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EFFICIENT SYNTHESIS AND CRYSTAL STRUCTURE OF NEW 1,4-ANSA-ANTHRAQUINONE

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Abstract – An ansa-anthraquinone with decamethylene-dioxa spacer was prepared by two-step or direct cyclization. The solid state structure was characterized by single crystal X-Ray diffraction analysis.

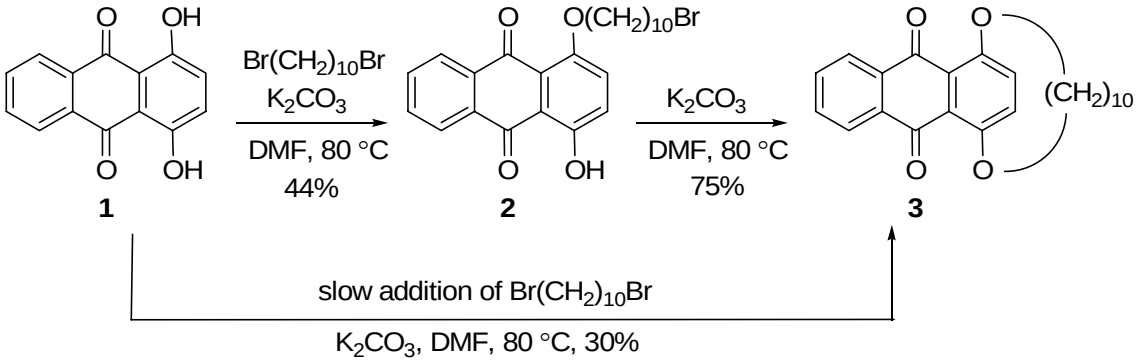
INTRODUCTION

Ansa-compounds, [n]paracyclophanes, have been of interest because of their unique structure and functionality.[1-8] Although their studies concerning benzene,[1-5] naphtalene,[6] and anthracene[6] nuclei were reported, anthraquinone has not been used as a key skeleton for synthesis of ansa compound. Anthraquinone is not only a fascinating chromophore due to its high fluorescence activity but also an important electrochemical redox system, furthermore anthraquinone is an valuable material for anthracene synthesis.[9] We thought that the introduction of ansa-bridge into anthraquinone will construct a new functionalized redox aromatic in a solution and that the ansa-bridge can behave like skipping rope.[8] In this paper, a new decamethylene-bridge dioxa-paracyclophane possessing anthraquinone (**3**) (Scheme 1), whose bridge-length was anticipated to give rise to free rope-skipping similarly to decamethylene-bridge dioxa-benzene,[1] was synthesized and the procedure was optimized. The molecule (**3**) was characterized by single-crystal X-Ray diffraction analysis.

RESULTS AND DISCUSSION

Our synthesis was performed as illustrated in Scheme 1. First, two-step Williamson ether synthesis from commercially available quinizarin (**1**: 1,4-dihydroxy-9,10-anthraquinone) was used. Reaction of **1** (0.16 M) with 2 molar amounts of 1,10-dibromodecane in the presence of K_2CO_3 in DMF at 80 ˚C gave mono-ether (**2**) in 44% yield. Then slow addition of **2** (6.7×10^{-3}M) into a solution of K_2CO_3 in DMF at 80 ˚C accomplished cyclization to afford the expected ansa-anthraquinone (**3**) in 75% yield. Next we

surveyed the direct synthesis of **3** from **1** and an equimolar amount of 1,10-dibromodecane. Very slow addition of 1,10-dibromodecane to **1** (0.01 M) in DMF and longer stirring led to the isolation of **3** in 30% yield. The yield was comparable to that obtained with the two-step synthesis. Both routes were practical for the isolation of **3**.



