Application of Horner–Emmons Olefination to the Crown-Ether Derivatives

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Abstract

An effective synthetic approach to the preparation of a new crown-ether vinylogs involving the Horner–Emmons olefination of carbonyl precursors with the use of C_2- and C_5-phosphonates was proposed. The effects of the conjugation chain length and the nature of the terminal polar functions in the phosphonate reagent on the yield and process stereoselectivity were discussed.

Introduction

Nowadays supramolecular complexes are widely used for the design and creation of advanced devices for analysis of pollution traces and ecological monitoring. Molecular recognition on the supramolecular level is a possible approach to the solution of this problem. The result of recognition is alteration of the electronic, optical and conformational properties that are responsible for signal generation and transduction [1–7].

Crown-ether receptors linked to various types of photosensitive systems are widely used as parts of ion-selective electrodes in the new generation of sensors and analytical devices [1–7]. A simple and promising linker is a conjugated double bond system with variable length and configuration. The presence of different terminal anchor groups in the linker chain made it possible to bind a macrocyclic ionophore to photosensitive systems such as surfaces of polymers and biomolecular ensembles [4–7]. Development of new synthetic methods for the introduction of crown-ether moiety into various types of molecules is in progress. In this paper, we describe the use of the classical Horner–Emmons olefination procedure as the most promising synthetic approach for the preparation of crown-ether vinylogs.

Experimental

^{1}H NMR spectra were recorded on a Bruker MSL-200 spectrometer in $CDCl_3$. Chemical shifts are given in ppm relative to hexamethyldisiloxane as an internal standard (δ 0.055 ppm), the spin–spin coupling constants are in Hz. The UV–Vis spectra were recorded on a Shimadzu UV-3100 spectrophotometer in acetonitrile at room temperature in quartz cells.

Electron impact (EI, IE = 70 eV) mass spectra were recorded on a Kratos model MS-30. Melting points were determined on an electrothermal melting point apparatus and were not corrected.

The qualitative composition of the reaction mixtures and the homogeneity of the compounds were determined by TLC on Kieselgel 60 F_{254} plates (Merck) or on Silufol UV-254 plates (Kavalier) in the following solvent mixtures: hexane–ethyl acetate, 2:1 (A); chloroform–methanol, 10:1 (B). The spots were visualized by spraying them with concentrated sulfuric acid. The preparative adsorption column chromatography was performed on Kieselgel 60 (0.040–0.063 mm, Merck).

Solvents were removed on a rotary evaporator in a vacuum at a temperature not higher than 35 °C. All reactions involving moisture- or oxygen-sensitive compounds and reagents were done under a dry argon atmosphere unless otherwise noted. Chemicals and solvents of analytical or reagent grade were purchased

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from commercial suppliers and used without purification.

Research grade triethyl phosphonoacetate (**21**) was purchased from Fluka. Other phosphonates (**22–24**) were synthesized by the Arbuzov reaction from appropriate chlorides with triethyl phosphite [8–10]. The starting carbonyl precursors, 4′-formyl-derivatives of benzo-15-crown-5 (**19**) and benzo-18-crown-6 (**20**) ethers, were prepared by the Duff formylation of unsubstituted macrocycles [11].

General procedure for Horner–Emmons olefination of carbonyl precursors (19, 20) with the use of C$_2$-(21, 22) and C$_5$-phosphonates (23, 24)

Ethyl 3-[(benzo-15-crown-5)-4′-yl]-2-propenoate (1): A 60% suspension of NaH in mineral oil (161 mg, 4.05 mmol) was washed with anhydrous hexane (3 × 5 mL), and anhydrous tetrahydrofuran (30 mL) was added to the residue. Then C$_2$-phosphonate (**21**) (0.9 mL, 4.05 mmol) was added dropwise using a syringe to the resulting mixture, which was vigorously stirred at 0 °C. After complete NaH disappearance (1 h), a solution of 4′-formylbenzo-15-crown-5 (**19**) (1 g, 3.37 mmol) in anhydrous tetrahydrofuran (10 mL) was added dropwise using a syringe to the resulting solution. The reaction mixture was stirred for 1 h and quenched with water (5 mL), acidified with 0.1 M aqueous hydrochloric acid to pH 5 and extracted several times with chloroform. The organic layers were combined, dried and concentrated. The crude product was purified by column chromatography on silica gel (eluent: chloroform–methanol mixtures with a 0–15% v/v gradient of methanol) to give pure compound (**1**). Recrystallization from methanol gave ester (**1**) as white crystals (yield: 0.9 g, 73%).

This general procedure was used for the preparation of several crowned esters (**1, 2, 7, 8**), nitriles (**3, 4, 9, 10**) and model compounds (**13, 16, 17**). The yields, isomer compositions, physico-chemical properties, ^{1}H NMR spectral data and other spectral parameters are summarized in Tables 1–3.

