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# Studies on Quinones. Part. 33.[1] Synthetic Approach to Podands Containing Quinone Fragments

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# STUDIES ON QUINONES. PART. 33.[1] SYNTHETIC APPROACH TO PODANDS CONTAINING QUINONE FRAGMENTS

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**Abstract**: The preparation and oxidative demethylation attempts of podands **3-5**, and **9** containing the 2,5-dimethoxyphenyl substituent are described. The reaction of alizarine **13** with chloroethanol afforded compounds **14** and **15**. The pathway formation of heterocycle **15** from **14** is proposed. The synthesis of podand **16** containing the cytotoxic 1-hydroxy-9,10-anthraquinone fragment as the terminal groups is reported.

The symmetrical dimerization of a ligand can lead to a very large increase of its binding affinity for a biological receptor as shown for example by dimers of daunomycin, 9-aminoacridine and pyridocarbazoles.[2] Continuing with our work on the synthesis of quinones with biological relevance we have initiated studies on the synthesis of quinone dimers joined by spacers with ability to interact with cations and small molecules. The podands,[3] a sort of acyclic crown ethers which has received little attention[4] in the design of new potentially bi-intercalant agents, was selected as a spacer for our purpose.

There are literature reports on the synthesis of podands linked to quinone nuclea *via* the reaction of 2,5-dimethoxybenzyl alcohol derivatives with glycol ditosylates and sodium hydride, followed by oxidative deprotection with cerium ammonium nitrate (CAN). Depending upon the structure of the podand precursors the oxidative demethylation provide macrocycles quinonoid compounds or podands bearing one or two 1,4-benzoquinone fragments as terminal groups.[5,6]

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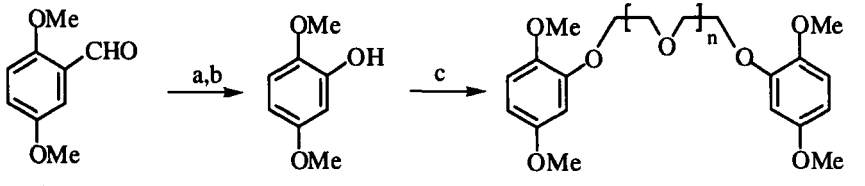
Recently we have reported the synthesis and *in vitro* antiprotozoan activity of podands linked to one and two benzo[*b*]thiophene fragments. These podands showed potent activities as cell growth inhibitor of the *Leishmania*.[7] In this communication we wish to describe our efforts on the synthesis of podands linked to a 2,5-dimethoxyphenyl group and the results on their oxidative deprotection. Also is reported the synthesis of a podand armed with the 1-hydroxy-9,10-anthraquinone cytotoxic fragment as terminal groups.

The synthesis of podands containing a latent 1,4-benzoquinone nucleus was firstly attempted by reaction of di-, tri- and tetraethylene glycol ditosylates with 2,5-dimethoxyphenol. The ditosylates were obtained by reaction of tosyl chloride with the corresponding glycols in pyridine solution following the reported procedure.[8] The preparation of 2,5-dimethoxyphenol **2** was performed by Bayer-Villiger reaction of 2,5-dimethoxybenzaldehyde **1** with *m*-CPBA according to the described method.[9] The reaction of **2** with the corresponding ditosylates (n = 1, 2, 3) was carried out in DMF in the presence of potassium carbonate at reflux for 24 hours. Under these conditions the corresponding podands **3-5** were generated in 89, 83 and 60% yield respectively (Scheme 1).

