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# Synthesis and Properties of a New Dye, Containing the Crown Ether Moiety

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We described two synthetic routes for preparation of new crown ether derivatives of polyenals, containing variable length of the conjugation chain.

*Keywords:* aromatic retinal analogs; polyenals; containing the crown ether moiety; synthesis

## Introduction

During a last ten years the design of a new synthetic methods for the introduction of crown ether moiety in the various type molecules is under extensive investigation. The derivatives of crown ethers are widely using as ion-selective electrode unit in various types of sensors. Earlier, several types of dyes, bearing chromophoric groups bound with

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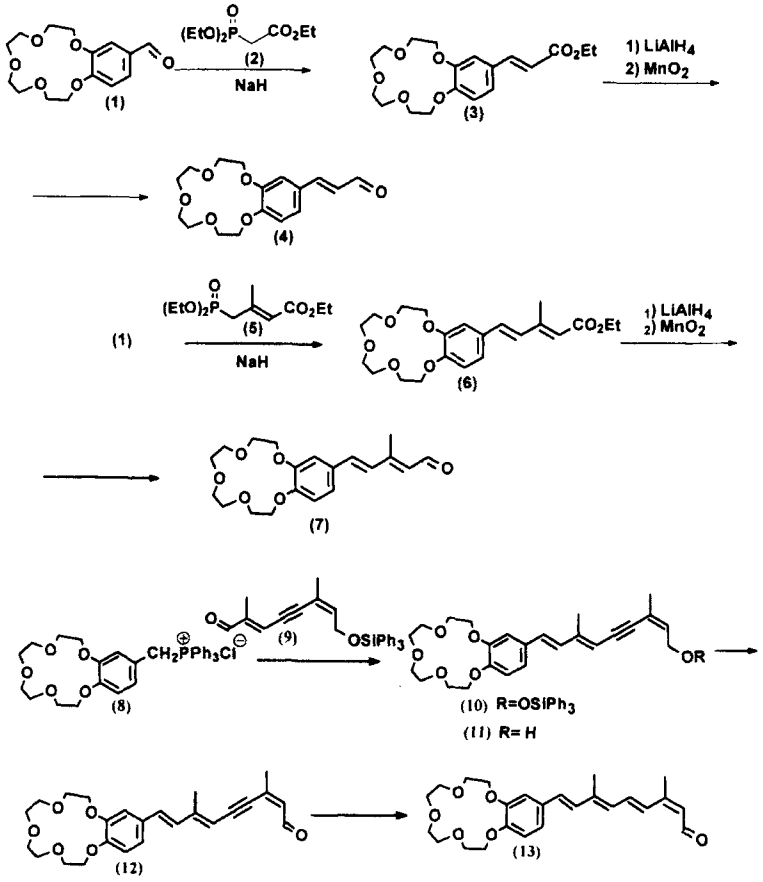
crown ethers derivatives via C=C- or butadiene linkers, were synthesized and their photochemical properties and ion-binding capability were investigated at Photochemistry Centre of RAS [1,2]. In present paper we describe the effective synthetic routes for preparation a new crown ethers polyenals derivatives (4,7,12,13), containing variable length of the conjugation chain.




Scheme 1.

Polyenals (12,13) structure is very similarly to the aromatic analogs of vitamine A aldehyde - retinal [3]. Its stereoisomers, bound via a protonated Schiff base with an ε-aminogroup of Lys-residue, are chromophore group in numerous light-transduction proteins family. Therefore, polyenals (12,13) and particularly its complexes with several metal cations, have a immense interest as appropriate route for introduction the electron-density labels into the chromophoric centre cavity of the retinal-chromoproteins.

**Polyenals synthesis.**

Two various synthetic routes, depicted on Scheme 1, have been proposed by us.

The first route for preparation of compounds (4,7) involved of Horner olefination of aldehyde (1) with $C_2$-(2) or $C_5$-(5) phosphonates. Starting compound (1) was prepared with 68% yield by Duff formylation of benzo-15-crown-5-ether, as described in [4]. Condensation of aldehyde (1) with $C_2$-phosphonate (2) gave ester (3) as pure E-isomer. Subsequent transformation of their ester group into hydroxyl function by $LiAlH_4$ and its oxidation by $MnO_2$ leads to aldehyde (4) with overall yield 22%. When analogous procedure has employed for aldehyde (1) and $C_5$-phosphonate (5) isomeric mixture of ester (6) was obtained in ratio E / Z 4:1 by $^1$H-NMR data. Then it was separated by column chromatography. Repeating of ester function transformation operation leads to aldehyde (7) with overall yield 16%.

The second approach consists in the introduction of crown ether moiety in the dye molecule by Wittig olefination of $C_{10}$ aldehyde (9) by

ilide, generated from triphenylphosphonium salt (8) under phase-transfer catalysis conditions, which were developed and successfully applied for aromatic retinal analog synthesis by us earlier [4]. Phosphonium salt (8) was prepared by quaternization of the correspondent chloromethyl derivative and $(C_6H_5)_3P$ with 50% yield as described in [3]. After isomers separation and removing of triphenylsilyl protective group the alcohol (11) was oxidized in polyenal (12) by $MnO_2$ in $CH_2Cl_2$. Semihydrogenation of the triple bond in the aldehyde (12) over Lindlar catalyst and thermoisomerisation of reaction mixture gave polyenal (13).

The structure of all compounds was clearly confirmed by IR-, UV- and $^1$H-NMR - spectroscopy. $^1$H-NMR-spectra data of polyenals (Brucker MSL-200 NMR spectrometer, $CDCl_3$), are present in Table 1.

