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Convenient synthesis of novel cyclophanes having plural hydroquinone or benzoquinone units from cyclic polyethers

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Abstract

This paper reports a facile way to prepare novel cyclophanes from cyclic polyethers (**1**). Cyclic polyethers (**1**) composed of functional methallyl 2,3-dimethylhydroquinone diether subunits were prepared by the reaction of 2,3-dimethylhydroquinone with methallyl dichloride. Cyclophanes having plural hydroquinone or benzoquinone units were obtained directly in high yields by the rearrangement and/or subsequent oxidation of the cyclic polyethers (**1**). © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: cyclophanes; hydroquinone units; benzoquinone units; Claisen rearrangement; oxidation.

A quinone–hydroquinone pair forms a redox system, and appears to play an important role in electrochemistry as well as in electron transfer during photosynthetic processes. Varieties of covalently linked porphyrin–quinone derivatives,[1] porphyrin–quinone cyclophanes,[2] and hydrogen-bonded complexes between porphyrin and quinone[3] have been prepared, and their photoinduced electron transfer was investigated as models of photosynthesis. Redox potentials are reported to be controlled by the structure of the quinone units.[4] In practice, the redox potentials for linear polymeric quinones or cyclic quinones differ from those of mono quinone derivatives due to different delocalization abilities and coulomb interaction energies of the unpaired electron over all the benzoquinone units.[4] Therefore, new cyclic quinones are quite attractive not only for the design of electron transfer systems, but also in host–guest chemistry. Some cyclic quinones have already been synthesized by the demethylation and subsequent oxidation of the corresponding *p*-dimethoxy-cyclophanes,[5] oxidation of the corresponding *p-tert*-butylcalix[4]arene[6] and several reaction steps from the corresponding calix[4]arene.[7] On the other hand, the molecular design of the starting material for a target compound is extremely important to find the best synthetic route in organic chemistry. The best synthetic route, especially when the starting material has many reacting sites, should be a minimum of reaction steps, and the selected reaction should have a good precedent of high yield without competing reactions. Recently, we have reported that cyclic

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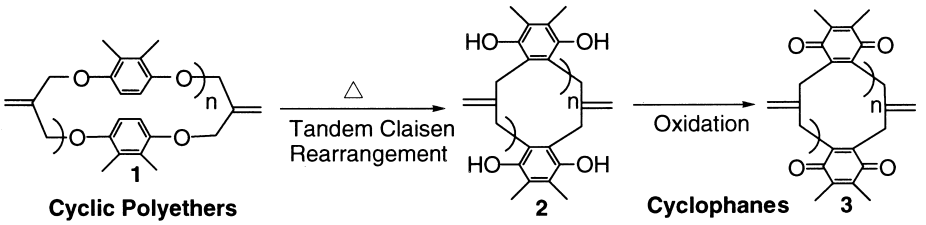
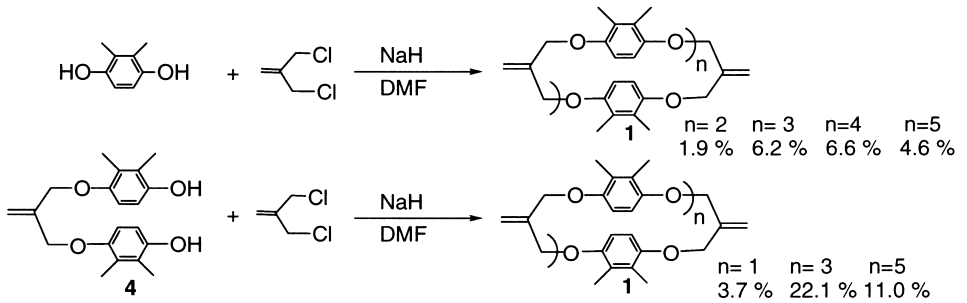
polyethers having methallyl diphenyl ether groups can be converted to the corresponding calixarene analogues[8] and crownophanes[9] via tandem (or double) Claisen rearrangement. These results enabled us to design new cyclic polyethers as precursors for novel cyclophanes having plural hydroquinone or benzoquinone units. In this paper, we report a facile way to synthesize novel cyclophanes from cyclic polyethers having methallyl 2,3-dimethylhydroquinone diether subunits via tandem Claisen rearrangement followed by oxidation (Scheme 1).



Scheme 1.

Cyclic polyethers (**1**) were prepared by the reaction of 2,3-dimethylhydroquinone with methallyl dichloride in the presence of sodium hydride according to the previously reported method.[10] The reaction method using **4** as the starting material instead of 2,3-dimethylhydroquinone turned out to be effective for preparing the cyclic polyethers, as shown in Scheme 2.[11]



Scheme 2.