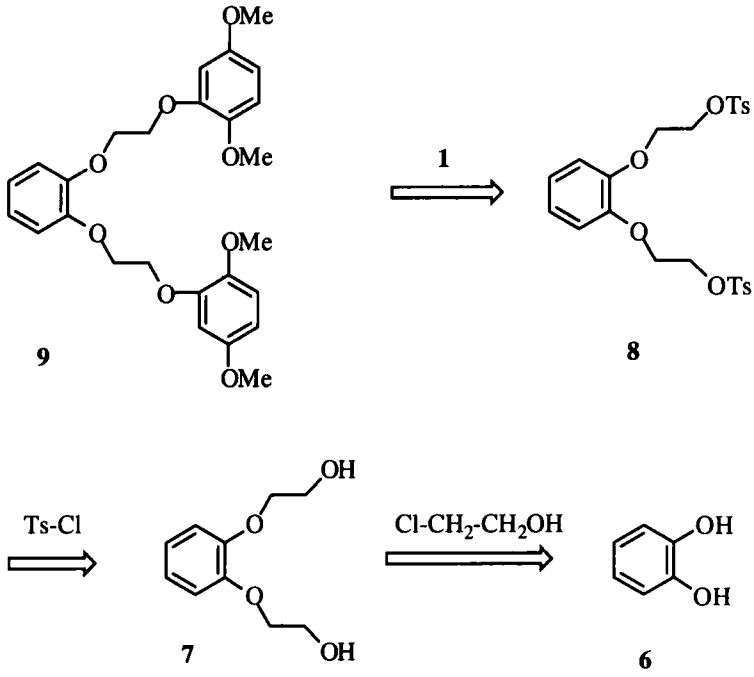
When the reaction of **2** with the corresponding ditosylates was carried out in aqueous sodium hydroxide solution for 12 hours at reflux, podands **3-5** were obtained in 83, 74 and 61% yield respectively.




**1** **2** **3-5**

**Reagents:** a) *m*-CPBA, $CH_2Cl_2$ ; b) NaOH, $H_2O$; c) TsO-(CH2-CH2-O)n-OTs , DMF, $K_2CO_3$

**Scheme 1**



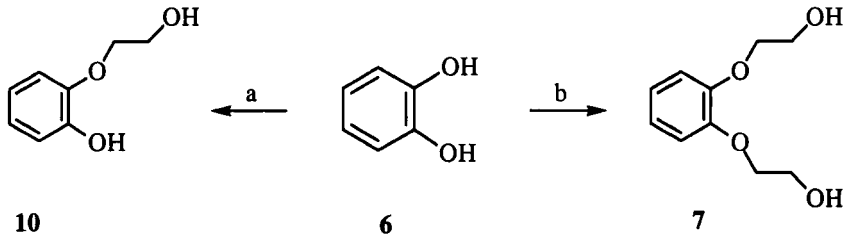

**Scheme 2**

The synthesis of compound **9** containing a semirigid podand spacer was also envisaged; the strategy planned to prepare **9** is outlined in Scheme 2.

The reaction of catechol with chloroethanol in the presence of sodium hydroxide in 2-methoxyethanol gave the monosubstitution product **10** in low yield (14%). All attempts to induce the formation of compound **7** by increasing the time reaction, or using chloroethanol as the solvent were unsuccessful. Nevertheless, when the reaction was carried in aqueous sodium hydroxide under nitrogen atmosphere, product **7** was isolated in 66% yield (Scheme 3).

Compound **7** was converted to the corresponding ditosylate **8** in 66% yield by reaction with tosyl chloride in pyridine solution. [10] Subsequent reaction of **8** with 2,5-dimethoxyphenol **2** in DMF provided podand **9** in 61% yield.

In order to release the quinones from the corresponding dimethylethers **3-5** the oxidative deprotection of podand **3** with nitric acid impregnated manganese



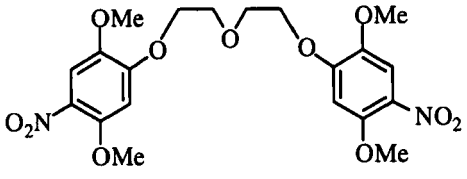

10 6 7

**Reagents:** a) $ClCH_2CH_2OH$, NaOH, $MeOCH_2CH_2OH$; b) $ClCH_2CH_2OH$, NaOH, $H_2O$

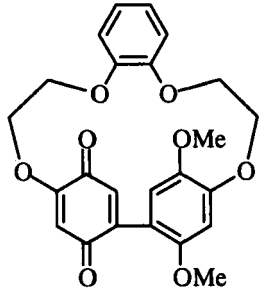
**Scheme 3**

dioxide[11] in dichloromethane was attempted. Tlc analysis of the reaction mixture indicated that a complex mixtures of products was generated. From this mixture, compound **11** was isolated in low yield. Podand **11** was prepared in 64% yield, however, by nitration of **3** with nitric acid in acetic acid solution. Oxidative deprotection of **3** with impregnated reagent under ultrasonic irradiation and also with CAN were unsuccessful.

