

Synthesis and characterization of coumarin-crown ethers

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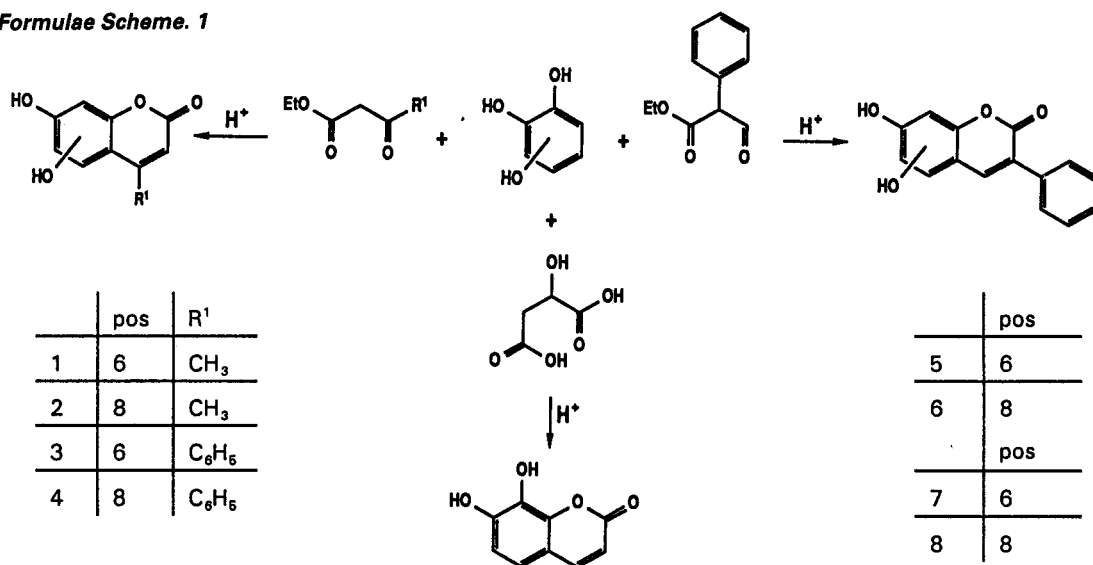
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Abstract Improving the preparation methods of some common dihydroxycoumarins, coumarin derivatives of the macrocyclic ethers were obtained in good yields. Dihydroxycoumarins reacted with dichlorides or ditosylates of polyethyleneglycols in the presence of DMF/H₂O/K₂CO₃ and macrocyclic ethers with a coumarin moiety were obtained with satisfactory yields. The structures of molecules obtained were proved with common methods of NMR, EI mass spectra and elemental analysis. Optical properties in acetonitrile and the association constants, K_a of Na⁺ ion with such molecules were now determined in water with a Na⁺ ion selective electrode.

INTRODUCTION

Since the discovery of crown ethers plenty of resembling molecules have been prepared to design the structural recognition in a ion-macrocyclic ether complex formation (ref.1). We have been working on this topic by synthesizing and searching on the mechanism of alkali metal-cyclic ether interactions with NMR (ref.2,3). Most recently we prepared some dihydroxycoumarins in good yields for obtaining their macrocyclic ether derivatives. The coumarins mostly display fluorescence spectra which is obviously observed in their macrocyclic ether derivatives. The stable chromophores attached to a macrocyclic ether as a probe of the optical spectroscopy could be used for any phase transfer process. In this work trihydroxy- or triacetoxybenzenes reacted with the some β -diketones, β -ketoaldehydes or d,l-malic acid in the presence of H₂SO₄ or CF₃COOH and gave desired coumarins (compounds 1-8), (ref.4). The coumarins were found to be stable enough in basic solutions to give Williamson synthesis for the crown ether preparations, Formulae Scheme 1.

Formulae Scheme. 1



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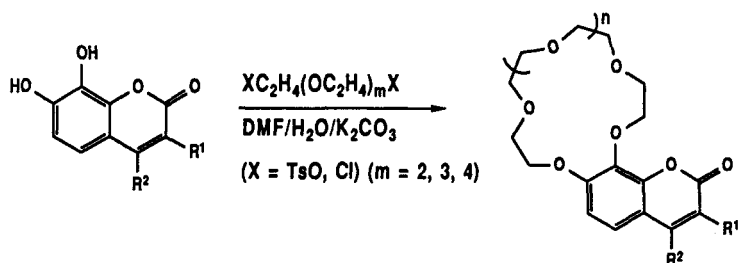
SYNTHESIS OF COUMARIN-CROWN ETHERS

The presented work deals to develop a method for the preparation of coumarin-crown ethers starting from accessible chemicals without high-dilution conditions. The anions of dihydroxycoumarins (compound 1-8) of strong nucleophilic power yielded with K^+ , Na^+ or Li^+ bases gave the corresponding cyclic products with an equimolar amount of dihalide or ditosylate of polyethyleneglycol in DMF / water. However, the procedure was improved after several attempts of preparations and various periods solvents, bases, temperatures were successively tried. Accordingly most versatile procedure which gave the macrocyclic ethers in appropriate yields (compound 9-26) is now presented, Formulae Scheme.2.

