali metal salts and crown ethers in acetonitrile and methanol showed decreases in conductivities of the solutions.

The object of the present work is the synthesis of some new coumestan and coumestan analog derivatives of crown ethers containing 4–6 oxygen atoms, 8,9-([1,4,7,10,13,16]hexaoxacyclopentadecino)-6*H*-benzofuro-[3,2-*c*][1]-benzopyran-6-one (**7c**), 1,3-dimethyl-8,9-([1,4,7,10,13,16]hexaoxacyclopentadecino)-6*H*-benzofuro[3,2-*c*]-[1]-benzopyran-6-one (**7f**), 2,3-dimethyl-8,9-([1,4,7,10,13]pentaoxacyclopentadecino)-6*H*-benzofuro[3,2-*c*]-[1]-benzopyran-6-one (**7g**), 1,4-dimethyl-8,9-([1,4,7,10,13]pentaoxacyclopentadecino)-6*H*-benzofuro[3,2-*c*][1]-benzopyran-6-one (**7h**), 6,7-([1,4,7,10,13]pentaoxacyclododecino)-3,3-dihydro-2*H*-dibenzofuran-1-one (**8b**), 6,7-([1,4,7,10,13,16]hexaoxacyclododecino)-3,3-dihydro-2*H*-dibenzofuran-1-one (**8c**), 6,7-([1,4,7,10,13,16]hexaoxacyclododecino)-3,3-dimethyl-3,4-dihydro-2*H*-dibenzofuran-1-one (**8f**) and a study of their conductance behaviour with Na$^+$-perchlorate in acetonitrile at 25 °C together with the structurally analog crown ethers (**7a**, **7b**, **7d**, **7e**, **8a**, **8d**) available from our early study [14].

The present work indicates 1:1 complex formation between the sodium ion and electrically neutral coumestan and coumestan analog crown ethers.

2. Experimental

The starting chemicals **2**, **3a**, **3b** were from Fluka or Merck. Initial compounds **1a**, **1b**, **4a**, **4b**, **5a**, **5b**, **7a**, **7b**, **7d**, **7e**, **8a**, **8d** and **8e** were available from our earlier study [14]. IR spectra were taken as KBr pellets with a JASCO FT-IR Spectrometer, model 5300. High resolution EI–MS were obtained with Fisons Instrument, model VG-ZABSPEC.

^{1}H NMR spectra were obtained with a Bruker Spectrometer, model AVANCE-400CPX and TMS were the internal standards. Melting points given are uncorrected. Combustion analyses were acquired with a LECO-932 CHN analyser.

Macrocycles **7a**–**7h** and **8a**–**8f** have been synthesized in our laboratories. Alkali perchlorate (NaClO$_4$, Merck) was recrystallized thrice with conductivity water. The salt was then heated below its decomposition temperature at reduced pressure. Acetonitrile (Merck; H$_2$O content less than 0.3%) was of analytical grade quality and was used without further purification.

3. The conductometric study of coumestano-crown ethers with NaClO$_4$ salt

All solutions were prepared in a dry box and transferred into the dry conductivity cell. All conductances were measured at 25 ± 0.05 °C. The measuring equipment consisted of a glass vessel (type Ingold) with an external jacket connected to a thermostatted water-bath (25 ± 0.05 °C) and a conductivity cell (Cole Parmer 19050-66 Model) with a conductometer (SUNTEX SC-170 Model).

The cell constant was determined to be 0.769 cm^{-1} at 25 °C by measuring the conductivity of aqueous potassium chloride solutions of different concentrations [15]. A value of the molar conductivity of the pure metal ion solution (Λ_{MA}) was obtained at the appropriate electrolyte concentration before any addition of ligand was made.

4. General procedure for the synthesis of 4-hydroxy-2*H*-[1]benzopyran-2-one (1c, 1d)

In a typical reaction, a mixture of 0.024 mmol of phenol, 0.024 mmol of malonic acid and 0.072 mmol of dry ZnCl$_2$ in 10 mL phosphorus oxychloride was heated with stirring at 60–65 °C for 35 h, cooled and decomposed with ice and water. The resulting crude product was collected and dissolved in 10% Na$_2$CO$_3$, filtered and the solution acidified. The separated coumarin gave, on recrystallization from dilute alcohol, pure 4-hydroxy-2*H*-chromen-2-one.

4.1. 4-Hydroxy-6,7-dimethyl-2H-[1]benzopyran-2-one (1c)

This compound was obtained in 58% yield, mp 248 °C (Lit. 243 °C [16]); IR (KBr): 3280 broad (OH), 1633/1666 shoulder (C=O) and 1595 (Ar-H) cm^{-1}; ^{1}H NMR (CDCl$_3$/DMSO-d_6, 400 Hz): δ 8.63 (4 O–H), 7.15 (s, Ar-H), 7.06 (s, Ar-H), 6.20 (s, 1H, lactone), 2.68 (s, 3H, CH$_3$) and 2.31 (s, 3H, CH$_3$).