The oxidative deprotection of podand **9** was examined in two parallel experiment with both oxidant reagents. The reaction with impregnated reagent afforded a complex reaction mixture; however, the reaction with CAN afforded the macrocycle **12** in 24% yield. The structure of compound **12** was established by the presence of two carbonyl carbons at δ179.2 and 180.4 ppm corresponding to the quinone nucleus. The presence of the substituted biphenyl system was deduced by




11




12

the signals of two aromatic protons at δ 6.73 and 6.68 ppm and two vinylic protons at δ 6.35 and 5.84 ppm.

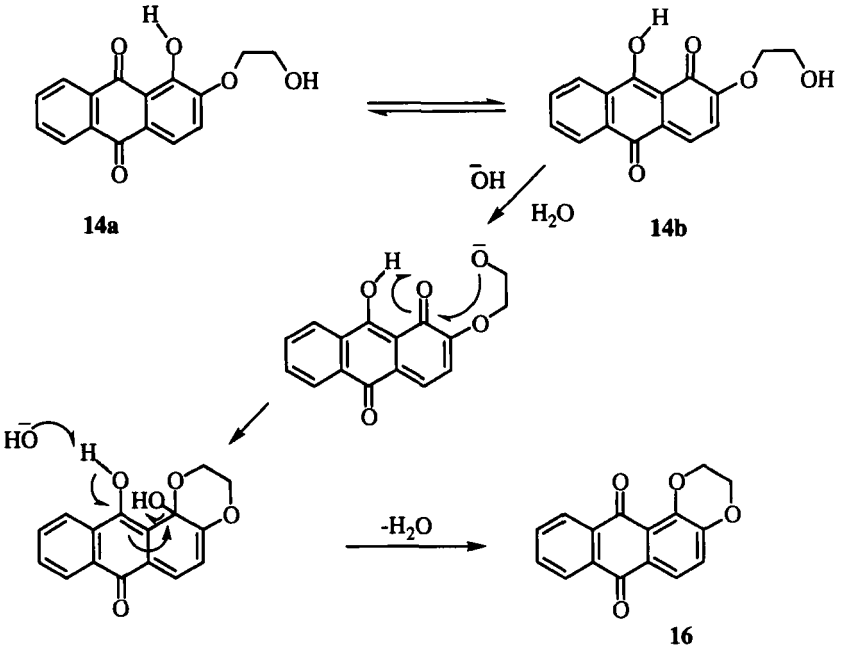
The above results indicate that the synthesis of podands having 1,4-benzoquinone nucleus as terminal groups by oxidative deprotection of podands type **3** is unsuccessful. On the basis of these results we decided to prepare podands linked to quinones by employing a strategy based on the coupling of functionalized quinones to the polyoxyethylene spacer.

The occurrence of the 1-hydroxy-anthraquinone system in a variety of cytotoxic compounds[12] led us to investigate the synthesis of podands containing this type of quinone substituent. Alizarin **13** was selected as a suitable precursor because it is easily available and the hydrogen bond interaction of the 1-hydroxy group would facilitate the selective alkylation of the 2-hydroxy group with glycol ditosylates. In order to confirm the major reactivity of the 2-hydroxy group to the O-alkylation we examined the reaction of alizarine **13** with chloroethanol. The reaction was carried out in DMF-potassium carbonate to afford two products which were isolated by preparative TLC. The more polar compound was characterized as the expected anthraquinone **14** (36%) and the less polar compound was identified as the angular quinone **15** (10%). Chang *et al* have reported the preparation of the cytotoxic quinone **15** in 21% yield, by reaction of alizarine **13** with 1,2-dibromoethane in DMF-potassium carbonate.[13]

This result confirm the reluctance of the *peri* hydroxy group of alizarin **13** to the alkylation reaction with chloroethanol. The formation of angular tetracyclic quinone **15** was rationalized by considering a tautomeric equilibrium between **14a** and the ana-quinone **14b**.