The rearrangement of cyclic polyethers (**1**) has been examined under various conditions. The rearrangement of a dimer (**1-2**, $n=1$) does not proceed, and even that of a trimer (**1-3**, $n=2$) results in partial rearrangement, probably since their ring sizes decrease gradually with progress of the rearrangement. Although the rearrangement of a tetramer (**1-4**, $n=3$) in the bulk or in some solvent systems (decahydronaphthalene or dimethyl sulfoxide) was accompanied by intramolecular cyclization, quantitative rearrangement could be accomplished by using *N,N*-dimethylaniline as solvent, which seems to prevent the excessive intramolecular cyclization promoted by hydrogen bonding with the resulting hydroquinone units.[12] Similarly, the quantitative rearrangement of a hexamer (**1-6**, $n=5$) was also confirmed by ^{1}H NMR, and the product could be isolated in 88% yield (Fig. 1A).[13] The oxidation reaction of **2** has been studied, and the hydroquinone units of **2** were rapidly oxidized with mild oxidants such as benzoquinone derivatives (chloranil, 2,5-dichlorobenzoquinone, *p*-benzoquinone) to yield quantitatively cyclophanes

(**3**) having benzoquinone units. Fig. 1 shows the ^{1}H NMR spectra of **2-6** and the mixture of **2-6** with 2,5-dichlorobenzoquinone (6.8 equiv.). In the ^{1}H NMR spectra of **2-6** with 2,5-dichlorobenzoquinone, the signals of OH protons of **2-6** completely disappeared, and signals assignable to **3-6** appeared at 4.47 and 3.09 ppm, respectively. Signals of 2,5-dichlorobenzoquinone and the corresponding hydroquinone appeared at 6.89 and 7.47 ppm, respectively.

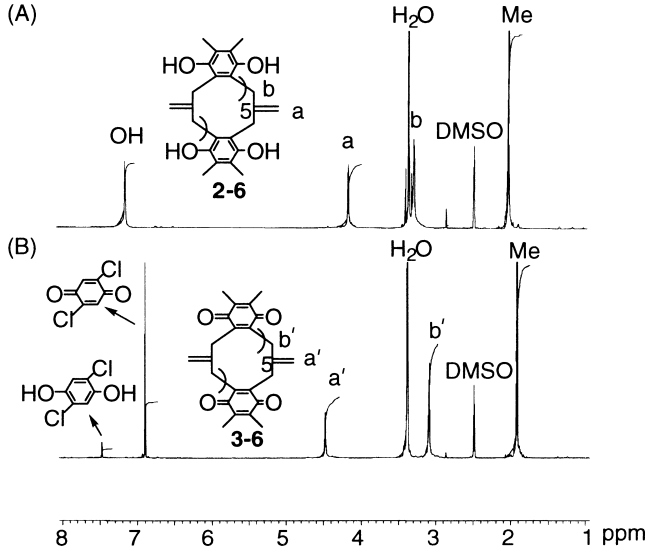


Figure 1. ^{1}H NMR spectra (500 MHz, DMSO-d_6) of **2-6** (A) and **2-6** with 2,5-dichlorobenzoquinone (6.8 equiv.) (B)

The solubility of the tetramer (**3-4**) is poor for common solvents but good only for CS_2, while the hexamer (**3-6**) has good solubility. Furthermore, one-pot synthesis of **3-6** from **1-6** via the rearrangement followed by the oxidation was carried out to give **3-6** in 94.1% overall yield. It is noteworthy that the reactions of compounds containing up to 12 reaction sites could be controlled completely through two reaction steps by selecting the appropriate starting material and synthetic route.

In conclusion, novel cyclic polyethers have been synthesized from 2,3-dimethylhydroquinone and methallyl dichloride. These cyclic polyethers proved to be quite useful precursors for novel cyclophanes having plural hydroquinone or benzoquinone units which could lead to new redox and electron transfer systems. This new synthetic scheme may be applicable to a general preparation method for hydroquinone or benzoquinone derivatives.