General procedure for the conversion of the terminal ester functional group into aldehyde

3-[(Benzo-15-crown-5)-4′-yl]-2-propenal (5): To a cooled (0 °C) solution of ester (**1**) (255 mg, 0.69 mmol) in anhydrous tetrahydrofuran (50 mL), LiAlH$_4$ (40 mg, 1.04 mmol) was added in several portions under vigorous stirring. The reaction was quenched with a water–diethyl ether mixture (25 mL, 1:4 v/v), the mixture was acidified with 0.1 M aqueous hydrochloric acid to pH 5, and the layers were separated. The aqueous phase was extracted several times with chloroform. The organic layers were combined, dried and concentrated. The

crude product was purified by column chromatography on silica gel (eluent: chloroform–methanol mixture with 0–30% v/v gradient of methanol) to give pure intermediate alcohol. In a 100-mL Erlenmeyer flask, the prepared alcohol was dissolved in anhydrous dichloromethane (50 mL), and active MnO$_2$ (150 mg) was added under vigorous stirring. The reaction mixture was stirred for 1 h at room temperature and filtered through a Celite layer (1 cm), which was washed with dichloromethane (100 mL). The filtrate was concentrated and the crude product was purified by column chromatography on silica gel (eluent: chloroform–methanol mixture with 0–15% v/v gradient of methanol) to give pure aldehyde (**5**) as yellow crystals (yield: 61 mg, 28%). This general procedure was used to prepare aldehydes (**5, 11**). The yields, physico-chemical properties, ^{1}H NMR spectral data and other spectral parameters are presented in Tables 1–3.
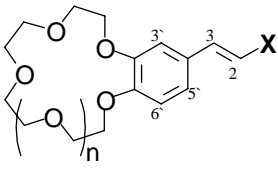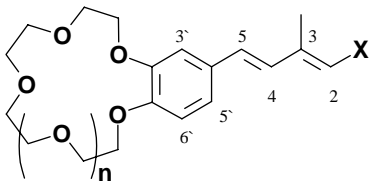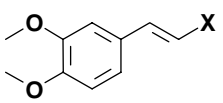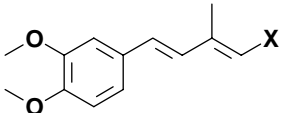
General procedure for the reduction of unsaturated nitriles

5-[(Benzo-15-crown-5)-4′-yl]-3-methylpenta-2,4-dienal (11): To a stirred solution of nitrile (**9**) (0.33 g, 0.92 mmol) in anhydrous toluene (25 mL), a solution of diisobutylaluminium hydride (0.9 mL, 1.5 M solution in toluene) was added dropwise using a syringe at −78 °C, and the mixture was stirred for 40 min at the same temperature. The reaction mixture was quenched with a suspension of wet silica gel (0.5 g) in 3 mL of methanol and allowed to warm to ambient temperature during 30 min. The solvent was evaporated and the crude residue was purified by column chromatography on silica gel (eluent: chloroform–methanol mixture with 0–15% v/v gradient of methanol) to give aldehyde (**11**) as yellow crystals (yield: 0.29 g, 86%).

This general procedure was used to prepare aldehydes (**5, 6, 12**) and model compounds (**15, 18**). The yields, isomer composition, physico-chemical properties, ^{1}H NMR spectral data and other spectral parameters are presented in Tables 1–3.

3,4-Dimethoxycinnamic acid nitrile (14): Powdered KOH (0.66 g 11.7 mmol) in anhydrous acetonitrile (30 mL) was refluxed for 3 min under argon and a solution of 3,4-dimethoxybenzaldehyde (1.71 g, 10.7 mmol) in anhydrous acetonitrile (10 mL) was added. The reaction mixture was carefully heated at 80 °C for 3 min, poured onto 100 g of cracked ice, and extracted several times with chloroform. The combined organic layers were dried and concentrated. The crude product was purified by column chromatography on silica gel (eluent: hexane–diethyl ether mixture, 1:2 v/v) to give pure compound (**14**). Recrystallization from methanol gave nitrile (**14**) as white crystals (yield: 1.55 g, 80%).

Table 1. Yields and isomer composition of the Horner–Emmons olefination products and their conversion into aldehydes

Structure	N	n	X	$(E\text{-} + Z\text{-})$ isomer yield, %	% of E-isomer
	1	1	—COOEt	73	100% 2E–
	2	2	—COOEt	70	100% 2E–
	3	1	—CN	86	90% 2E–
	4	2	—CN	53	64% 2E–
	5	1	—CHO	28 (from (**1**))	100% 2E–
				57 (from (**3**))	
	6	2	—CHO	70 (from (**4**))	100% 2E–
	7	1	—COOEt	46	87% 2E,4E–
	8	2	—COOEt	41	86% 2E,4E–
	9	1	—CN	54	90% 2E,4E–
	10	2	—CN	60	71% 2E,4E–
	11	1	—CHO	86 (from (**9**))	94% 2E,4E–
				35 (from (**7**))	
	12	2	—CHO	56 (from (**10**))	81% 2E,4E–
	13	–	—COOEt	51	100% 2E–
	14	–	—CN	80	75% 2E–
	15	–	—CHO	80 (from (**14**))	100% 2E–
	16	–	—COOEt	85	100% 2E,4E–
	17	–	—CN	90	90% 2E,4E–
	18	–	—CHO	58 (from (**17**))	80% 2E,4E–

Results and discussion

The classical Horner–Emmons olefination procedure is a unique method for the design of conjugated double bond systems in various types of molecules [5, 6, 12, 13]. The advantages are:

1. high reactivity of phosphonate anions towards different types of carbonyl compounds,
2. ready availability of the starting materials and reagents,
3. high regio- and stereoselectivity,
4. simple separation of by-products from the key alkenes.