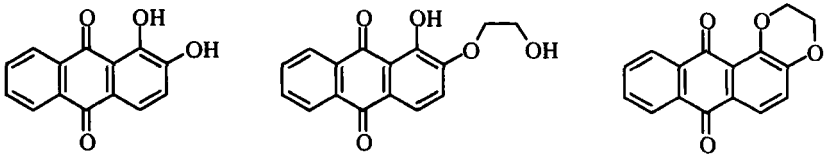
The unstable tautomer **14b** can undergo a base-induced cyclization to produce an hemiketal intermediate which *via* dehydration affords the angular tetracyclic quinone **15** (Scheme 4).

We investigate the reaction of alizarine with ethylene glycol ditosylate, potassium carbonate in DMF. The reaction gave the expected podand **16** in 31%



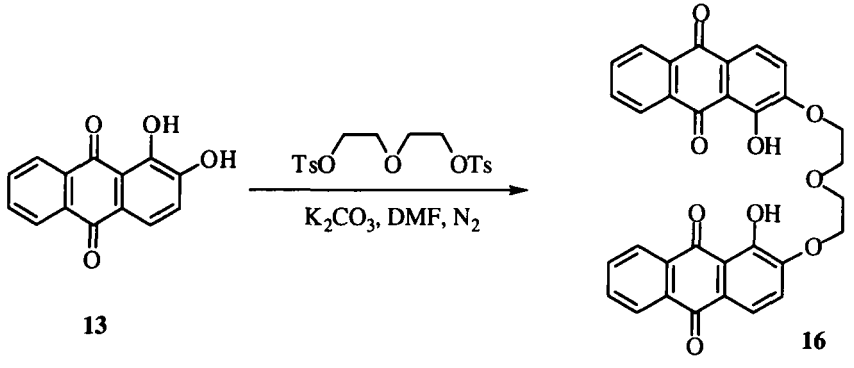

Scheme 4

yield accompanied by alizarin **13**. Attempts to improve the yield of **16** either by using prolonged reaction times or excess ethylene glycol were unsuccessful.



**13** **14** **15**

The structure of dimer **16** was confirmed by $^1$H NMR. The appearence of a singlet at δ12.93 ppm corresponding to the chelated protons together with the signals of the methylene protons of the spacer at δ4.09 and 4.36 ppm confirmed that the two quinone fragments in **16** are linked to the 2-position of the anthraquinone skeleton.




13 16

In summary, we have prepared a variety of podands bearing aromatic and quinone substituents as the terminal groups. These results could be extended to the preparation of podands containing bioactives quinones for biological and host-guest supramolecular studies.[14] The synthesis of new podands containing carbo- and heterocyclic cytotoxic fragments are in progress.

## Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. FTIR spectra were recorded on a Bruker vector 22-FT spectrophotometer for KBr disc and the wave numbers are given in $cm^{-1}$. The $^1H$- and $^{13}C$-NMR spectra were determined on a Bruker AC-200P spectrometer in deuteriochloroform. Chemical shifts are reported in $\delta$ ppm downfield to TMS, and *J*-values are given in Hertz. Low resolution mass spectra were obtained on a VG-12-250 spectrometer at 70 eV. Silica gel Merck 60 (70-230 mesh) and DC-Alufolien $60F_{254}$ were normally used for preparative column and analytical TLC, respectively. Elemental analysis were done at Instituto de Química General (C.S.I.C), Madrid Spain. All reagents were commercial quality. Solvent used in extraction were distilled prior to use. Silica gel Merck 60 (70-230 mesh) and DC-Alufolien $60F_{254}$ were normally used for preparative column and analytical TLC, respectively. Preparation of di-, tri- and tetraethyleneglycol ditosylates were performed according to a reported method.[8] Compound **2** was obtained from commercially available 2,5-dimethoxybenzaldehyde by using the reported procedure.[9]

**Preparation of podands 3-5. Typical Procedure**

Method A:

A suspension of diethylene glycol ditosylate (300 mg, 0.725 mmol), 2,5-dimethoxyphenol **2** (230 mg, 1.52 mmol), potassium carbonate (210 mg) in DMF (10 mL) was refluxed under nitrogen atmosphere for 24 h. The reaction mixture was diluted with water and extracted with chloroform (3 x 20 mL). The organic extract was washed thoroughly with 5% hydrochloric acid and finally with water. The dried solution was evaporated *in vacuo* to yield crude 1,5-*bis*(2,5-dimethoxyphenoxy)-3-oxapentane **3** (244 mg, 89%). Podand **3** was purified by column chromatography on silica gel (4:1 petroleum ether-chloroform); white needles mp: 103-105 °C (ethanol); Anal. Calcd. for $C_{20}H_{26}O_7$: C, 63.49; H, 6.93. Found: C, 63.71; H, 7.10%;$\nu_{max}$:1520, 1230, 1040 and 1020: $\delta_H$: 3.74 (s, 6H, 2 x OMe), 3.80 (s, 6H, 2 x OMe), 3.95 (t, 4H, $J$ = 5 Hz, 2- and 4-H), 4.18 (t, 4H, $J$ = 5 Hz, 1- and 5-H), 6.41 (dd, 2H, $J$ = 8.7 and 3.0 Hz, 4'-H), 6.56 ( d, 2H, $J$ = 3 Hz, 6'-H), 6.79 ( d, 2H, $J$ = 8.7 Hz, 3'-H); $\delta_C$: 55.6, 56.7, 68.6, 69.8, 102.4, 104.1, 113, 144, 149, 154.2.

**1,8-*Bis*(2,5-dimethoxyphenoxy)-3,6-dioxaoctane 4**

Prepared from triethylene glycol ditosylate (300 mg, 0.655 mmol), 2,5-dimethoxyphenol **2** (200 mg, 1.31 mmol), potassium carbonate (180 mg) in DMF (10 mL). The crude podand **4** (229 mg, 83%) was purified by column chromatography on silica gel (chloroform); white plates mp. 110-112 °C (ethanol); Anal. Calcd. for $C_{22}H_{30}O_8$: C, 62.55; H, 7.16. Found: C, 62.81; H, 7.30%; $\nu_{max}$ : 1500, 1230, 1040 and 1020: $\delta_H$: 3.74 (s, 6H, 2 x OMe), 3.74 ( s, 4H, 4- and 5-H), 3.80 ( s, 6H, 2 x OMe ), 3.88 (t, 4H, $J$ = 5 Hz, 2- and 7-H), 4.16 (t, 4H, $J$ = 5 Hz, 1- and 8-H), 6.41 (dd, 2H, $J$ = 8.7 and 3 Hz, 4'-H), 6.55 (d, 2H, $J$ = 3 Hz, 6'-H), 6.78 (d, 2H, $J$ = 8.7 Hz, 3'-H); $\delta_C$: 55.7, 56.8, 68.6, 69.7, 70.9, 102.4, 104.2, 113, 144.1, 149.3, 154.3.

**1,11-Bis(2,5-dimethoxyphenoxy)-3,6,9-trioxaundecane 5**

Prepared from tetraethylene glycol ditosylate (300 mg,0.60 mmol) 2,5-dimethoxyphenol **2** (184 mg, 1.20 mmol), potassium carbonate (160 mg) in DMF (10 mL). The crude podand **5** was isolated as an oil (167 mg, 60%) and an analytical sample was obtained by column chromatography on silica gel; HRMS Calcd. for $C_{24}H_{34}O_9$: 466.22083. Found: 466.22095; $\nu_{max}$ : 1500, 1220, 1110 : $\delta_H$: 3.74 (s,

6H, 2 x OMe), 3.79 (s, 6H, 2 x OMe), 3.62-3.88 (m, 12H, 2-, 4-, 5-, 7-, 8-,10-H), 4.15 (t, 4H, $J$ = 5 Hz, 1- and 11-H), 6.40 (dd, 2H, $J$ = 8.7 Hz, 4'-H), 6.54 (d, 2H, $J$ = 3 Hz, 6'-H), 6.78 (d, 2H, $J$ = 8.7 Hz, 3'-H); $\delta_C$: 55.7, 56.8, 68.5, 69.6, 70.6, 70.8, 102.3, 104, 112.9, 144, 149, 154.