Schiff bases of polyenals (12,13) by condensation with n-butylamine have synthesized and carried out the preliminary study the spectral properties in protonated and unprotonated forms. We plan to prepare from our aldehydes serie by its condensation with several dyes, possesses methyl group a numerous range new derivatives and then to conduct a detail investigation their spectral properties and ion-binding capability. These works are now in progress and its results will publish lately.

**Interaction of analog (12) with bacterioopsin.**

The synthesized analog (12) was tested further in recombination with bacterioopsin, from apomembranes H.salinarium. Apomembranes obtained from purple membranes by hydroxylaminolysis at pH 7.0 and 0 - 5°C and intensive illumination.

TABLE 1 Parametres of polyenic compounds NMR-spectra.

| N | $^1$H-NMR-spectra data |
|---|---|
| (3) | 1.35 (m, 3H, $CH_3CH_2O$), 3.75 (m, 8H, $CH_2O$), 3.90 (m, 4H, $CH_2O$), 4.17 (m, 4H, $CH_2O$), 5.95 (d, 1H, J 8.1, 6'-H), 6.43 (d, 1H, J 16, 2-H), 7.40 (s, 1H, 2'-H), 7.44 (d, 1H, J 8.1, 5'-H), 7.64 (d, 1H, J 16, 3-H). |
| (4) | 3.69 (m, 8H, $CH_2O$), 3.85 (m, 4H, $CH_2O$), 4.07 (m, 4H, $CH_2O$), 6.51 (dd, 1H, J 16/8, 2-H), 6.80 (d, 1H, J 8.1, 6'-H), 7.33 (d, 1H, J 16, 3-H). 7.40 (s, 1H, 2'-H), 7.44 (d, 1H, J 8.1, 5'-H), 9.57 (d, 1H, J 8, CHO). |
| (6) | 1.31 (m, 3H, $CH_3CH_2O$), 2.40 (s, 3H, $CH_3$), 3.75 (m, 8H, $CH_2O$), 3.89 (m, 4H, $CH_2O$), 4.15 (m, 4H, $CH_2O$), 5.95 (s, 1H, 2-H), 6.85 (d, 1H, J 16, 4-H), 6.96 (d, 1H, J 8.1, 6'-H), 7.07 (d, 1H, J 16, 5-H), 7.40(s, 1H, 2'-H), 7.44 (d, 1H, J 8.1, 5'-H). |
| (7) | 2.40 (d, 3H, J 0.5, $CH_3$), 3.71 (m, 8H, $CH_2O$), 3.89 (m, 4H, $CH_2O$), 4.12 (m, 4H, $CH_2O$), 6.03 (d, 1H, J 8, 2-H), 6.84 (d, 1H, J 16, 4-H), 6.96 (d, 1H, J 8.1, 6'-H), 7.12 (d, 1H, J 16, 5-H), 7.40 (s, 1H, 2'-H), 7.44 (d, 1H, J 8.1, 5'-H), 10.12 (d, 1H, J 8, CHO). |
| (11) | 1.82 (s, 3H, 7-$CH_3$), 2.22 (s, 3H, 3-$CH_3$), 3.8...4.2 (m, 16H, $CH_2O$), 4.36 (d, 2H, J 7, 1-$CH_2$), 5.65 (s, 1H, 6-H), 6.61 (d, 1H, J 16, 8-H), 6.76 (d, 1H, J 16, 9-H), 6.82 (t, 1H, J 7, 2-H), 6.92 (s, 1H, arom.), 6.95 (s, 2H, arom.). |
| (12) | 2.12 (s, 3H, 7-$CH_3$), 2.16 (s, 3H, 3-$CH_3$), 3.8...4.2 (m, 16H, $CH_2O$), 5.72 (s, 1H, 6-H), 6.1(d, 1H, J 8, 2-H), 6.8 (m, 2H, 8,9-H), 6.98 (m, 3H, arom.), 10.7 (d, 1H, J 8, CHO) |

Resynthesis of pigment conducted by addition of analog solution in methanol to a suspension apomembranes in a buffer(protein concentration - 2.03 mg/ml, 25°C, pH 6.0, 5 mM MES). It was revealed, that the formation of a pigment with $\lambda_{max}$ 461 nm takes place already during one hour. The comparison of new pigment optical density with bacteriorhodopsin optical density (ε 63000 $M^{-1}$ $cm^{-1}$, at 560 nm), has allowed to estimate ε of a new pigment (10000 $M^{-1}$ $cm^{-1}$).

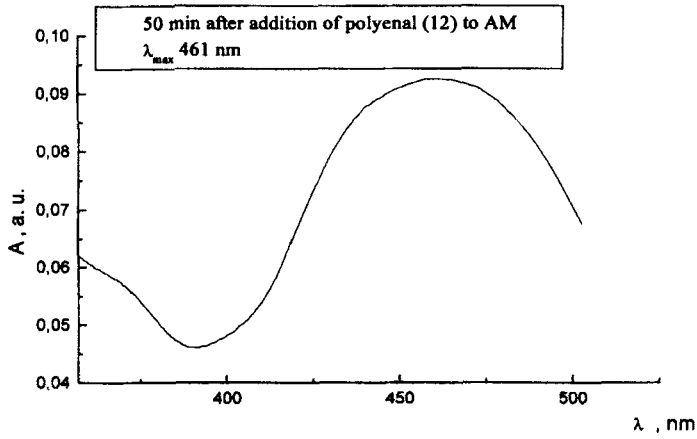



Fig. 1. Spectrophotometric control of bacteriorhodopsin analog' formation process from polyenal (12) and apomembranes from Halobacterium salinarium. Protein concentration - 2.03 mg/ml, 25$^0$C, pH 6.0, 5 mM MES.

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