Anal. Calcd for C$_{11}$H$_{10}$O$_3$: C, 69.47; H, 5.26. Found: C, 69.68; H, 5.46.

4.2. 4-Hydroxy-5,8-dimethyl-2H-[1]benzopyran-2-one (1d)

This compound was obtained in 58% yield, mp 258 °C (ethanol) (Lit. 261–262 °C [17]). IR (KBr): 3147/3150 (OH), 1687 (C=O) cm^{-1}; ^{1}H NMR (CDCl$_3$/DMSO-d_6, 400 Hz): δ 7.23–8.83 (q, Ar-H and 4-OH), 6.23 (s, 1H, lactone), 2.67 (s, 3H, CH$_3$) and 2.20 (s, 3H, CH$_3$).

Anal. Calcd for C$_{11}$H$_{10}$O$_3$: C, 69.47; H, 5.26. Found: C, 69.20; H, 5.16.

5. General procedure for the preparation of compounds 4c and 4d

In a typical reaction, a mixture of **1c** or **1d** and 0.02 mol catechol was stirred in 60 mL acetone/water (1:1) with an oxidizing mixture KIO_3/CH_3COONa at 25 °C in the presence of nitrogen for 60 min. The precipitated product was filtered and washed with hot water. Each of the compounds listed below was recrystallized from ethanol.

5.1. 8,9-Dihydroxy-2,3-dimethyl-6H-benzofuro[3,2-c][1]-benzopyran-6-one (4c)

This compound was obtained in 64% yield, mp 268 °C (ethanol) (Lit. 262 °C [18]). The IR spectrum of **4c** (in KBr) showed absorption bands at 3380 (OH), 1710 (C=O, lactone), 1600−1800 (C=C, furan and aromatic) and 1240 (C−O, stretching) cm^{-1}; ^{1}H NMR (CDCl$_3$/DMSO-d_6, 400 Hz) of **4c** showed singlets at δ 9.52 (2 O−H), 8.2 (Ar-H), two singlets at 7.4 (Ar-H), 2.39 (3H, Ar-CH$_3$) and 2.38 (3H, Ar-CH$_3$); ^{13}C NMR (CDCl$_3$): δ 157.8, 157.5, 152.2, 149.7, 146.7, 144.9, 133.2, 133.1, 125.8, 121.0, 114.1, 105.5, 105.2, 99.1, 22.3, 22.

Anal. Calcd for $C_{17}H_{12}O_5$: C, 68.92; H, 4.05. Found: C, 68.88; H, 3.96.

5.2. 8,9-Dihydroxy-1,4-dimethyl-6H-benzofuro[3,2-c][1]-benzopyran-6-one (4d)

This compound was obtained in 66% yield, mp >300 °C. The IR spectrum of **4d** (in KBr) showed absorption bands at 3370 (OH), 1680 (C=O, lactone), 1600−1800 (C=C, furan and aromatic) cm^{-1}; ^{1}H NMR (CDCl$_3$/DMSO-d_6, 400 Hz) of **4d** showed doublets at δ 9.50 (2 O−H), 7.4−7.8 (Ar-H), singlets at 7.6, 7.7 (Ar-H), 2.86 (s, 3H, CH$_3$) and 2.51 (s, 3H, CH$_3$); ^{13}C NMR (CDCl$_3$): δ 158.1, 157.6, 152.3, 149.6, 147.0, 144.8, 133.3, 133.1, 126.1, 121.0, 105.5, 105.3, 99.2, 22.6, 22.3, 19.68.

Anal. Calcd for $C_{17}H_{12}O_5$: C, 68.92; H, 4.05. Found: C, 68.30; H, 4.08.

6. General procedure for the synthesis of coumestan and coumestan analog derivatives of crown ethers (7a−7h and 8a−8f)

The typical procedure for the cyclisation reaction leading to macrocyclic ethers **7a−7h** and **8a−8f** is as follows. A mixture of *o*-dihydroxy compounds **4a−4d** and **5a−5b** (5 mmol) polyethyleneglycol ditosylate or dichloride (5 mmol) and 10 mmol Me$_2$CO$_3$ was dissolved in 120 mL of CH$_3$CN 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, Fluka) with chloroform gave pure ethers **7a−7h** and **8a−8f**.

