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Synthesis and structure of sterically hindered *o*-benzoquinone carboxylic acid

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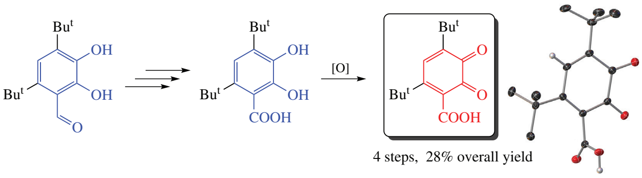
2,4-Di-*tert*-butyl-5,6-dioxocyclohexa-1,3-diene-1-carboxylic acid, an oxidized analogue of sterically hindered pyrocatechuic acid, was obtained from 4,6-di-*tert*-butyl-2,3-dihydroxybenzaldehyde in four stages. The electrochemical reduction of this compound proceeds in two stages: the first reduction wave (E_{red1} = –0.24 V) is irreversible, while the second stage is partially reversible ($E_{1/2,\mathrm{red2}}$ = –0.65 V). The molecular structure of the *o*-quinone carboxylic acid in the crystalline state was comfirmed by single-crystal X-ray analysis.

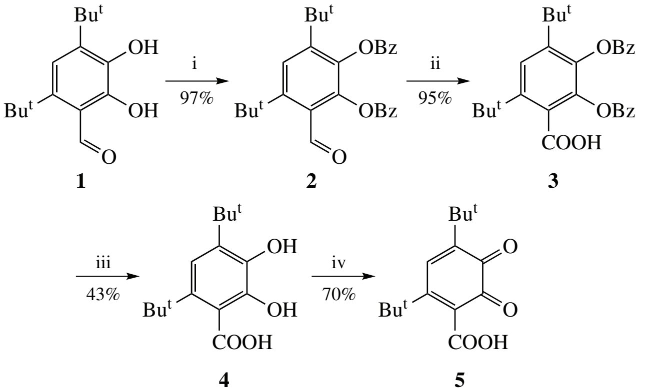


4 steps, 28% overall yield

Keywords: catechol, *o*-quinone, pyrocatechuic acid, oxidation, X-ray, cyclic voltammetry.

Pyrocatechuic (2,3-dihydroxybenzoic) acid and its derivatives are represented widely in the chemistry of biologically active compounds (siderophores and antioxidants),[1–6] as well as ligands for supramolecular[7–12] and coordination chemistry.[13–16] In all studies, these compounds are represented in the reduced (catecholic) form while highly reactive oxidized forms (semiquinone and quinone) have not been isolated.[17–19] It is known that the oxidized form of catechols is stabilized by sterically hindered substituents (*e.g*., *tert*-butyl groups), so such derivatives can be obtained.[20–23] In the present work, we report on the synthesis of sterically hindered derivative of pyrocatechuic acid as well as its corresponding *o*-benzoquinone carboxylic acid.

4,6-Di-*tert*-butyl-2,3-dihydroxybenzaldehyde **1**, a well-known precursor for the synthesis of new sterically hindered catechols and quinones,[24–32] was used in this work as the starting material. Direct oxidation of its aldehyde group into the carboxy one is not selective and is accompanied by oxidation reactions of the catechol fragment. Therefore, the catechol fragment was protected with ester groups at the first stage of the synthesis (Scheme 1). The resulting compound **2** was oxidized into acid **3** in a two-phase DCM–H_2O system at room temperature with $NaClO_2$. The protective groups in compound **3** were removed with hydrazine hydrate, which additionally prevented the oxidation of acid **4** with atmospheric oxygen. Oxidation of compound **4** to *o*-quinone **5** was carried out in an acidic medium (HNO_3 in AcOH).



Scheme 1 *Reagents and conditions*: i, PhC(O)Cl, Et_3N, CH_2Cl_2, 0 °C; ii, $NaClO_2$, H_2NSO_3H, CH_2Cl_2, room temperature; iii, $N_2H_4\cdot H_2O$, H^+, MeOH, 60 °C; iv, HNO_3, AcOH, room temperature.

