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LETTERS

Reaction of benzoquinones and naphthoquinones with 1,8-diamino-3,6-dioxanonane and with 1,11-diamino-3,6,9-trioxaundecane

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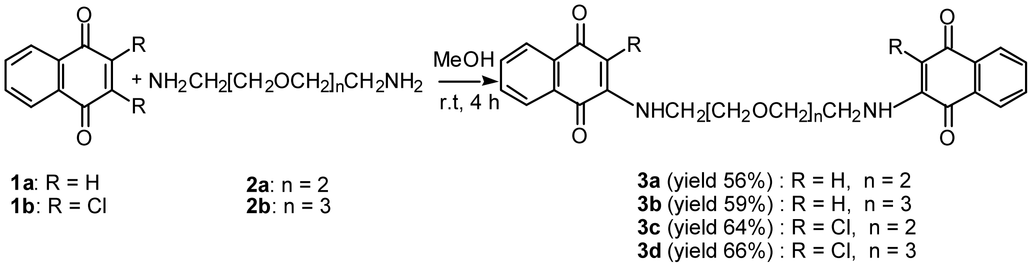
Abstract—Reaction of 1,4-naphthoquinone or 2,3-dichloro-1,4-naphthoquinone with α,ω-diamino-derivatives of poly(alkylenoxides) leads to the formation of α,ω-bis(quinonyl) amines. A similar reaction with chloranil, bromanil, dichlorodicyanobenzoquinone, *S*-phenylbenzoquinone and 1,4-benzoquinone itself, leads to the formation of quinoid crown ethers. © 2003 Published by Elsevier Science Ltd.

The reaction of polyoxypropylenediamines (Jeffamine D-400, D-2000 and others) with 1,4-benzoquinone leads to the formation of polyamine-benzoquinone polymers (PAQs) which upon coating on metals exhibit excellent corrosion resistance.[1–4] A shorter Jeffamine, the 1,11-diamino-3,6,9-trioxaundecane, reacts with *p*-fluoranil to form a macrocycle containing the difluoroquinone unit.[5] Such macrocyclic compounds bearing quinone rings, have attracted considerable attention.[6–10] The physical proximity of the electroactive quinone group to the ion-binding crown moiety, opens exciting possibilities, offering the ability to couple a redox reaction with ion binding properties. Host–guest complexes can be formed in which the reduced (hydroquinonic) form is a much stronger ligating donor than the neutral (quinonic) form. This property might be used to develop chromogenic or electrochemical methods for the detection or separation of a variety of metal cations. It is also well known that quinone bearing macrocycles, e.g. geldanamycins and ansamycins are among the most potent antibiotics and antitumour agents.[11,12] Quinone-containing crown ethers, represent a coupled system in which two mechanisms mutually influence each other, and hence might add to our understanding of the analogous biologically active compounds.

In the present communication we show that the reaction of polyoxyalkylene diamines with naphtho-



Scheme 1. Synthesis of bis-quinonopolyoxyalkylenediamines.

Keywords: quinones; bis-quinonylamines; crown ethers; polyoxyethylenediamines.

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quinones yields the appropriate *N*,*N*′-bis(quinonyl) amines, while the same reaction with various 1,4-benzoquinones, produces quinoid crown ethers.

As expected, 1,4-naphthoquinone (**1a**) or 2,3-dichloro-1,4-naphthoquinone (**1b**) reacted with triethyleneglycol diamine (**2a**) (Jeffamine-148) or with tetraethyleneglycol diamine (**2b**) (Jeffamine-192) yielding the appropriate *N*,*N*′-bis(quinonyl) amines **3a**–**d** in average to good yields (Scheme 1).