6.1. 8,9-([1,4,7,10,13,16]Hexaoxacyclooctadecino)-6H-benzofuro[3,2-c][1]-benzopyran-6-one (7c)

Compound **4a** (1.48 g, 5 mmol), K$_2$CO$_3$ (1.40 g, 10 mmol), CH$_3$CN (120 mL) and **6c** (2.73 g, 5 mmol) reacted as described above to afford **7c**, 0.34 g (14.4%), mp 160 °C (acetonitrile); IR (KBr): 3100 (C−H, arom.), 2890 (CH$_2$), 2850−2950 (C−H, alkyl), 1749 (lactone), 1618 (C=C), 1278 (C−O, aryl), 1128 (C−H, alkyl) cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 Hz): δ 7.90 (d, 1H, Ar-H), 7.68 (s, 1H, Ar-H), 7.44 (m, 1H, Ar-H), 7.34 (m, 2H, Ar-H), 7.23 (s, 1H, Ar-H), 4.4 (t, 2H, OCH$_2$), 4.30 (t, 2H, OCH$_2$), 4.22 (t, OCH$_2$), 3.90 (t, 2H, OCH$_2$), 3.80 (m, 4H, 2OCH$_2$), 3.78 (m, 8H, 4OCH$_2$); ^{13}C NMR (CDCl$_3$): δ 163.0, 160.02, 158.64, 153.6, 151.47, 151.25, 149.88, 131.80, 125.07, 121.86, 117.82, 117.73, 113.23, 112.79, 109.77, 106.53, 101.70, 73.02, 72.61, 72.51, 72.35, 71.73, 71.65, 71.01, 70.20, 69.88; MS: m/z 470 (M$^+$), 294 (M$^+$ − C$_8$H$_{16}$O$_4$), 268, 210, 139; for C$_{25}$H$_{26}$O$_9$ HRMAS Calcd 470.1889; Found: 470.1871.

Anal. Calcd for C$_{25}$H$_{26}$O$_9$: C, 63.80; H, 5.53. Found: C, 63.72; H, 5.50.

6.2. 1,3-Dimethyl-8,9-([1,4,7,10,13,16]-hexaoxacyclooctadecino)-6H-benzofuro[3,2-c]-[1]-benzopyran-6-one (7f)

Compound **4b** (1.48 g, 5 mmol), K$_2$CO$_3$ (1.40 g, 10 mmol), CH$_3$CN (120 mL) and **6c** (2.73 g, 5 mmol) reacted as described above to afford **7f**, 0.640 g (13%), mp 215 °C (benzene); IR (KBr) 3100 (C−H, arom.), 2950−2960 (C−H, alkyl), 1750 (lactone), 1620 (C=C), 1285 (C−O, aryl), 1080−1140 (O−C, alkyl) cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 Hz): δ 4.40 (t, OCH$_2$), 3.89 (m, 2H, 2OCH$_2$), 3.81 (m, 8H, 4OCH$_2$), 3.75 (t, 2H, OCH$_2$), 3.71 (m, 4H, 2OCH$_2$), 2.76 (s, 3H, Ar-CH$_3$), 2.40 (s, 3H, Ar-CH$_3$); ^{13}C NMR (CDCl$_3$): δ 162.22, 160.35, 155.77, 152.06, 150.94, 149.84, 143.38, 136.05, 128.71, 117.45, 117.10, 111.54, 107.22, 106.25, 99.44, 79.72, 79.08, 78.01, 72.76, 72.70, 72.56, 71.53, 71.45, 23.52, 22.93; MS: m/z 498 (M$^+$), 322 (M$^+$ − C$_8$H$_{16}$O$_4$), 296, 225.

Anal. Calcd for C$_{27}$H$_{30}$O$_9$: C, 65.06; H, 6.02. Found: C, 65.09; H, 6.08.

6.3. 2,3-Dimethyl-8,9-([1,4,7,10,13]-pentaoxacyclopentadecino)-6H-benzofuro[3,2-c]-[1]-benzopyran-6-one (7g)

Compound **4c** (1.48 g, 5 mmol), Na$_2$CO$_3$ (1.1 g, 10 mmol), CH$_3$CN (120 mL) and **6b** (1.15 g, 5 mmol)