Scheme 1

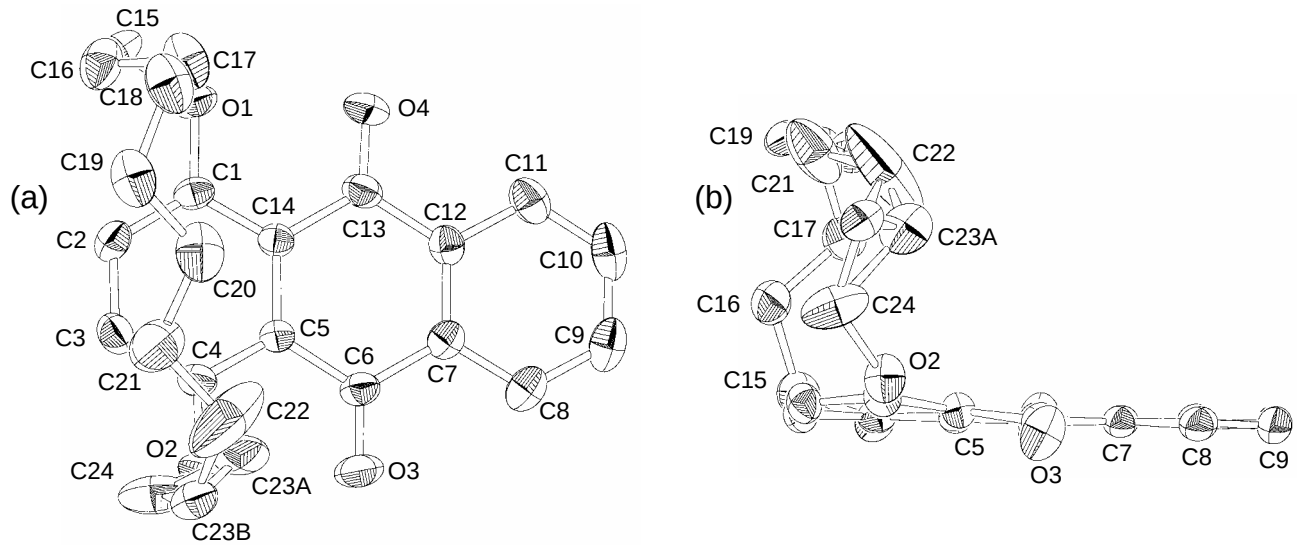


Figure 1. Molecular structure of **3** viewed from (a) the top and (b) the side directions

The X-Ray crystallographic analysis of **3** reveals the structural features of the molecule in the solid state (Figure 1). The anthraquinone moiety is slightly deformed from planarity. Thus the side oxygen atoms are not on the plane of the aromatic ring due to the steric repulsion between them. Short intramolecular distances were observed between the peripheral oxygen atoms (O1···O4 and O2···O3 are 2.57 and 2.62 Å, respectively), which are much shorter than the sum of the van der Waals radii. Further, the anthraquinone ring is not planar but takes a somewhat twisted conformation. The displacements of atoms O1, O2, O3, O4, C3, C4 , and C5 relative to the plane of the benzene fragment C7-C12 are 0.08, -0.60, 0.20, 0.08, -0.17, -0.30, and -0.12 Å, respectively. Another feature is the existence of the disorder of one methylene in the bridge, in which methylene C23 shows two atomic positions with occupancy factors for C23A and C23B of 0.5, respectively.

In the ^{1}H NMR spectrum of **3** in $CDCl_3$ at room temperature, the bridge proton signals except the methylene protons adjacent to the oxygen atom were observed in the range of 0.70-1.75 ppm, whose values suggest little effect of the ring current of the aromatic ring on the bridge, namely rope-skipping in the solution. Moreover, two methylene protons adjacent to the oxygen atom appeared as broad singlets at 4.37 and 4.54 ppm, indicating the anisotropic effect of the carbonyl oxygen atoms.

To survey the optical properties of **3**, UV-vis spectral measurements were carried out. For comparison, a non-ansa 1,4-dipropoxy-9,10-anthraquinone[9] (**4**) was also examined. The absorption maxima of **3** and **4** were observed at 409 (log ε 3.64) and 420 (log ε 3.73) nm, respectively. The blue shift of **3** compared to **4** may be ascribed to non-planarity of anthraquinone moiety in solution.

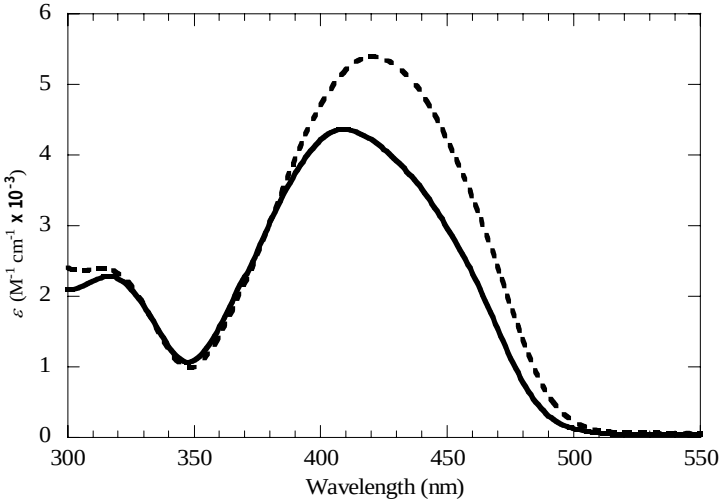


Figure 2. UV-vis spectra of **3** (solid line) and **4** (dotted line) in $CHCl_3$

In summary, we have successfully established an efficient synthetic method for the preparation of 1,4-ansa-anthraquinone by two-step or direct cyclization. The molecular structure was confirmed by X-Ray analysis unambiguously.

EXPERIMENTAL

Melting points were measured on a Yanaco Melting Point apparatus and are uncorrected. Elemental analysis was carried out on a Yanaco MT-5 CHN corder. IR spectra were measured on a Shimadzu FTIR-8400 spectrometer. ^{1}H and ^{13}C spectra were recorded on a Bruker-Biospin DRX500 FT spectrometer at 500 and 126 MHz, respectively. UV-vis spectra were taken on a HITACHI U3500. DMF was distilled from CaH_2. All other chemicals were commercially available and were used as received.