These facile reactions were performed at room temperature, in methanol, using (in the case of **1b**) 1 equiv. of Na_2CO_3. All analytical and spectroscopic data confirmed the bis-quinone structure and using ^{13}C NMR it was possible to distinguish between the carbons adjacent to the nitrogens ($\delta = 42$ ppm) and those in the proximity of the oxygens ($\delta = 70$ ppm).[13]

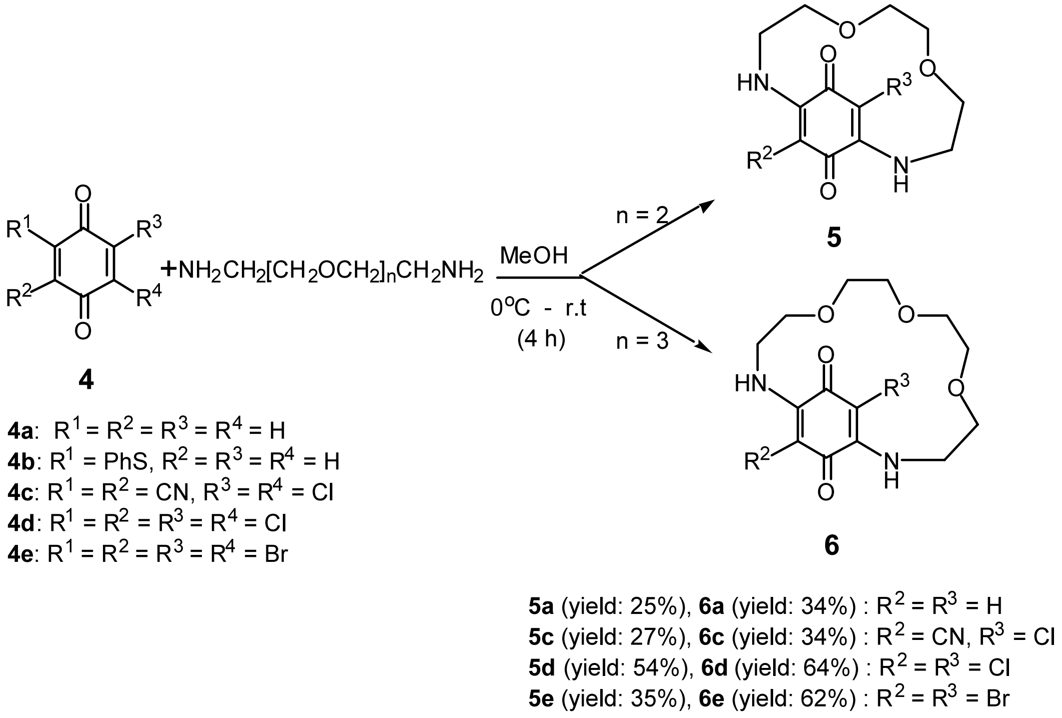
The parallel reaction of Jeffamine-192 with 1,4-benzoquinone **4a** resulted mainly in polymerization, however, the formation of a low molecular weight product (22% yield) was also observed. Isolation and identification proved that a cyclization reaction had taken place yielding the 2,5-disubstituted quinoid-crown ether **6a**. In order to extend the scope of this cyclization, and to improve the yields of the quinone containing macrocycles, we conducted the reaction of both Jeffamines-148 and 192 with various substituted 1,4-benzoquinones (Scheme 2).

Reacting benzoquinones bearing good leaving groups, e.g. tetrachlorobenzoquinone (**4d**) and tetrabromobenzoquinone (**4e**), with 2 equiv. of the Jeffamines, gave good yields (up to 64%) of the macrocycles. The reactions were performed under normal conditions, and no special techniques or high dilutions were needed. The polyoxyalkylenic nature of the Jeffamines seems to form a transition state with the quinone, which favors cyclization over dimerization (traces) and polymerization (15–20%).[14]

Reaction of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (**4c**) with the Jeffamines yielded similar macrocyclic quinones **5c** and **6c**. This result was unexpected since the cyano groups in DDQ are poor leaving groups, which are not substituted when reacted with normal amines. In the present case the polyoxyethylenic nature of the reactant and the conformation at the transition state might induce cyano group displacement. This ability of the Jeffamines to substitute poor leaving groups attached to the quinonic ring was also observed in the reaction with *S*-phenyl-1,4-benzoquinone **4b**. Jeffamine-192 gave the appropriate quinonic crown ether **6a** (yield 34%) after unexpected substitution of the thiophenoxy group.

Figure 1 shows the molecular structure of the macrocyclic benzoquinone **6a**.[15] It can be seen that the molecule has no symmetry, belongs to the $P2_1/c$ space group and the benzoquinone ring adopts a planar configuration.