reacted as outlined above to obtain **7g**, 0.31 g (13.6%), mp 206–208 °C (acetonitrile); IR (KBr) 3150 (C–H, arom.), 2950–2960 (C–H, alkyl), 1750 (lactone), 1610 (C=C), 1290 (C–O, aryl), 1080–1150 (O–C, alkyl) cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 Hz): δ 7.52 (s, 1H, Ar-H), 7.49 (s, 1H, Ar-H), 7.25 (s, 1H, Ar-H), 7.16 (s, 1H, Ar-H), 4.22 (t, 2H, OCH$_2$), 3.97 (t, 2H, OCH$_2$), 3.96 (t, 2H, OCH$_2$), 3.8 (t, 2H, OCH$_2$), 3.78 (s, 4H, 4 OCH$_2$), 2.77 (s, 3H, CH$_3$), 2.36 (s, 3H, CH$_3$); ^{13}C NMR (CDCl$_3$): δ 161.43, 159.16, 154.32, 153.67, 152.13, 151.46, 150.16, 143.15, 135.25, 134.43, 123.22, 119.84, 118.30, 117.67, 116.63, 99.89, 99.63, 79.58, 79.31, 73.20, 73.14, 72.51, 72.40, 21.84, 21.23; MS: m/z 454 (M$^+$), 426 (M$^+$ – CO), 322 (M$^+$ – C$_6$H$_{12}$O$_3$), 296, 238.

Anal. Calcd for C$_{25}$H$_{26}$O$_8$: C, 66.07; H, 5.72. Found: C, 66.22; H, 5.84.

6.4. 1,4-Dimethyl-8,9-([1,4,7,10,13]-pentaoxacyclopentadecino)-6H-benzofuro[3,2-c]-[1]-benzopyran-6-one (7h)

Compound **4d** (1.48 g, 5 mmol), Na$_2$CO$_3$ (1.1 g, 10 mmol), CH$_3$CN (120 mL) and **6b** (1.15 g, 5 mmol) reacted as described above to obtain **7h**, 0.24 g (10.5%), mp 184 °C (acetonitrile); IR (KBr) 3100 (C–H, arom.), 2950–2960 (C–H, alkyl), 1745 (lactone), 1620 (C=C), 1280 (C–O, aryl), 1076–1140 (O–C, alkyl) cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 Hz): δ 7.57 (d, 2H, Ar-H), 7.19 (d, 1H, Ar-H), 7.19 (d, 2H, Ar-H), 7.07 (d, 2H, Ar-H), 4.5 (m, 4H, 2OCH$_2$), 4.2 (m, 4H, 2OCH$_2$), 3.98 (s, 8H, 4OCH$_2$), 2.85 (s, 3H, Ar-CH$_3$), 2.50 (s, 3H, Ar-CH$_3$); ^{13}C NMR (CDCl$_3$): δ 162.63, 160.40, 157.41, 154.07, 151.38, 150.17, 133.88, 133.78, 128.10, 126.26, 117.67, 114.05, 108.17, 106.71, 99.64, 73.19, 73.13, 72.49, 71.54, 71.46, 23.03, 18.10; MS: m/z 454 (M$^+$), 426 (M$^+$ – CO), 322 (M$^+$ – C$_8$H$_{16}$O$_4$).

Anal. Calcd for C$_{25}$H$_{26}$O$_8$: C, 66.08; H, 5.72. Found: C, 65.95; H, 5.76.

6.5. 6,7-([1,4,7,10,13]Pentaoxacyclopentadecino)-3,3-dihydro-2H-dibenzofuran-1-one (8b)

Compound **5a** (1.1 g, 5 mmol), the tetraethyleneglycol ditosylate **6b** (2.3 g, 5 mmol) and Na$_2$CO$_3$ (1.1 g, 20 mmol) in absolute acetonitrile (120 mL) reacted as described above to afford **8b** 0.13 g (8%), viscous; IR (KBr) 3100 (C–H, aryl), 2850–2995 (C–H, alkyl), 1650 (C=O), 1200–1300 (C–O, aryl) cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 Hz): δ 7.06 (s, 1H), 7.58 (s, 1H), 4.16 (m, 8H), 3.82 (m, 4H), 3.78 (s, 4H), 2.52 (t, 2H), 2.4 (t, 2H), 2.23 (p, 2H), 1.17 (s, 6H); ^{13}C NMR (CDCl$_3$): δ 196.81, 172.00, 171.88, 151.21, 151.12, 149.69, 149.21, 131.74, 129.82, 118.54, 118.11, 107.03, 99.36, 72.56, 72.16, 71.59, 71.45, 63.51, 39.69, 25.70, 24.48; MS: m/z 376 (M$^+$), 244 (M$^+$ – C$_6$H$_{12}$O$_3$), 189, 163.

Anal. Calcd for C$_{20}$H$_{24}$O$_7$: C, 63.83; H, 6.41. Found: C, 63.74; H, 6.40.