Method B:

A mixture of diethylene glycol ditosylate (300 mg, 0.725 mmol), 2,5-dimethoxyphenol **2** (230 mg, 1.52 mmol), sodium hydroxide (61 mg, 1.52 mmol) in water (4 mL) was refluxed under nitrogen atmosphere for 12 h. The reaction mixture was acidified with dil. hydrochloric acid, extracted with chloroform and the dried extract was evaporated affording podand **3** in 83 % yield.

Under similar conditions podands **4** and **5** were prepared in 74 and 61 % yields respectively.

**1-Hydroxy-2-(2-hydroxyethyloxy)benzene 10**

A solution of catechol **6** (300 mg, 273 mmol), chloroethanol (436 mg, 5.45 mmol), sodium hydroxide in 2-methoxyethanol (7 mL) was heated to 100-102°C for 2 days. The reaction mixture was diluted with water and extracted with ethyl ether (3x20 mL). The dried extract was evaporated *in vacuo* and the residue was purified by column chromatography (chloroform) to afford **10** (168 mg, 40%) as a white solid mp 96-99 °C; Anal. Calcd. for $C_8H_{10}O_3$: C, 62.31; H, 6.54. Found: C, 62.46; H, 6.16%; $\nu_{max}$: 3400-3200, 1490, 1260, 1110 and 1040; $\delta_H$: 3.99 (t, 2H, $J$ = 4 Hz, 2´-H), 4.14 (t, 2H, $J$ = 4 Hz, 1´-H), 6.90 (m, 4H, 3-, 4-, 5-, and 6-H); $\delta_C$: 61.4, 70.7, 113.5, 115.6, 120.2, 122.5, 145.9, 146.5; LRMS, m/z (%): 154 (27.4, $M^+$), 110 (100).

**1,2-*Bis*(2-hydroxyethoxy)benzene 7**

A solution of cathecol **6** (600 mg, 5.46 mmol), sodium hydroxide (437 mg, 10.9 mmol ) and water (12 mL) was magnetically stirred under nitrogen atmosphere for 1h. To this mixture was added chloroethanol (0.98 g, 11.9 mmol) and then refluxed for 24 h. The resulting mixture was acidified with diluted hydrochloric acid and extracted with chloroform (3x20 mL). The dried organic extract was evaporated *in vacuo* and the residue was purified by column chromatography on silica gel

(chloroform) to provided pure **7** (713 mg, 66%); mp 82-84 °C (lit.[10] 93-94°C); Anal. Calcd. for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.24; H, 7.23%; $\nu$-max:3600-3200, 1490, 1260, 1110 and 1060: $\delta_H$: 3.35 (br s, 2H, exchangeable with $D_2O$, 2 x OH), 3.93 (t, 4H, $J$ = 4 Hz , 2´-H), 4.13 (t, 4H, $J$ = 4 Hz, 1´-H), 6.98 (s, 4H, 3, 4, 5, 6-H); $\delta_C$: 61.3, 72.2, 116.5, 122.7, 149.3.

**1,2-*Bis*(2-hydroxyethoxy)benzene ditosylate 8**

To a stirred solution of **7** (300 mg, 1.52 mmol) in pyridine (1 mL) at 0°C was added tosyl chloride (696 mg, 3.65 mmol) and the mixture was left with stirring for 3h at 0°C and then was freezing overnight. The mixture was diluted with ice-water (10 mL), stirred for 1h and extracted with chloroform (3 x 20 mL). The extract was washed with 5% hydrochloric acid (5 x 20 mL), water and dried. Evaporation of the solvent afforded compound **8** as white solid (445 mg, 58%). Compound **8** was purified by column chromatography on silica gel (chloroform), mp:87-90 °C (lit.[10] 95.5-97°C) ; Anal. Calcd. for $C_{24}H_{26}O_8S_2$: C, 56.90; H, 5.17; S, 12.66 Found: C, 56.92; H, 5.18; S, 12.73%; $\delta_H$: 2.43 (s, 6H, 2 x Me), 4.16 (t, 4H, 5 Hz, 2'-H), 4.33 (t, 4H, $J$ = 5 Hz, 1'-H), 6.86 (m, 4H, 3-, 4-, 5-, 6-H), 7.34 (d, 4H, $J$ = 8 Hz, Ar-H), 7.80 (d, 4H, $J$ = 8 Hz, Ar-H); $\delta_C$: 21.6, 67.4, 68.3, 116.4, 122.7, 128, 130, 133, 145, 148.5.