The amidic nature of the NH groups can be seen clearly. Thus, the C(3)–C(4) and C(1)–C(6) distances (1.515 and 1.519 Å, respectively) are larger than those of the other two single bonds in the quinone ring C(3)–C(2) and C(5)–C(6) (1.400 and 1.413 Å, respectively). This reflects the resonance structure of **6a** and the charge distribution from N(1) and N(2) to the quinonic oxygens.



4a: $R^1 = R^2 = R^3 = R^4 = H$
4b: $R^1 = PhS$, $R^2 = R^3 = R^4 = H$
4c: $R^1 = R^2 = CN$, $R^3 = R^4 = Cl$
4d: $R^1 = R^2 = R^3 = R^4 = Cl$
4e: $R^1 = R^2 = R^3 = R^4 = Br$

5a (yield: 25%), **6a** (yield: 34%) : $R^2 = R^3 = H$
5c (yield: 27%), **6c** (yield: 34%) : $R^2 = CN$, $R^3 = Cl$
5d (yield: 54%), **6d** (yield: 64%) : $R^2 = R^3 = Cl$
5e (yield: 35%), **6e** (yield: 62%) : $R^2 = R^3 = Br$

Scheme 2. Synthesis of quinoid crown ethers.

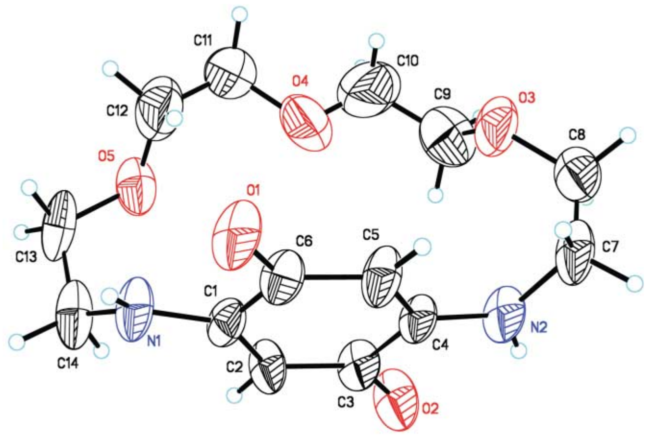


Figure 1. Single-crystal X-ray structure of benzoquinonodiaza crown ether-192 (**6a**).

A different behavior was observed with the macrocyclic quinone **5e** (see Fig. 2).[16] Here, the quinone ring, bears two bromine atoms and is bonded to a rather short chain (10 atoms). The striking difference is that in this molecule the quinone ring is non-planar. It adopts a boat-like, bent configuration with torsion angles of 18.6 and 24.5°.[17] It would appear that due to ring strain, the two ends of the Jeffamine, are unable to reach far enough and close the ring without distorting the quinone. Further investigations into the synthetic aspects of quinonic crown ethers are currently under way.

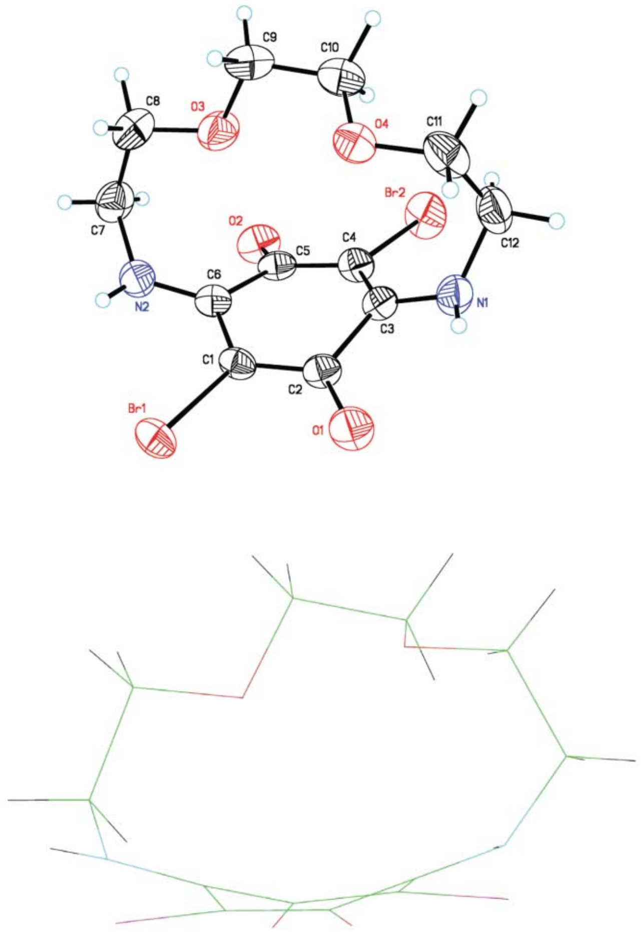


Figure 2. Single-crystal X-ray structure of dibromobenzoquinonodiaza crown ether-148 (**5e**). The lower view shows the boat-like configuration of the quinonic ring.