6.6. 6,7-([1,4,7,10,13,16]-Hexaoxacyclooctadecino)-3,3-dihydro-2H-dibenzofuran-1-one (8c)

Compound **5a** (1.1 g, 5 mmol), the pentaethyleneglycol ditosylate **6c** (2.73 g, 5 mmol) and K$_2$CO$_3$ (1.4 g, 10 mmol) in acetonitrile (120 mL) reacted as described above to give **8c**, 0.25 g (12%), mp 104 °C (acetonitrile); IR (KBr) 3100 (C–H, arom.), 2860–3000 (C–H, alkyl), 1650 (C=O), 1200–1300 (C–O, aryl) cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 Hz): δ 4.18 (m, 8H), 3.84 (m, 4H), 3.78 (s, 4H), 2.8–3.2 (t, 2H), 2.1–2.8 (t, 2H), 2.4–2.5 (t, 2H); ^{13}C NMR (CDCl$_3$): δ 196.82, 172.01, 171.88, 151.21, 151.12, 149.37, 149.21, 131.74, 129.82, 118.54, 118.11, 107.03, 99.36, 72.56, 72.16, 71.59, 71.45, 71.35, 71.19, 70.58, 63.51, 39.69, 25.70, 24.48; MS: m/z 420 (M$^+$), 288 (M$^+$ – C$_6$H$_{12}$O$_3$), 101, 79.

Anal. Calcd for C$_{22}$H$_{28}$O$_8$: C, 62.85; H, 6.66. Found: C, 63.02; H, 6.68.

6.7. 6,7-([1,4,7,10,13,16]-Hexaoxacyclooctadecino)-3,3-dimethyl-3,4-dihydro-2H-dibenzofuran-1-one (8f)

Compound **5b** (1.23 g, 5 mmol), the pentaethyleneglycol ditosylate **6c** (2.73 g, 5 mmol) and K$_2$CO$_3$ (1.4 g, 10 mmol) in absolute acetonitrile (120 mL) reacted as described above to give **8f**, 0.40 g (18%), mp 96 °C (acetonitrile); IR (KBr) 3100 (C–H, arom.), 2800–2990 (C–H, alkyl), 1650 (C=O), 1200–1300 (C–O, aryl) cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 Hz): δ 4.03–4.2 (m, 4H), 3.8–3.9 (m, 4H), 3.65–3.67 (t, 4H), 3.57 (4H), 3.53–3.54 (d, 2H), 2.93 (s, 2H), 2.33 (s, 2H), 1.07 (s, 6H); ^{13}C NMR (CDCl$_3$): δ 196.15, 171.01, 151.64, 149.85, 149.55, 118.32, 117.52, 107.55, 100.05, 73.05, 72.99, 72.83, 72.72, 72.51, 71.78, 71.65, 71.58, 54.21, 39.82, 37.26, 30.64; MS: m/z 448 (M$^+$), 316 (M$^+$ – C$_6$H$_{12}$O$_3$), 129.

Anal. Calcd for C$_{24}$H$_{32}$O$_8$: C, 64.28; H, 7.14. Found: C, 64.18; H, 7.04.

7. Results and discussion

7.1. Organic synthesis

Starting compounds of 4-hydroxy-2H-[1]benzopyran-2-one derivatives **1a–1d** were prepared from the corresponding phenols that reacted with malonic acid in POCl$_3$/dry ZnCl$_2$ mixture.

Coumestan compounds, 6H-benzofurano[3,2-c][1]-benzopyran-6-one, **4a–4d** were synthesized from **1a–1d** reacting with catechol **2**, adopting Wanzlick's

dehydrogenative coupling procedure [8]. Coumestan analog products, 6,7-dihydroxy-3,4-dihydro-2H-dibenzofuran-1-one **5a** and 6,7-dihydroxy-3,3-dimethyl-3,4-dihydro-2H-dibenzofuran-1-one **5b**, were obtained by reacting catechol **2** with cyclohexane-1,3-dione **3a** and 3,3,-dimethylcyclohexane-1,3-dione **3b** in the presence of $K_3[Fe(CN)_6]/CH_3COONa/H_2O$/acetone mixture, respectively. The preparation of crown ethers was performed by cyclic condensation of 8,9-dihydroxycoumestan **4a–4d** and coumestan analog derivatives **5a**, **5b** with polyethyleneglycol dichloride or polyethyleneglycol ditosylate, in the order named.