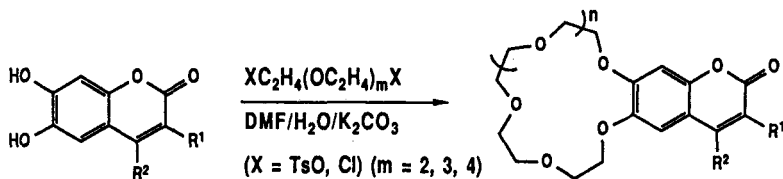
The general procedure is as follows ; Dihydroxycoumarin and dichloride or ditosylate of polyethyleneglycol and K_2CO_3 were dissolved in water/DMF (15/85). The mixture was heated for 36-48 h at 70-80 °C under dry nitrogen during stirring. The cooled mixture was diluted with water then extracted with chloroform or dichloromethane. Evaporated extracts dried on alumina usually gave pure raw products which were crystallized from suitable solvents. The yields, analytical data and detailed spectral information will be soon reported.

The structural elucidations were carried out with elemental analysis, electron impact mass spectra, 1H NMR and IR spectra of the desired molecules. High purity of the compounds were obtained using column chromatography (dichloromethane / aliminiumoxid 90, MERCK) and used for complex stability measurements. Generally, the mass spectra of the molecules featured a strong molecular ion peak and a fragmentation pattern in agreement with the proposed structures. 1H NMR and 2D spectra of the molecules interestingly exhibited distinctive aliphatic and aromatic proton pattern. Particularly well resolved spectra in the range of 3-5 ppm allowed us to estimate the first order coupling constants.

Formulae Scheme. 2



	n	R ¹	R ²
9	0	H	CH ₃
10	1	H	CH ₃
11	2	H	CH ₃
12	1	H	H
13	2	H	H
14	1	H	C ₆ H ₅
15	2	H	C ₆ H ₅
16	1	C ₆ H ₅	H
17	2	C ₆ H ₅	H



	n	R ¹	R ²
18	0	H	CH ₃
19	1	H	CH ₃
20	2	H	CH ₃
21	1	H	H
22	2	H	H
23	1	H	C ₆ H ₅
24	2	H	C ₆ H ₅
25	1	C ₆ H ₅	H
26	2	C ₆ H ₅	H

COMPLEXATION OF COUMARIN-CROWN ETHERS WITH Na⁺

Coumarin-crowns were soluble in $CHCl_3$ or CH_2Cl_2 as they are free or complexed forms so that they could be used as phase transfer carriers or liquid membrane systems. They even gave solid, stable and nonhygroscopic crown ether complexes with Na^+ which mostly decomposed over 200 °C. The polar structure of the coumarin moiety behaves as a functional group enabling the aromatic structure more soluble in aqueous phase as a complexed coronand molecule.

The Na^+ complex formation of coumarin derivatives of macrocyclic ethers were investigated in water by the potentiometric method with a Na^+ selective glass electrode, ORION model 86-11 Ross electrode with an ion-meter from SCHOTT model CG804 at 25 °C with the minimum identical cation / ligand concentrations, (L_0) of 0.001 mol l⁻¹. The K_a values were estimated from the equation of $1/K_a[L_0] = (1-nP')^n(1-mP')^m/P'$ where P' is the measured mole fraction of complexed ion (refs.5,6). The results obtained according to our recently developed analytical method are summarized in Table 1. The association constants, K_a of various degrees of complex formations are shown (refs.3,6).

We have demonstrated that five oxygen member of coumarin ether ring binds strongly to the cation even in water, although, the difference compared to binding role of six oxygen member cyclic ether is not that much. Accordingly multiple complexation observed even in water displays the strong ion-dipole interactions involved in solution as it is indicated with the higher values of association constants, K_a of higher complexing degrees. In any case the results are in agreement with our reported NMR-complexation studies. As a comprehension we also determined the complexing behavior of the common crown ethers likewise 15-crown-5, 18-crown-6 and their benzo derivatives at similar experimental conditions according to our procedure and the results are displayed in Table 1.

Table 1. Complexation parameters of Coumarin-crown ethers with Na^+ obtained with the potentiometric measurements at 25°C in water.