In the present paper we describe an effective synthetic route for the preparation of crown-ether vinylogs (**1–12**) with variable length of the conjugated chain and different crown-ether ring size. Also, we synthesized the corresponding reference compounds (**13–18**), in which crown-ether moiety was replaced by related structure of 3,4-dimethoxyphenyl residue. This fragment has similar electron-donating properties but it lacks cation-binding ability. Comparison of their properties allowed us to distinguish between the influence of the crown-ether complexation on the chromophore properties and buffer effects.

Because of the scarcity of published data describing the use of the Horner–Emmons olefination in the crown-ether family, it was necessary to study the influence of the structures of the phosphonate and the carbonyl precursor on the degree of conversion and stereoselectivity of the process. We found that the optimal conditions for this reaction are as follows: 0 °C; NaH as the base, tetrahydrofuran as the solvent, and an aldehyde–phosphonate–base molar ratio of 1:1.2:1.2.

The compounds (**1–4**, **7–10**) were synthesized by the Horner–Emmons olefination of 4′-formyl-derivatives of monobenzo-crown ethers with C_2- and C_5-phosphonate anions (**21–24**), containing ester or nitrile terminal groups (Scheme 1).

The influence of a set of parameters such as the chain length, the presence of the methyl group, and the nature of terminal polar functions in the phosphonate molecule and the macrocycle size on the yields and stereoselectivity of this reaction was studied (see Table 1). Analysis of these data shows that Horner olefination preferably

Table 2. ^{1}H NMR spectral data, physico-chemical properties and other spectral parameters of the major E-isomer of compounds (**1–18**)