**1,2--*Bis* [2-(2,5-dimethoxyphenoxy)ethoxy]benzene 9**

A mixture of ditosylate **8** (329 mg, 0.65 mmol), 2,5-dimethoxyphenol **2** (200 mg, 1.3 mmol), potassium carbonate (180 mg) in DMF (10 mL) was refluxed under nitrogen atmosphere for 14 h. The reaction mixture was acidified with dil. hydrochloric acid and then extracted with chloroform (3x20 mL). The organic extract was washed thoroughly with 5% hydrochloric acid and with water. The dry solution was evaporated *in vacuo* to yield **9** (236 mg, 77%) which was purified by column chromatography on silica gel (chloroform), mp 121-123 °C; Anal. Calcd. for $C_{26}H_{30}O_8$: C, 66.37; H, 6.43. Found: C, 66.25; H, 6.35%; $\nu_{max}$:1500, 1250, 1220 and 1040: $\delta_H$: 3.73 (s, 6H, 2 x OMe), 3.80 (s, 6H, 2 x OMe), 4.38 (m, 8H, 1´- and 2´-H), 6.42 (dd, 2H, $J$ = 8.8 and 3 Hz, 4´-H), 6.61 (d, 3H, $J$ = 3 Hz, 6´-H), 6.80 (d, 2H, $J$ = 8.8 Hz, 3´-H), 6.96 (m, 4H, 3-, 4-, 5-, 6-H); $\delta_C$: 55.6, 56.8, 67.7, 68.0 102.6, 104.3, 113.2, 115.6, 122.0, 144.0, 149.0, 149.2, 154.3.

**Reaction of podand 3 with cerium ammoniun nitrate**

To a solution of compound **3** ( 100 mg, 0.264 mmol) in acetonitrile ( 6 mL) was added with stirring a solution of CAN ( 600 mg, 1.09 mmol) in water (6 mL). The mixture was mantaining with stirring for 30 min at rt and diluted with water. The mixture was extracted with chloroform (3x10 mL) and the dry organic layer evaporated under reduced pressure. The residue was cromatographied on preparative TLC (chloroform) and from the yellow band (Rf = 0.42) 1,8-*bis*(2,5-dimethoxy-4-nitrophenoxy)-3,6-dioxaoctane **11** was isolated as yellow solid (4 mg); mp 200-202 °C; HRMS Calcd. for $C_{20}H_{24}N_2O_{11}$: 468.13801. Found: 468.13864 : $\nu_{max}$: 1520, 1265 and 1025; $\delta_H$: 3.86 (s, 6H, 2 Hz, 1- and 5-H), 6.65 (s, 2H, 6'-H), 7.57 (s, 2H, 3'-H). Podand **11** was prepared in 64% yield by nitration of **3** ( 290 mg, 0.794 mmol) with concentrated nitric acid (0.1 mL) in acetic acid solution (1 mL) at 5-12°C for 1 h.