Accordingly, **4a** condensed with **6a**, **6b** and **6c** to afford the crown ethers **7a**, **7b** and **7c**, respectively. Compound **4b** reacted with **6a**, **6b** and **6c** to provide the crown ethers **7d**, **7e** and **7f**, respectively. **4c** reacted with **6b** to give the crown ether **7g**. **4d** reacted with **6b** to give the crown ether **7h**. **5a** reacted with **6a**, **6b** and **6c** to afford the crown ethers **8a**, **8b** and **8c**, respectively. Accordingly **5b** reacted with **6a**, **6b** and **6c** to provide **8d**, **8e** and **8f**, respectively, in the presence of alkali metal carbonate in CH_3CN (Scheme 1). Chromatography of the residue on silica gel (chloroform) afforded the coumestan-crown ethers **7a–7h** 10–14%, the coumestan analog derivatives of crown ethers **8a–8f** 8–18%. The characterization of novel crown ethers, given in the experimental part, was made using NMR, IR, TLC, mass spectroscopy and elemental analysis. The 400 MHz ^1H NMR spectra of the benzofuran derivatives of crown ethers **7a–7h** and **8a–8f** in deuteriochloroform indicate the presence of crown ether moieties (δ 3.78–4.16, multiplets). The integration showed the presence of appropriate number of protons. The aromatic methyl groups (2.76, 2.36, 2.77) at 1,3,4 positions each a singlet represent three hydrogens. The characteristic aromatic signals for each crown ether confirm the structure. The ^{13}C NMR spectra show, in addition to aromatic, aromatic methyl and crown ether signals, one resonance for carbonyl carbons. The compounds **7a–7h** exhibited in their IR spectra $\nu C{=}O$ ~1750 cm^{-1} which is characteristic of 2-pyrone moiety, while the compounds **8a–8f** showed in their IR spectra the appearance of a band at 1650 cm^{-1} which further corroborated the structure. The spectral data of the known compounds (**7a**, **7b**, **7d**, **7e**, **8a**, **8d**) were in accordance with that of literature [14].

7.2. Complexation equilibria in acetonitrile; conductometric measurements

Various methods to calculate the stability constants from measurements of properties involving factors such as molar conductivity etc. have been described in the literatures [9,10].

When a crown compound forms a (M:L) complex with a cation, the equilibrium equation is written as

$$M^{m+} + L \rightleftharpoons ML^{m+} \tag{1}$$
$$\alpha C_M \quad C_L - (1-\alpha)C_M \quad (1-\alpha)C_M$$
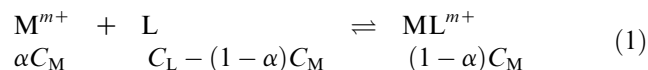
where M^{m+}, L, and α are the cation, crown compound, and fraction of free cations, respectively. Thus the equilibrium constants, K_e of complex formation, were calculated using Eqs. (2)–(13)

$$K_e = [ML^{m+}]/[M^{m+}][L] \tag{2}$$

$$C_M/C_L = 1 \tag{3}$$

$$C_M = [M^{m+}] + [ML^{m+}] \tag{4}$$

$$C_L = [L] + [ML^{m+}] \tag{5}$$

$$\alpha = [M^{m+}]/C_M \tag{6}$$

$$P = [ML^{m+}]/C_M = K_e[L]/(1 + K_e[L]) \tag{7}$$

The observed conductivity, κ, is given by

$$\kappa = \kappa_M^{m+} + \kappa_{ML}^{m+} \tag{8}$$

The molar conductivities are

$$\Lambda_{MAm} = \kappa_{MA}^{m+}/[M^{m+}] \tag{9}$$

$$\Lambda_{ML}^{m+} = \kappa_{ML}^{m+}/[ML^{m+}] \tag{10}$$

$$\Lambda = \kappa/C_M \tag{11}$$

$$\Lambda = \alpha \Lambda_M^{m+} + (1-\alpha)\Lambda_{ML}^{m+} \tag{12}$$

As a result of Eq. (12), Eq. (2) can be transformed into

$$K_e = (\Lambda_M^{m+} - \Lambda)/((\Lambda - \Lambda_{ML}^{m+})[L]) \tag{13}$$

where

$$[L] = C_L - C_M P$$

and

$$[L] = C_L - C_M(\Lambda_M^{m+} - \Lambda)/(\Lambda_M^{m+} - \Lambda_{ML}^{m+}).$$

Notations: C_M and C_L are the total concentrations of alkali metal and crown ether, respectively; $[M^{m+}]$, $[L]$ and $[ML^{m+}]$ are the concentrations of uncomplexed cation, uncomplexed crown ether and complexed cation,

	R	R₁	R₂	R₃	R₄
1a	-	H	H	H	H
1b	-	CH₃	H	CH₃	H
1c	-	H	CH₃	CH₃	H
1d	-	CH₃	H	H	CH₃
3a	H	-	-	-	-
3b	CH₃	-	-	-	-
4a	-	H	H	H	H
4b	-	CH₃	H	CH₃	H
4c	-	H	CH₃	CH₃	H
4d	-	CH₃	H	H	CH₃
5a	H	-	-	-	-
5b	CH₃	-	-	-	-

	m	X
6a	2	OTs
6b	3	Cl
6c	4	OTs

	R₁	R₂	R₃	R₄	n
7a	H	H	H	H	0
7b	H	H	H	H	1
7c	H	H	H	H	2
7d	CH₃	H	CH₃	H	0
7e	CH₃	H	CH₃	H	1
7f	CH₃	H	CH₃	H	2
7g	H	CH₃	CH₃	H	1
7h	CH₃	H	H	CH₃	1