No.	^{1}H NMR data	R_f	Mp, °C (Lit. mp, °C) [reference]	Analysis: C, H, %	MS, m/z, (I_{rel}, %)
1	1.30 (t, 3H, J 7.0 Hz, OCH$_2$CH_3), 3.73 (s, 8H, CH$_2$O), 3.89 (m, 4H, CH$_2$O), 4.13 (m, 4H, CH$_2$O), 4.22 (q, 2H, J 7.0 Hz, CH$_3$CH_2O), 6.25 (d, 1H, J 16.0 Hz, 2-H), 6.80 (d, 1H, J 8.1 Hz, 6'-H), 7.02 (s, 1H, 3'-H), 7.06 (dd, 1H, J 8.1/1.5 Hz, 5'-H), 7.57 (d, 1H, J 16.0 Hz, 3-H)	0.5^B	84–86	For C$_{19}$H$_{26}$O$_7$ calcd: C, 62.28; H, 7.15. Found: C, 62.30; H, 7.13	366(M$^+$, 73), 234(89), 189(100), 162(77), 89(81)
2	1.32 (t, 3H, J 7.0 Hz, OCH$_2$CH_3), 3.72 (m, 12H, CH$_2$O), 3.90 (m, 4H, CH$_2$O), 4.15 (m, 4H, CH$_2$O), 4.18 (q, 2H, J 7.0 Hz, CH$_3$CH_2O), 6.25 (d, 1H, J 16.0 Hz, 2-H), 6.81 (d, 1H, J 8.1 Hz, 6'-H), 7.02 (s, 1H, 3'-H), 7.05 (dd, 1H, J 8.1/1.5 Hz, 5'-H), 7.57 (d, 1H, J 16.0 Hz, 3-H)	0.3^B	89–91	For C$_{21}$H$_{30}$O$_8$ calcd: C, 61.45; H, 7.37. Found: C, 61.41; H, 7.39	410(M$^+$, 41), 234(100), 189(58), 162(45), 73(37)
3	3.70 (s, 8H, CH$_2$O), 3.85 (m, 4H, CH$_2$O), 4.10 (m, 4H, CH$_2$O), 5.66 (d, 1H, J 16.0 Hz, 2-H), 6.80 (d, 1H, J 8.1 Hz, 6'-H), 6.90 (s, 1H, 3'-H), 6.98 (dd, 1H, J 8.1/1.5 Hz, 5'-H), 7.26 (d, 1H, J 16.0 Hz, 3-H)	0.5^B	97–99	For C$_{17}$H$_{21}$NO$_5$ calcd: C, 63.94; H, 6.63. Found: C, 64.11; H, 6.61	319(M$^+$, 33), 187(100), 172(62), 131(63), 103(38)
4	3.69 (m, 12H, CH$_2$O), 3.93 (m, 4H, CH$_2$O), 4.18 (m, 4H, CH$_2$O), 5.70 (d, 1H, J 16.0 Hz, 2-H), 6.86 (d, 1H, J 8.1 Hz, 6'-H), 6.96 (s, 1H, 3'-H), 7.02 (dd, 1H, J 8.1/1.5 Hz, 5'-H), 7.28 (d, 1H, J 16.0 Hz, 3-H)	0.45^B	63–65	For C$_{19}$H$_{25}$NO$_6$ calcd: C, 62.80; H, 6.93. Found: C, 62.96; H, 6.85	363(M$^+$, 30), 187(100), 172(87), 131(69), 103(47)
5	3.73 (s, 8H, CH$_2$O), 3.90 (m, 4H, CH$_2$O), 4.13 (m, 4H, CH$_2$O), 6.55 (dd, 1H, J 16.0/8.0 Hz, 2-H), 6.84 (d, 1H, J 8.1 Hz, 6'-H), 7.05 (d, 1H, J 1.5 Hz, 3'-H), 7.11 (dd, 1H, J 8.1/1.5 Hz, 5'-H), 7.36 (d, 1H, J 16.0 Hz, 3-H), 9.62 (d, 1H, J 8.0 Hz, CHO)	0.48^B	99–101 (105–106) [15]	For C$_{17}$H$_{22}$O$_6$ calcd: C, 63.34; H, 6.88. Found: C, 63.31; H, 6.81	322(M$^+$, 92), 190(98), 134(85), 106(100), 78(96)
6	3.69 (m, 12H, CH$_2$O), 3.95 (m, 4H, CH$_2$O), 4.18 (m, 4H, CH$_2$O), 6.56 (dd, 1H, J 16.0/1.5 Hz, 2-H), 6.89 (d, 1H, J 8.1 Hz, 6'-H), 7.05 (d, 1H, J 1.5 Hz, 3'-H), 7.11 (dd, 1H, J 8.1/1.5 Hz, 5'-H), 7.36 (d, 1H, J 16.0 Hz, 3-H), 9.62 (d, 1H, J 8.0 Hz, CHO)	0.3^B	66–68 (75–76) [15]	For C$_{19}$H$_{26}$O$_7$ calcd: C, 62.28; H, 7.15. Found: C, 62.49; H, 7.18	366(M$^+$, 84), 190(100), 162(87), 106(75), 73(68)
7	1.27 (t, 3H, J 7.0 Hz, OCH$_2$CH_3), 2.37 (s, 3H, CH$_3$), 3.74 (s, 8H, CH$_2$O), 3.90 (m, 4H, CH$_2$O), 4.13 (m, 4H, CH$_2$O), 4.14 (q, 2H, J 7.0 Hz, CH$_3$CH_2O), 5.84 (s, 1H, 2-H), 6.64 (d, 1H, J 16.0 Hz, 4-H), 6.81 (d, 1H, J 8.1 Hz, 6'-H), 6.84 (d, 1H, J 16.0 Hz, 5-H), 6.97 (s, 1H, 3'-H), 7.03 (dd, 1H, J 8.1/1.5 Hz, 5'-H)	0.5^B	103–105	For C$_{22}$H$_{30}$O$_7$ calcd: C, 65.01; H, 7.44. Found: C, 65.15; H, 7.51	406(M$^+$, 67), 202(41), 201(100), 173(48), 129(49)
8	1.27 (t, 3H, J 7.0 Hz, OCH$_2$CH_3), 2.36 (s, 3H, CH$_3$), 3.69 (m, 12H, CH$_2$O), 3.91 (m, 4H, CH$_2$O), 4.16 (m, 4H, CH$_2$O), 4.16 (q, 2H, J 7.0 Hz, CH$_3$CH_2O), 5.84 (s, 1H, 2-H), 6.63 (d, 1H, J 16.0 Hz, 4-H), 6.82 (d, 1H, J 8.1 Hz, 6'-H), 6.85 (d, 1H, J 16.0 Hz, 5-H), 6.99 (s, 1H, 3'-H), 7.00 (dd, 1H, J 8.1/1.5 Hz, 5'-H)	0.3^B	85–87	For C$_{24}$H$_{34}$O$_8$ calcd: C, 63.98; H, 7.61. Found: C, 64.05; H, 7.39	450(M$^+$, 12), 201(100), 129(29), 115(33), 71(29)
9	2.23 (s, 3H, CH$_3$), 3.74 (s, 8H, CH$_2$O), 3.90 (m, 4H, CH$_2$O), 4.13 (m, 4H, CH$_2$O), 5.25 (s, 1H, 2-H), 6.65 (d, 1H, J 16.0 Hz, 4-H), 6.80 (d, 1H, J 8.1 Hz, 6'-H), 6.81 (d, 1H, J 16.0 Hz, 5-H), 6.97 (s, 1H, 3'-H), 6.99 (dd, 1H, J 8.1/1.5 Hz, 5'-H)	0.42^B	117–119	For C$_{20}$H$_{25}$NO$_5$ calcd: C, 66.84; H, 7.01. Found: C, 66.95; H, 6.90	359(M$^+$, 64), 227(35), 212(100), 143(29), 73(32), 71(40)
10	2.22 (s, 3H, CH$_3$), 3.85 (m, 12H, CH$_2$O), 3.92 (m, 4H, CH$_2$O), 4.15 (m, 4H, CH$_2$O), 5.24 (s, 1H, 2-H), 6.63 (d, 1H, J 16.0 Hz, 4-H), 6.74 (d, 1H, J 16.0 Hz, 5-H), 6.81 (d, 1H, J 8.1 Hz, 6'-H), 6.97 (s, 1H, 3'-H), 7.03 (dd, 1H, J 8.1/1.5 Hz, 5'-H)	0.25^B	102–104	For C$_{22}$H$_{29}$NO$_6$ calcd: C, 65.49; H, 7.24. Found: C, 65.63; H, 7.31	403(M$^+$, 32), 213(32), 212(100), 186(27), 156(26)
11	2.34 (s, 3H, CH$_3$), 3.74 (s, 8H, CH$_2$O), 3.90 (m, 4H, CH$_2$O), 4.14 (m, 4H, CH$_2$O), 6.03 (d, 1H, J 8.0 Hz, 2-H), 6.72 (d, 1H, J 16.0 Hz, 4-H), 6.82 (d, 1H, J 8.1 Hz, 6'-H), 6.97 (d, 1H, J 1.5 Hz, 3'-H), 7.03 (d, 1H, J 1.5 Hz, 3'-H), 10,12 (d, 1H, J 8.0 Hz, CHO)	0.45^B	121–123	For C$_{20}$H$_{20}$O$_6$ calcd: C, 66.28; H, 7.23. Found: C, 66.43; H, 7.14	362(M$^+$, 74), 201(100), 187(92), 115(57), 71(59)