**Reaction of podand 9 with cerium ammoniun nitrate**

To a solution of compound **9** ( 100 mg, 0.212 mmol) in acetonitrile ( 5 mL) was added with stirring a solution of CAN ( mg, mmol) in water (4 mL). The mixture was mantaining with stirring for 30 min at rt and diluted with water. The mixture was extracted with chloroform (3x10 mL) and the dry organic layer evaporated under reduced pressure. The residue was cromatographied on preparative TLC and from the red-brown band compound **12** was isolated as a brown solid (16.15 mg, 24%); $\nu_{max}$ : 1620, 1600, 1510 and 1210; $\delta_H$: 3.77 (s, 3H, OMe), 3.84 (s, 3H, OMe), 3.89 (t, 2H, $J$ = 4 Hz, $CH_2$), 4.13 (t, 2H, $J$ = 4 Hz, $CH_2$), 4.40 (m, 4H, 2 x $CH_2$), 5.84 (s, 1H, vinylic), 6.35 (s, 1H, vinylic), 6.68 (s, 1H, Ar-H), 6.73 (s, 1H, Ar-H), 6.98 (m, 4H, Ar-H); $\delta_C$: 56.6, 56.9, 61.3, 67.9, 68.2, 71.8, 100.2, 102.6, 114.2, 114.9, 115.7, 122.2, 122.3, 129.5, 143.7, 148.9, 150.4, 151.8, 168.8, 179.2, 180.4. Compound **12** turned black-green upon exposure to atmosphere for 12-24 h. As a result of its instability, a satisfactory elemental analysis for this compound could not be obtained.

**Reaction of alizarin 13 and 2-chloroethanol**

A solution of **13** (300 mg, 1.25 mmol), potassium carbonate (180 mg) in DMF (5 mL) was magnetically stirred at rt for 3h under nitrogen atmosphere.

Chloroethanol (120 mg, 1.49 mmol) was added to the mixture a then refluxed under nitrogen atmosphere for 48 h. The resulting mixture was acidified with 12N hydrochloric acid and extracted with chloroform (3 x 20 mL). The organic extract was washed with 5% hydrochloric acid, water and dried over sodium sulfate. The solvent was evaporated off to afford a residue (0.143 mg) which was chromatographied on silica gel. Elution with chloroform gave angular quinone **15** ($R_f$=0.60 , 34 mg, 10%), m.p: 230-232 °C (lit.[12] 233-235 °C ), alizarin **13** ($R_f$ = 0.33, 15 mg) and anthraquinone **14** ($R_f$ = 0.16, 90 mg, 36%), mp 203-205 °C; HRMS Calcd. for $C_{16}H_{12}O_5$: 284.06847. Found: 284.06870 : $\nu_{max}$: 3576, 3552, 3422, 1666, 1634 1590, 1458, 1267; $\delta_H$: 3.92 (quint., 2H, *J* = 5 and 5 Hz, 2´-H), 4.25 (t, 2H, *J* = 5 Hz, 1´-H), 4.99 (t, 1H, *J* = 5 Hz, exchangeable with $D_2O$, OH), 7.41 (d, 1H, *J* = 8.5 Hz, 3-H), 7.82 (d, 1H, *J* = 8.5 Hz, 3-H), 7.92 (m, 2H, 6- and 7-H), 8.29 (m, 2H, 5- and 8-H), 12.91 (s, 1H, OH).

**Reaction of alizarin 13 with diethylene glycol ditosylate**

A suspension of alizarine **13** (200 mg, 0.833 mmol), diethylene glycol ditosylate, (157 mg, 0.416 mmol) potassium carbonate (120 mg) in DMF (3 mL) was refluxed for 26 h under nitrogen atmosphere. Work-up afforded a crude that was cromatographied on silica gel (chloroform) to gave alizarin **13** and 1,5-*bis*(1-hydroxy-8,10-dioxo-2-anthroxy)-3-oxapentane **16** ( 71 mg, 31%, Rf = 0.20); mp 238-241 °C; LRMS: 550.2 ($M^+$, 17%); $\nu_{max}$ : 3440, 1665, 1636, 1591; $\delta_H$: 4.09 (t, 4H, *J* = 4 Hz, 2- and 4-H), 4.36 (t, 4H, *J* = 4 Hz, 1- and 5-H), 7.19 (d, 2H, *J* = 8.5 Hz, 3'-H), 7.73 ( m, 6H, 4'-, 6'- and 7'-H), 8.36 (m, 4H, 5'- and 8'-H), 12.91 (s, 2H, OH); $\delta_C$: 69.1, 69.8, 116, 117.5, 120.8, 125.3, 126.8, 127.2, 133.2, 133.7, 133.9, 134.6, 152.9, 153.1, 181.2, 188.9.

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