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11. Dimer **1-2** ($n=1$): colorless crystals, mp 217–219°C; ^{1}H NMR (500 MHz, $CDCl_3$) $\delta=2.10$, 4.49, 5.26, 6.15 ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 12.87, 69.98, 111.12, 117.89 126.96, 143.48, 151.24 ppm. Mass calcd (found) for $C_{24}H_{28}O_4$: 380.48 (380). Trimer **1-3** ($n=2$): colorless crystals, mp 126–128°C; ^{1}H NMR (500 MHz, $CDCl_3$) $\delta=2.14$, 4.56, 5.30, 6.48 ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 12.32, 70.02,110.37, 114.37, 127.28, 142.54, 151.25 ppm. Mass calcd (found) for $C_{36}H_{42}O_6$: 570.73 (570). Tetramer **1-4** ($n=3$): colorless crystals, mp 194–196°C; ^{1}H NMR (500 MHz, $CDCl_3$) $\delta=2.11$, 4.57, 5.37, 6.60 ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 12.59, 69.95, 109.72, 115.29, 123.75, 142.24, 151.42 ppm. Mass calcd (found) for $C_{48}H_{56}O_8$: 760.97 (760). Pentamer **1-5** ($n=4$): colorless crystals, mp 135–138°C; ^{1}H NMR (500 MHz, $CDCl_3$) $\delta=2.16$, 4.58, 5.39, 6.64 ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 12.22, 69.61, 109.27, 114.53, 127.06, 141.58, 151.01 ppm. Mass calcd (found) for $C_{60}H_{70}O_{10}$: 951.21 (950). Hexamer **1-6** ($n=5$): colorless crystals, mp 163–165°C; ^{1}H NMR (500 MHz, $CDCl_3$) $\delta=2.17$, 4.58, 5.38, 6.64 ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 12.63, 69.99, 109.68, 114.80, 127.48, 141.95, 151.39 ppm. Mass calcd (found) for $C_{72}H_{84}O_{12}$: 1141.45 (1141).
12. Rearrangement, typical procedure: compound **1-4** (0.16 g, 0.21 mmol) was dissolved in *N,N*-dimethylaniline (2 ml). After oxygen was removed, the solution was stirred under an argon atmosphere at 190°C for 3.5 h. After the reaction mixture was poured into the $CHCl_3$:hexane mixed solvent (volume ratio 1:1), **2-4** (138 mg, 86.2%) was separated by filtration. Tetramer **2-4** ($n=3$): colorless crystals, mp > 240°C (decomp.); ^{1}H NMR (500 MHz, DMSO-d_6) $\delta=2.06$, 3.33, 3.98, 7.19 ppm; ^{13}C NMR (125 MHz, DMSO-d_6) 12.80, 33.67, 106.69, 121.77 122.03, 145.67, 146.78 ppm. Mass calcd (found) for $C_{48}H_{56}O_8$: 760.97 (760). Pentamer **2-5** ($n=4$): colorless crystals, mp 162–164°C; yield 80.5%; ^{1}H NMR (500 MHz, DMSO-d_6) $\delta=2.07$, 3.32, 4.19, 7.20 ppm; ^{13}C NMR (125 MHz, DMSO-d_6) 14.31, 31.32, 108.61, 122.41, 124.18, 146.31, 147.74 ppm. Mass calcd (found) for $C_{60}H_{70}O_{10}$: 951.21 (948). Hexamer **2-6** ($n=5$): colorless crystals, mp 125–128°C; yield 88.0%; ^{1}H NMR (500 MHz, DMSO-d_6) $\delta=2.04$, 3.35, 4.15, 7.11 ppm; ^{13}C NMR (125 MHz, DMSO-d_6) 13.1, 33.62, 108.33, 121.87, 123.90, 145.96, 147.42 ppm. Mass calcd (found) for $C_{72}H_{84}O_{12}$: 1141.45 (1141).
13. Oxidation reaction, typical procedure: to a solution of **2-6** (0.118 mg, 0.093 mmol) in $CHCl_3$ (15 ml) was added 2,5-dichlorobenzoquinone (8 equiv.). The reaction mixture was stirred for 30 min at room temperature. After the solvent was removed, **3-6** (106 mg, 89.8%) was isolated by preparative HPLC eluted with $CHCl_3$. Tetramer **3-4** ($n=3$): yellow crystals, mp > 240°C(decomp.); yield 85%; ^{1}H NMR (500 MHz, CD_2Cl_2) $\delta=2.03$, 3.16, 4.48 ppm; ^{13}C NMR (125 MHz, CD_2Cl_2) 12.96, 34.24, 109.17, 141.52 141.65, 143.24, 187.06 ppm. Mass calcd (found) for $C_{48}H_{48}O_8$: 752.90 (753). Pentamer **3-5** ($n=4$): yellow crystals, mp > 240°C (decomp.); yield 81%; ^{1}H NMR (500 MHz, $CDCl_3$) $\delta=2.02$, 3.20, 4.54 ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 12.50, 33.09, 110.83, 140.87, 142.73, 142.77, 186.56 ppm. Mass calcd (found) for $C_{60}H_{60}O_{10}$: 941.13 (942, M+1). Hexamer **3-6** ($n=5$): yellow crystals, mp > 240°C (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$) $\delta=2.01$, 3.21, 4.55 ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 12.89, 33.34, 111.69, 141.18, 143.21, 143.28, 186.97 ppm. Mass calcd (found) for $C_{72}H_{72}O_{12}$: 1129.36 (1131, M+2).