No.	^{1}H NMR	R_f	mp (°C)	Elemental analysis	MS
12	2.35 (s, 3H, CH$_3$), 3.69 (m, 12H, CH$_2$O), 3.93 (m, 4H, CH$_2$O), 4.18 (m, 4H, CH$_2$O), 6.03 (d, 1H, J 8.0 Hz, 2-H), 6.71 (d, 1H, J 16.0 Hz, 4-H), 6.82 (d, 1H, J 8.1 Hz, 6'-H), 6.98 (d, 1H, J 16.0 Hz, 5-H), 7.02 (d, 1H, J 1.5 Hz, 3'-H), 7.03 (d, 1H, J 8.1 Hz, 5'-H), 10,12 (d, 1H, J 8.0 Hz, CHO)	0.25^B	101–103	For C$_{22}$H$_{30}$O$_7$ calcd: C, 65.01; H, 7.44. Found: C, 65.28; H, 7.26	406(M$^+$, 91), 215(63), 201(100), 115(83), 73(64)
13	1.31 (t, 3H, J 7.0 Hz, OCH$_2$C*H*$_3$), 3.88 (s, 6H, CH$_3$O), 4.23 (q, 2H, J 7.0, OC*H*$_2$CH$_3$), 6.28 (d, 1H, J 16.0 Hz, 2-H), 6.84 (d, 1H, J 8.1 Hz, 6'-H), 7.03 (d, 1H, J 1.5 Hz, 3'-H), 7.07 (dd, 1H, J 8.1/1.5 Hz, 5'-H), 7.60 (d, 1H, J 16.0 Hz, 3-H)	0.37^A	49–51 (61) [16]	For C$_{13}$H$_{16}$O$_4$ calcd: C, 66.09; H, 6.83. Found: C, 66.11; H, 6.82	236(M$^+$, 100), 191(78), 164(37), 91(18), 77(31)
14	3.90 (s, 6H, CH$_3$O), 5.70 (d, 1H, J 16.0 Hz, 2-H), 6.85 (d, 1H, J 8.1 Hz, 6'-H), 6.90 (d, 1H, J 1.5 Hz, 3'-H), 7.02 (dd, 1H, J 8.1/1.5 Hz, 5'-H), 7.30 (d, 1H, J 16.0 Hz, 3-H)	0.28^A	82–84 (88–90) [17]	For C$_{11}$H$_{11}$NO$_2$ calcd: C, 69.83; H, 5.86. Found: C, 70.13; H, 5.97	189(M$^+$, 100), 174(66), 146(53), 91(34), 76(36)
15	3.90 (s, 6H, CH$_3$O), 6.59 (dd, 1H, J 16.0/8.0 Hz, 2-H), 6.88 (d, 1H, J 8.1 Hz, 6'-H), 7.06 (d, 1H, J 1.5 Hz, 3'-H), 7.13 (dd, 1H, J 8.1/1.5 Hz, 5'-H), 7.40 (d, 1H, J 16.0 Hz, 3-H), 9.64 (d, 1H, J 8.0 Hz, CHO)	0.27^A	79–81 (83–84) [18,19]	For C$_{11}$H$_{12}$O$_3$ calcd: C, 68.74; H, 6.29. Found: C, 68.57; H, 6.15	192(M$^+$, 100), 162(87), 91(42), 77(33), 58(48)
16	1.27 (t, 3H, J 7.0 Hz, OCH$_2$C*H*$_3$), 2.38 (s, 3H, CH$_3$), 3.88 (s, 3H, CH$_3$O), 3.90 (s, 3H, CH$_3$O), 4.16 (q, 2H, J 7.0 Hz, CH$_3$C*H*$_2$O), 5.86 (s, 1H, 2-H), 6.67 (d, 1H, J 16.0 Hz, 4-H), 6.82 (d, 1H, J 8.1 Hz, 6'-H), 6.86 (d, 1H, J 16.0 Hz, 5-H), 6.98 (s, 1H, 3'-H), 7.00 (dd, 1H, J 8.1/1.5 Hz, 5'-H)	0.5^A	54–56	For C$_{16}$H$_{20}$O$_4$ calcd: C, 69.55; H, 7.30. Found: C, 69.41; H, 7.12	276(M$^+$, 58), 204(45), 203(100), 202(53), 188(56)
17	2.24 (s, 3H, CH$_3$), 3.88 (s, 6H, CH$_3$O), 5.27 (s, 1H, 2-H), 6.68 (d, 1H, J 16.0 Hz, 4-H), 6.83 (d, 1H, J 16.0 Hz, 5-H), 6.84 (d, 1H, J 8.1 Hz, 6'-H), 6.97 (s, 1H, 3'-H), 7.03 (dd, 1H, J 8.1/1.5 Hz, 5'-H)	0.25^A	73–75	For C$_{14}$H$_{15}$NO$_2$ calcd: C, 73.34; H, 6.59. Found: C, 73.17; H, 6.68	229(M$^+$, 100), 214(69), 198(96), 183(29), 154(28)
18	2.34 (s, 3H, CH$_3$), 3.87 (s, 3H, CH$_3$O), 3.90 (s, 3H, CH$_3$O), 6.03 (d, 1H, J 8.0 Hz, 2-H), 6.74 (d, 1H, J 16.0 Hz, 4-H), 6.83 (d, 1H, J 8.1 Hz, 6'-H), 6.98 (d, 1H, J 16.0 Hz, 5-H), 7.00 (s, 1H, 3'-H), 7.04 (d, 1H, J 8.1 Hz, 5'-H), 10.11 (d, 1H, J 8.0 Hz, CHO)	0.3^A	97–99 (94–95) [20]	For C$_{14}$H$_{16}$O$_3$ calcd: C, 72.39; H, 6.94. Found: C, 72.45; H, 6.72	232(M$^+$,100), 203(77), 172(68), 166(64), 131(63)