	R	n
8a	H	0
8b	H	1
8c	H	2
8d	CH₃	0
8e	CH₃	1
8f	CH₃	2
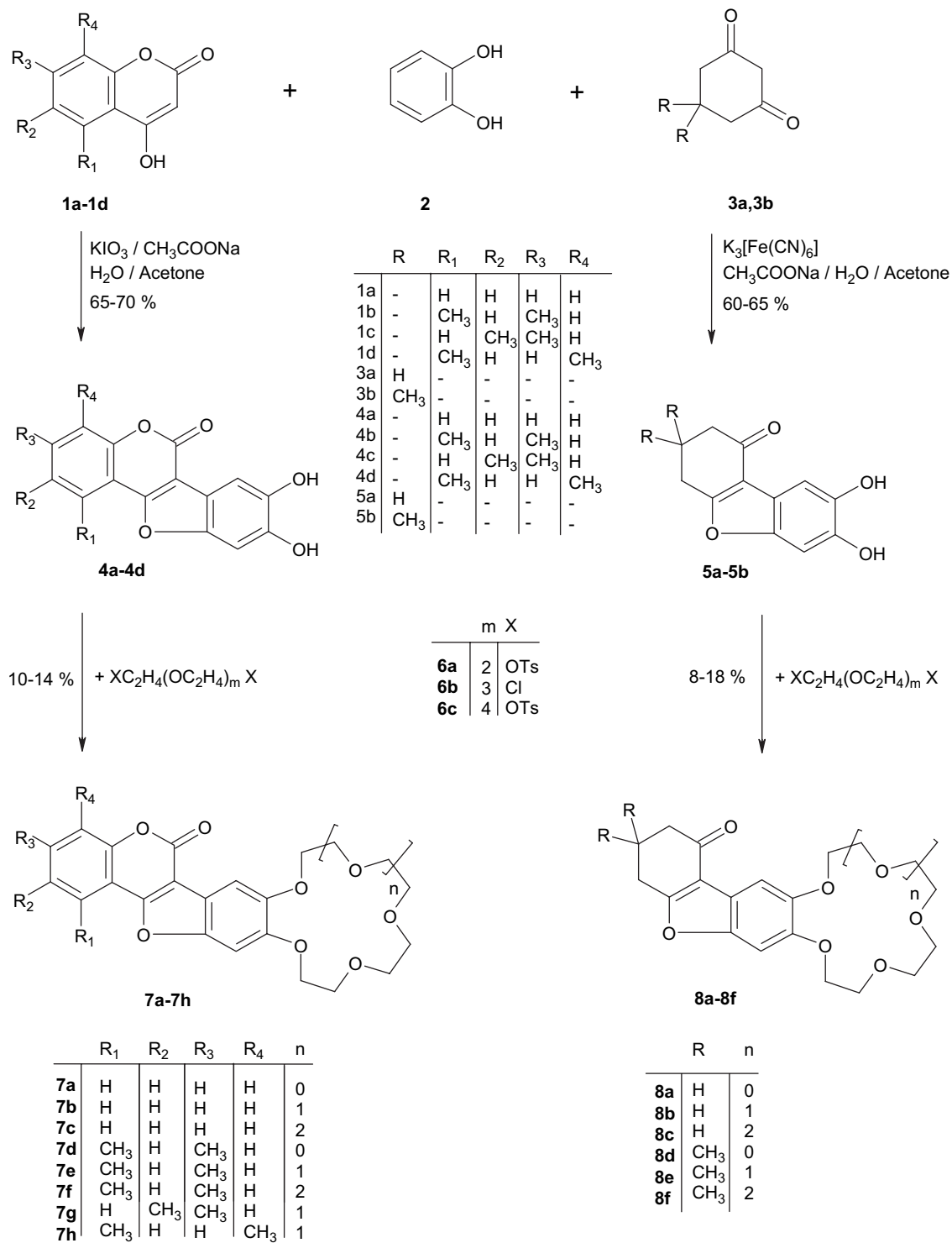
Scheme 1.

respectively; P is the experimental mole fraction of the complexed cation or the ligand [Eqs. (1)−(13)], κ_M^{m+}, κ_{ML}^{m+} are the observed conductivities of the electrolyte and the crown compound−electrolyte complex, respectively; Λ_M^{m+} and Λ_{ML}^{m+} are the designated molar conductivities of the electrolyte and the crown compound−electrolyte complex, respectively.