Two-step Procedure for the Synthesis of 3

A mixture of quinizarin (963 mg, 4.01 mmol), 1,10-dibromodecane (2.42 g, 8.06 mmol), K_2CO_3 (553 mg, 4.00 mmol) in DMF (25 mL) was stirred at 80 ˚C for 3 h. After cooling to rt, water was added, and the mixture was extracted with $CHCl_3$ and the organic phase was washed with brine. The combined extracts

were dried over Na_2SO_4, and then the solvent was evaporated. Column chromatography on silica gel ($CHCl_3$-hexane, 1:1) followed by washing with hexane gave mono-ether (**2**) as an orange solid. Yield: 811 mg (44%). mp 77-79 ˚C. IR(KBr) ν 2916.2, 1666.4, 1645.0, 1597.2, 1467.7, 1427.2, 1352.0, 1283.2, 1255.6, 1238.2, 1039.6, 783.0 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.27-1.45 (m, 10H), 1.53-1.60 (m, 2H), 1.83-1.96 (m, 4H), 3.41 (t, J = 6.8 Hz, 2H), 4.13 (t, J = 6.7 Hz, 2H), 7.31 (d, J = 9.4 Hz, 1H), 7.40 (d, J = 9.4 Hz, 1H), 7.75-7.82 (m, 2H), 8.29 (t, J = 8.3 Hz, 2H), 13.05 (s, 1H, OH). ^{13}C NMR ($CDCl_3$) δ 25.88, 28.16, 28.74, 29.29, 29.33, 29.35, 29.40, 32.81, 34.11, 70.43, 115.90, 119.45, 125.46, 126.26, 126.34, 127.34, 132.28, 133.20, 134.72, 135.07, 153.93, 157.44, 181.45, 188.99. Anal. Calcd for $C_{24}H_{27}O_4Br$: C, 62.75; H, 5.92%. Found: C, 62.91; H, 5.97%.

To a suspension of K_2CO_3 (416 mg, 3.01 mmol) in DMF (15mL), a solution of mono-ether (**2**) (139 mg, 0.30 mmol) in DMF (30 mL) was added dropwise at 80 ˚C over 2.5 h. The mixture was stirred at 80 ˚C for 6 h, and allowed to be cooled to rt. Water was added, and the mixture was extracted with $CHCl_3$, the organic phase was washed with brine and dried over Na_2SO_4. After removal of the solvent, column chromatography on silica gel ($CHCl_3$-AcOEt, 5:1) afforded ansa-anthraquinone (**3**) as a yellow solid. Yield: 86 mg (75%). mp 162-164 ˚C. IR(KBr) ν 2933.5, 1666.4, 1360.8, 1249.8 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.70-1.32 (m, 12H), 1.69-1.75 (m, 4H), 4.34 (brs, 2H), 4.54 (brs, 2H), 7.43 (s, 2H), 7.73 (dd, J = 3.2, 5.7 Hz, 2H), 8.20 (dd, J = 3.2, 5.7 Hz, 2H). ^{13}C NMR ($CDCl_3$) δ 23.75, 26.68, 27.32, 28.59, 71.10, 124.49, 126.57, 126.71, 133.39, 134.23, 154.88, 182.77. Anal. Calcd for $C_{24}H_{26}O_4$: C, 76.17; H, 6.92%. Found: C, 76.15; H, 7.04%.

Direct Procedure for the Synthesis of 3

To a mixture of quinizarin (241 mg, 1.00 mmol) and K_2CO_3 (692 mg, 5.00 mmol) in DMF (100 mL), a solution of 1,10-dibromodecane (302 mg, 1.00 mmol) in DMF (10 mL) was added at 80 ˚C over 9.5 h, and then the mixture was stirred at 80 ˚C for 12.5 h and cooled to rt. Water was added, and the mixture was extracted with $CHCl_3$, and the organic phase was washed with brine and dried over Na_2SO_4. After evaporation of the solvent, column chromatography on silica gel ($CHCl_3$-AcOEt, 5:1) afforded above stated ansa-anthraquinone (**3**). Yield: 112 mg (30%).

X-Ray Crystal Structure Analysis of 3

Crystal data: $C_{24}H_{26}O_4$, Fw = 378.47, yellow prism, monoclinic, space group $P2_1/a$, a = 11.679(1), b = 15.249(1), c = 11.812(1) Å, β = 114.891(5)˚, V = 1908.2(4) $Å^3$, Z = 4, D_{calcd} = 1.317 g cm^{-3}, T = 173 K, R = 0.087 [I > 2sigma(I)], R_w = 0.182 (all data), 15207 reflections measured, 14805 unique, R_{int} = 0.036. X-ray data were collected on a Rigaku/MERCURY CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71070 Å). The structure was solved by a direct method using SIR92.[10] The positions of C23A and C23B were found from Fourier maps. The non-hydrogen atoms were refined

anisotropically by full-matrix least-squares. The positions of hydrogen atoms were calculated geometrically. All of the calculations were performed using the teXsan program package.[11] The crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as CCDC614155. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44-1223-336-033; e-mail: deposit@ccdc.ca.ac.uk].

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