Table 3. UV–vis spectral data for *E*-isomers of compounds (**1–18**) and their complexes with various metal cations

No.	λ_{max}, nm ($\varepsilon \times 10^{-4}$, M^{-1} cm^{-1}) of compound without metal salt	λ_{max}, nm ($\Delta\lambda_{max} = \lambda_{ML} - \lambda_L$), of complex with cation		
		Mg^{2+}	Ba^{2+}	La^{3+}
1	321 (1.78)	298 (−23)	308 (−13)	307 (−14)
2	322 (1.70)	313 (−9)	312 (−10)	308 (−14)
3	321 (1.80)	298 (−23)	308 (−13)	317 (−4)
4	323 (1.71)	320 (−3)	310 (−13)	310 (−13)
5	330 (2.06)	304 (−26)	305 (−25)	315 (−15)
6	332 (1.95)	323 (−9)	319 (−13)	310 (−22)
7	338 (2.66)	320 (−18)	325 (−13)	321 (−17)
8	341 (3.40)	337 (−4)	328 (−13)	322 (−19)
9	340 (3.24)	320 (−20)	326 (−14)	321 (−19)
10	342 (3.40)	339 (−3)	329 (−13)	323 (−19)
11	356 (3.26)	335 (−21)	338 (−18)	335 (−21)
12	359 (2.80)	353 (−6)	342 (−17)	336 (−23)
13	321 (1.88)	321 (0)	321 (0)	321 (0)
14	321 (2.00)	321 (0)	321 (0)	321 (0)
15	332 (2.46)	332 (0)	332 (0)	332 (0)
16	340 (2.90)	340 (0)	340 (0)	340 (0)
17	341 (3.14)	341 (0)	341 (0)	341 (0)
18	358 (3.40)	358 (0)	358 (0)	358 (0)

follows *E*-selectivity for the newly formed bond with moderate or high yields of products in all series of compounds (**1–4**, **7–10**, **13–14** and **16–17**). The configuration of the new C=C bond and the isomer ratio in the products were determined using ^{1}H NMR spectroscopy by comparing the integral intensities of proton signals in the polyene chain (doublets with *J* 16.0 Hz and *J* 12.0 Hz for *E*- and *Z*-isomers, respectively). Irrespective of the carbonyl precursor structure, C$_2$-phosphonate (**21**) with the ester terminal group formed only *E*-isomers of compounds (**1, 2, 13**), while C$_2$-phosphonate (**22**) with the nitrile group gave mixtures of 2*E*-/2*Z*-isomers (see Table 1). For C$_5$-phosphonates (**23, 24**) *E*-stereoselectivity of olefination was observed only for new C$_4$=C$_5$ bond formation, while the C$_2$=C$_3$ double bond was isomerized in some cases to give 2*E*,4*E*/2*E*,4*Z*-isomer mixtures, due to the use of phosphonates (**23, 24**) as isomer mixtures (*E*-/*Z*-, 60:40) and/or the additional possibility of *E*→*Z*-isomerization in the process of anion generation. A reason of 100% *E*-selectivity for the newly formed C$_4$=C$_5$ bond is the low probability of formation of the 4*Z*-isomer caused by the steric effect of the methyl group. Therefore, after olefination procedure with phosphonates (**23, 24**) we obtained an olefin mixture with a content of the predominant 2*E*,4*E*-isomer ranging from 70% to 100% (see Table 1). The series of model compounds (**13–18**) was synthesized via the same route.

Transformation of the ester group of intermediate esters (**1, 2, 7, 8, 13, 16**) into the hydroxymethyl function via LiAlH$_4$ reduction followed by MnO$_2$ oxidation leads to aldehydes. For conversion of the nitrile group into the aldehyde function we used a one-step procedure of

DIBAL reduction. The *E*→*Z*-isomerization that accompanies the nitrile group transformation into aldehyde function through DIBAL reduction was observed in several cases (for nitriles **9, 10, 17**).