In the present work, the determination of equilibrium constants, log K_e of Na$^+$ ion with **7a**−**7h** and **8a**−**8f**, the only monomeric and electrically neutral crown compounds in acetonitrile, using conductometric measurements at 25 °C for the thermodynamic interpretations of the cation−macrocyclic ether interactions have been studied.

Although the ligand−ion exchange rate and role of mother solvent mainly orients the ligand selectivity, the binding power of the ion−dipole interactions primarily depends on the number of oxygen as well as molecular conformations of a macromolecule [11].

The binding power of sodium ion with **7a**−**7h** and **8a**−**8f** coumestano-crown ethers for acetonitrile solution with conductometric studies at 25 °C has been measured. The equilibrium constants and free energies, ΔG^θ of crown compound−cation complexes in acetonitrile have been estimated from Eqs. (1)−(13) and given in Table 1. Accordingly, in the acetonitrile-crown ether solutions, ions are most probably structured as axially complexed ion-pairs with a 1:1 ratio of unit one complex [12]. The new determined log K_e values of NaClO$_4$ for the coumestano-crown ether compounds in acetonitrile decreased in the order of **7f** > **8b** > **7b** > **7d** > **8c** > **7e** > **8a** > **7c** > **8d** > **7h** > **7a** > **8f** > **8e** (**7g** was precipitated as an unsolvated solid complex). This indicates that complexation occurs between the coumestano-crown ethers and the sodium metal ions, and that the coumestano-crown ether−alkali metal ion complexes are less mobile than the free sodium metal ions. In the previous study [13], it was found that stabilities of the 1:1 complexes of 18C6, 15C5 and 12C4 with NaClO$_4$ in 85% dioxan−water mixture are 0.80, 0.57 and 0.67, respectively. In this study, results for synthesized 14 coumestano-crown ethers with NaClO$_4$ in acetonitrile at 25 °C are obtained and compared with previous results for 18C6, 15C5 and 12C4 with the same alkali salt in 85% dioxan−water mixture. And we have previously obtained much smaller log K_e values [11] for 18C6, 15C5 and 12C4 with NaClO$_4$ in 85% dioxan−water mixture than in this study (see Table 1). As seen in Table 1, log K_e values calculated for coumestano derivatives of 18CR6, 15CR5 and 12CR4 series were found to be {2.92, 2.26, 1.33, 0.33}, {2.79, 2.77, 2.05, 0.98, 0.06} and {2.34, 1.42, 1.24, 0.79}, respectively. This indicates that all coumestano-crown ethers form complexes that are less mobile than the corresponding alkali metal ions [9]. Two factors may be responsible for this negligible change in κ inspite of a decrease in different coumestano-crown ether derivatives: (1) ions most probably form ion-pairs, and scarcely any complexation occurs between the crown compounds and the cations; (2) mobilities of a resulting crown compound−cation complex and the corresponding cation are not equal at the same concentration [9].

The thermodynamic parameter values ($-\Delta G^\theta$) of 1:1 complexation reaction between crown ethers and sodium ion in acetonitrile determined by conductometric methods are given in Table 1. The log K_e values determined by conductometry agree with those values determined by other methods [9,11].

It is found that stabilities of complexes of the Na$^+$ ions with crown compounds at 25 °C are affected not only by the relative sizes of the cation and the crown ether cavity but also by the different coumestano "side arm" and the influence of acetonitrile solvent.

As a result of this study, it is observed that, for the Na$^+$ complexes with coumestano-crown ethers in acetonitrile, the log K_e values are dependent on the chemical characteristics of all ligands and solvents, indicating that the electrostatic ion−dipole forces, that are a function of the macroscopic dielectric constant of the solvent and on the dipole moment of the ligands that depends on the different side arm, are the strongest factors in the complexation processes.

Table 1
The log K_e and $-\Delta G^\theta$ (kcal/mol)

Coumestano-crown ethers	log K_e	$-\Delta G^\theta$
7a	0.79	1079.04
7b	2.77	3777.43
7c	1.33	1815.70
7d	2.34	3195.00
7e	2.05	2793.07
7f	2.91	3976.92
7g	[a]	−
7h	0.98	1331.87
8a	1.42	1933.49
8b	2.79	3801.32
8c	2.26	3076.30
8d	1.24	1694.03
8e	0.06	−81.27
8f	0.33	450.18

Values for the interactions of different coumestano-crown ethers with NaClO$_4$ in acetonitrile at 25 °C by a conductometric study.
Correlation coefficient: 0.999.
  [a] Precipitated as an unsolvated solid complex.

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