Acknowledgements

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13. *Selected data for **3a***: bright-orange crystals (56%); mp 150–152°C (from methanol); ^{1}H NMR (500 MHz, DMSO-d_6): δ 3.33 (t, 4H, $J=5.6$); 3.57 (bs, 4H); 3.63 (t, 4H, $J=5.6$); 5.70 (s, 2H); 7.26 (bt, 2H, $J=5.7$); 7.64 (dt, 2H, $J=1.5$, 7.5); 7.76 (dt, 2H, $J=1.5$, 7.5); 7.86 (ddd, 2H, $J=0.5$, 1.5, 7.5); 7.90 (ddd, 2H, $J=0.5$, 1.5, 7.5); ^{13}C NMR (500 MHz, DMSO-d_6): δ 181.4s, 148.4s, 134.8d, 133.1d, 132.1s, 130.3s, 125.9d, 125.3d, 99.8d, 69.7t, 67.7t, 41.8t; MS: 461 (MH$^+$), 460 (M$^+$); HRMS found: 460.1626; calcd for $C_{26}H_{24}N_2O_6$: 460.1634.
14. *Selected data for **6d***: dark-red crystals (64%); mp 193–195°C (from chloroform); ^{1}H NMR (500 MHz, CDCl$_3$): δ 3.48–3.52 (m, 8H); 3.60 (m, 4H); 3.71–3.80 (m, 2H); 4.42 (bs, 2H); 6.52 (bs, 2H); ^{13}C NMR: (200 MHz, CDCl$_3$): δ 173.6s, 148.5s, 103.3s, 70.93t, 70.80t, 43.51t; MS: 364(M$^+$), 329 (M$^+$–Cl); HRMS found: 364.0600; calcd for $C_{14}H_{18}Cl_2N_2O_5$: 364.0593.
15. *X-ray data for **6a***: $C_{14}H_{20}N_2O_5$, $M=296.32$, monoclinic, $a=7.581(10)$, $b=14.385$ (19), $c=14.464$ (18) Å, $U=1554$ (3) Å^3, space group $P2_1/c$, $Z=4$, $D_{\text{calcd}}=1.27$ Mg/m^3, μ(Mo Kα) $=0.097$ mm^{-1}. Crystal dimensions 0.32×0.35×

0.78 mm. Data were measured at 295 K on a standard Bruker SMART 6K CCD diffractometer [l(Mo Kα)] = 0.711069 Å, graphite monochromator. The structure was solved by direct methods and refined by least-squares in full-matrix approximation. Hydrogen atoms were placed to the calculated positions and were refined using the 'riding model' SHELXTL [Bruker AXS, 1998] software package for calculations and drawing. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

16. *X-ray data for **5e***: $C_{12}H_{14}Br_2N_2O_4$, $M = 410.07$, monoclinic, $a = 9.623(4)$, $b = 9.464(4)$, $c = 15.787(7)$ Å, $U = 1427.6(10)$ Å^3, space group $P2_1/c$, $Z = 4$, $D_{calcd} = 1.908$ Mg/m^3, μ(Mo Kα) = 5.692 mm^{-1}. Crystal dimensions 0.64×0.44×0.32 mm. Data were measured at 295 K on a standard Bruker SMART 6K CCD diffractometer with graphite monochromated Mo Kα radiation. The structure was solved by direct methods and refined by least-squares in full-matrix approximation. Hydrogen atoms were placed to the calculated positions and were refined using the 'riding model' SHELXTL [Bruker AXS, 1998] software package for calculations and drawing. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.
17. Crystallographic data (excluding structure factors) for the structures in this paper, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 203258 and 203259. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).