An alternative synthetic route based on direct condensation of 3,4-dimethoxybenzaldehyde with KOH/CH$_3$CN [14] was tested for the preparation of nitrile (**14**).
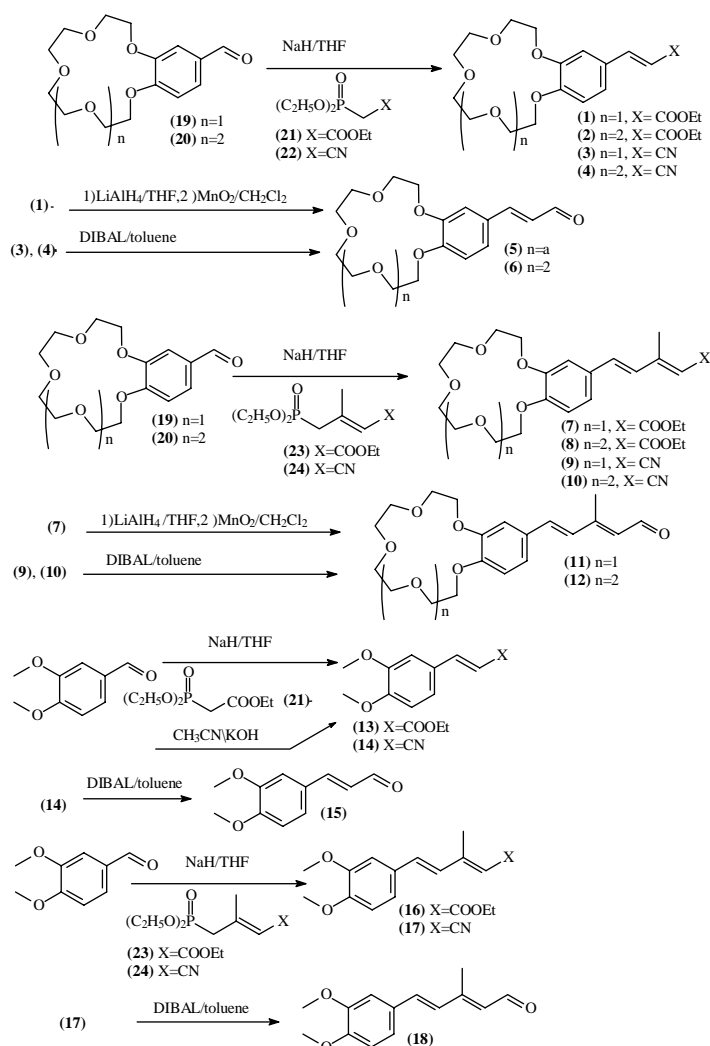
The individual *E*-isomers were isolated by recrystallization or additional separation by column chromatography. The structure of all compounds was confirmed by ^{1}H NMR, mass spectrometry and elemental analysis data.

Finally, four series of compounds (**1–6**, **7–12**, **13–15** and **16–18**) containing monobenzo-15-crown-5- and monobenzo-18-crown-6-ether or 3,4-dimethoxyphenyl fragments with different length of the conjugation chain and different nature of the terminal polar group were prepared.

A preliminary investigation of spectral properties and ion-binding capability was conducted for the crowned and reference compounds.

The electronic absorption spectra of all compounds under study exhibit two groups of bands located in the 200–240 and 270–400 nm spectral regions (Figure 1). For convenience, we used only long-wavelength bands.

Comparison of the spectral characteristics of the crown-ether vinylogs with identical terminal groups but different sizes of the crown-ether fragment has demonstrated almost complete coincidence of the spectral characteristics of these compounds and the corresponding 3,4-dimethoxyphenyl analogs containing no crown-ether fragments (Table 3). This means that long-wavelength absorption of these compounds is due to the same

Scheme 1.

system of conjugated bonds. The position of the long-wavelength absorption bands depends on the length of the conjugated chain and the nature of the terminal group. An increase in the chain length and the electron-withdrawing capability of the terminal groups results in bathochromic shifts of the absorption bands (see Table 3).

Unlike the 3,4-dimethoxyphenyl analogs, the introduction of metal salts into solutions of crown-ether vinylogs in acetonitrile induces hypsochromic shifts of absorption bands (cf. curves 1 and 2; 3 and 4 in Figure 1, Table 3). The observed spectral changes are due to complex formation between the metal ions and the crown-ether fragments. The hypsochromic shift depends on the nature of the metal ion (see Table 3 and Figure 2). This shift is due to the decrease in the electron-donating ability of the oxygen atoms in the macroheterocycle. The magnitude of the shift is determined by the efficiency of metal ion binding by the crown-ether moiety.

Analysis of the concentration dependences of the hypsochromic shift upon complexation shows that magnesium ions interact most efficiently with a small crown-ether fragment (see Table 3). This is due to the close conformity between the sizes of the interacting species. When the barium cation interacts with mono-benzo-15-crown-5 ether fragments, no binding selectivity is observed due to its greater ion radius compared to that of magnesium (see Table 3). The lanthanum ions with an intermediate ion radius induce a hypsochromic shift close to or even greater than that observed for barium ions. This may be attributed to a higher charge density of lanthanides.

This part of the work is now in progress and the final results will be published in the near future.