Compnd. Number	Ring Size	Arom. group	Log $K_a^{(a)}$	$-\Delta G^\ominus$	Log $K_a^{(b)}$	$-\Delta G^\ominus$	Log $K_a^{(c)}$	$-\Delta G^\ominus$
10	5	7,8-Benzopyran-	4.55	2687	11.42	6645	-	-
11	6	7,8-Benzopyran-	4.32	5552	10.94	6458	11.69	6906
13	6	7,8-Benzopyran-	4.77	2815	10.75	6344	11.50	6790
19	5	6,7-Benzopyran-	4.84	2861	11.80	6969	12.56	7418
20	6	6,7-Benzopyran-	3.69	2181	10.16	6101	10.90	6438
18C6	6	-	5.80	3429	13.46	7948	14.23	8396
15C5	5	-	5.81	3431	12.57	7422	13.42	7920
B15C5	5	Benzo-	4.87	2877	11.42	6736	12.21	7210
B18C6	6	Benzo-	4.97	2934	11.63	6868	12.43	7338

(a) Association constant of ; $\text{CE} + \text{A}^+ \rightarrow \text{CEA}^+$; ΔG , in cal mol⁻¹ at 25 °C
 (b) Association constant of ; $2\text{CE} + \text{A}^+ \rightarrow \text{CE}_2\text{A}^+$
 (c) Association constant of ; $\text{CE} + 2\text{A}^+ \rightarrow \text{CEA}_2^+$

OPTICAL SPECTRA OF COUMARIN-CROWN ETHERS

Although we have investigated the complexing role of coumarin-crowns via potentiometry, the optical behavior of such compounds are quite promising to investigate the various aspects of ion-dipole interactions of such compounds. Table 2 summarizes the absorption and fluorescence spectral data of coumarin-crowns (compounds 10-24). The absorption maxima (λ_{max}) of UV spectra originated from $\pi-\pi^*$ transitions shows bathochromic shifts in 6,7-benzopyrene derivatives and especially in 3-phenyl derivatives, because of electron donating of substituent into coumarin ring. The similar effects are observed on the fluorescence spectra of emission maximas, Table 2. From this aspect we are now working on novel structures and their optical behaviors on the complexation.

Table 2. Optical data for the coumarin-crown ethers in acetonitrile at 25 °C (#)

Comp.	$\lambda_{\text{max abs UV}}$ (nm)	λ_{ext}	λ_{ems}	Comp.	$\lambda_{\text{max abs UV}}$ (nm)	λ_{ext}	λ_{ems}
10	313.20	357	447	19	339.60	311	412
11	314.00	366	457	20	323.00	374	414
12	314.20	360	405	21	342.00	382	421
13	313.20	362	439	22	342.50	386	421
16	335.60	310	423	23	346.80	390	461
17	357.50	287	440	24	346.60	392	460

(#) Obtained with Perkin Elmer Luminescence spectrometer model LS-50 and with Shimadzu UV-VIS spectrophotometer model UV-160A.

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REFERENCES

1. R.M. Izatt, K. Pawlak, J.S. Bradshaw and R. L. Bruening, *Chem.Rev.* **91**, 1721-2085 (1991).
2. a. H. Hoşgören and Ç. Erk, *Polymer Bull.* **5**, 47 (1981). b. Ç. Erk, *Fresenius Z.Anal.Chem.* **316**, 477 (1983). c. Ç.Erk, *Makromol.Chem.Rapid. Communic.* **5**, 269 (1984). d. Ç. Erk, *Synt.Communic.* **19**, 49 (1989). e. Ç. Erk, *Liebigs Ann.Chem.* 1083 (1991).
3. a. Ç. Erk, *Appl.Spectrosc.* **40**, 100 (1986). c. Ç.Erk, *J.Mol.Liqs.* **40**, 1 (1989), Ç. Erk, *J.Phys.Chem.* **94**, 8617 (1990). d. Ç. Erk, *J.Mol.Liqs.* **48**, 17 (1991).
4. a. R. D. H. Murray, J. Mendez and S. A. Brown, *Natural Coumarins*, p 131, Wiley, New York (1982). b. M. Bulut and Ç. Erk, ESOC7, Abstracts, Namur, Belgium, 1991 c. M.Bulut and Ç. Erk, *Org.Proced. Prep.Int.* (1992) in press, d. M. Bulut, *Chim.Acta Turcica*, (1991), in press. e. M. Bulut and Ç. Erk, *Synthetic Communic.* **22**, 1259 (1992).
5. a. M. Bulut and Ç. Erk, *J.Org.Chem.* (1992), submitted. b. M. Bulut and Ç. Erk, *Chem.Ber.* (1992), submitted. c. M. Bulut, A. Göçmen and Ç. Erk, (1992), unpublished results.
6. a. Ç. Erk, *Thermochim.Acta* **131**, 125 (1988). b. Ü. Çakır and Ç. Erk, *ibid* **178,67**(1990). c. Ç. Erk, *Analyst*, (1991), submitted. d. G. Savaş, A.Göçmen and Ç. Erk, *Analyst*, submitted.