Conclusion

We elaborated an effective synthetic route for the preparation of new crown-ether vinylogs with a variable length of the conjugated bonds, different crown-ether ring size and terminal polar groups. We also prepared the corresponding reference compounds.
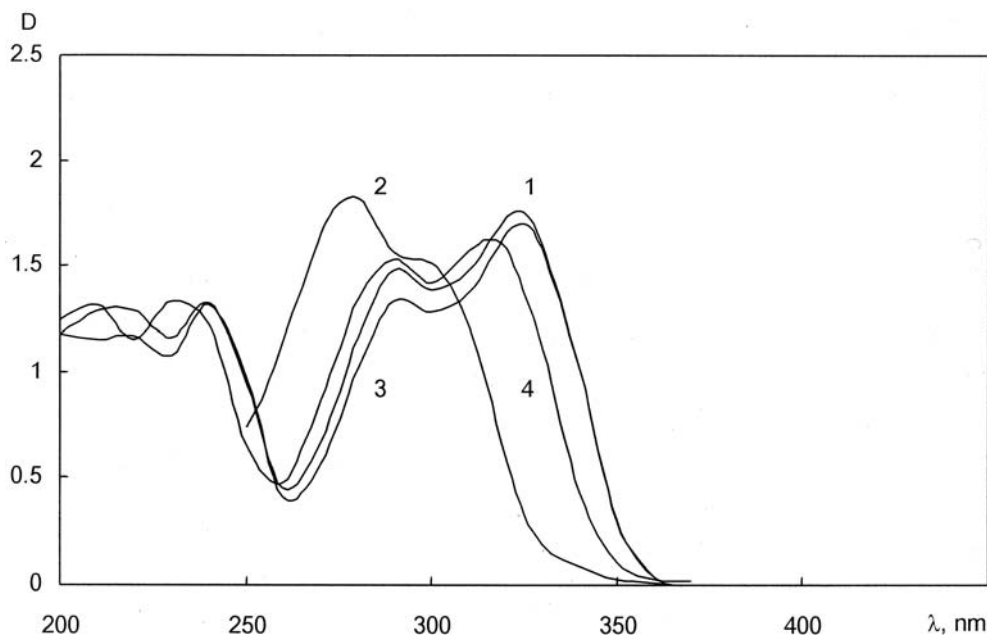
Figure 1. UV–vis spectra of nitriles (**3**, **4**) in acetonitrile without (curves 1, 3) and after addition magnesium perchlorate (curves 2, 4).
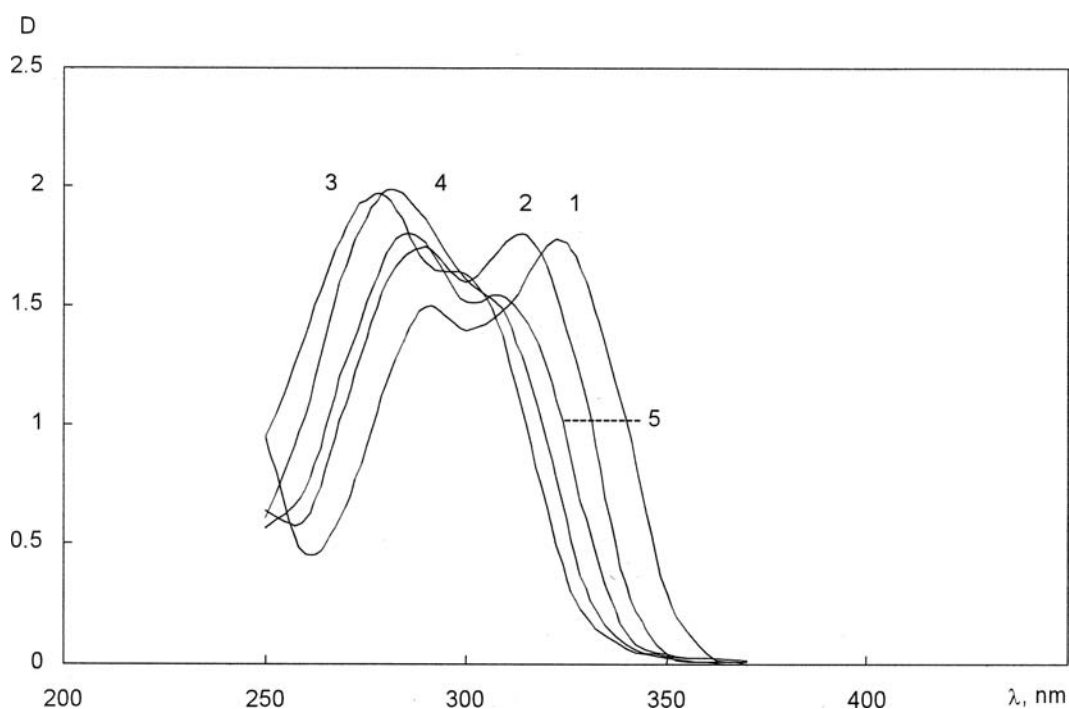

Figure 2. UV–vis spectra of nitrile (**3**) in acetonitrile without (curve 1) and after the addition of Li (curve 2), Mg (curve 3), Ca (curve 4) and Ba (curve 5) perchlorates ($c_L = 2 \times 10^{-4}$ M^{-1}, $c_M/c_L = 10^3$).

Acknowledgements

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