The overall yield of *o*-quinone carboxylic acid **5** from catechol carbaldehyde **1** was 28% in four stages. Compound **5** is well-solubile in diethyl ether, acetic acid, and hexane but it is poorly water-soluble at pH < 6. All compounds obtained were characterized by IR, ^{1}H, ^{13}C NMR spectroscopy and elemental analysis. The *o*-quinone carboxylic acid **5** was characterized by X-ray structural analysis and cyclic voltammetry.

The molecular structure of *o*-quinone **5** is shown in Figure 1. The alternation of double and single bonds in the ring characteristic of *o*-quinones is observed in compound **5** in accordance with X-ray diffraction data.[†] The carboxy group is orthogonally (~83°) arranged relative to the plane of the quinone ring and is not conjugated to it.

[†] The crystals suitable for X-ray analysis were grown from a mixture of hexane and diethyl ether.

Crystal data for **5**. $C_{15}H_{20}O_4$, M = 264.31, space group $P2(1)/c$, 100 K, a = 12.8317(5), b = 10.0684(5) and c = 11.5712(5) Å, β = 104.932(4)°, Z = 4, V = 1444.46(11) Å^3, d_{calc} = 1.215 g cm^{-3}, $F(000)$ = 568. Red prism-shaped single crystal with dimensions 0.33×0.16×0.10 mm was selected and intensities of 28716 reflections were measured using an Agilent Xcalibur E diffractometer (ω-scans, λ[MoKα] = 0.71073 Å, μ = 0.087 mm^{-1}, $2\theta_{\max}$ = 61.01°). After merging of equivalents and absorption correction, 4413 independent reflections (R_{int} = 0.0499) were used for the structure solution and refinement. Final R factors: R_1 = 0.0412

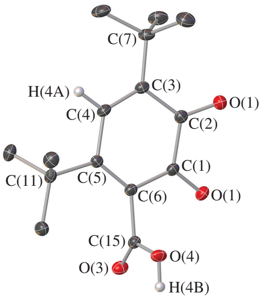


Figure 1 Molecular structure of compound **5**. Hydrogen atoms are not shown except for H(4A) and H(4B). Selected bond lengths (Å) and angles (°): C(1)–O(1) 1.2178(12), C(2)–O(2) 1.2199(13), C(15)–O(3) 1.2064(13), C(15)–O(4) 1.3302(13), O(1)–C(1)–C(6) 122.1(1), O(1)–C(1)–C(2) 118.1(1), O(2)–C(2)–C(3) 125.4(1), O(2)–C(2)–C(1) 117.2(1), O(3)–C(15)–O(4) 125.1(1).

The O(2)···H(4B) 2.02 Å and O (1)···H(4B) 2.31 Å distances are less than the sum of the van der Waals radii, which indicates the formation of hydrogen bonds in the crystal. Thus, a chain structure is formed in the crystal due to the formation of hydrogen bonds of the carboxyl group of one molecule with the oxygen atoms of the *o*-quinone of the neighboring one (Figure 2). Steric repulsion between the *tert*-butyl substituent and the carboxy group can also be noted. This is expressed in a significant deviation of the angles C(5)–C(6)–C(15) [130.1(1)°] and C(6)–C(5)–C(11) [126.9(1)°] from 120°.

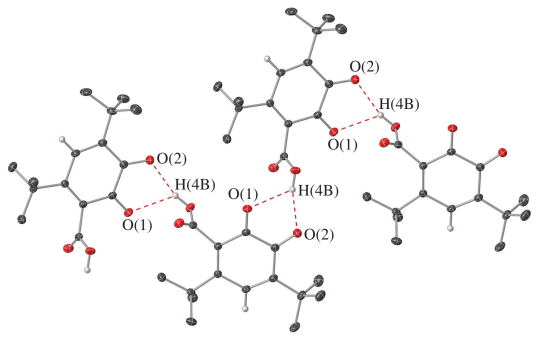


Figure 2 Chain structure of molecules **5** in the crystal.

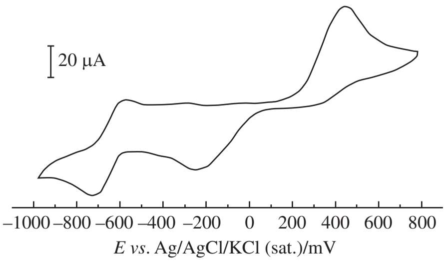
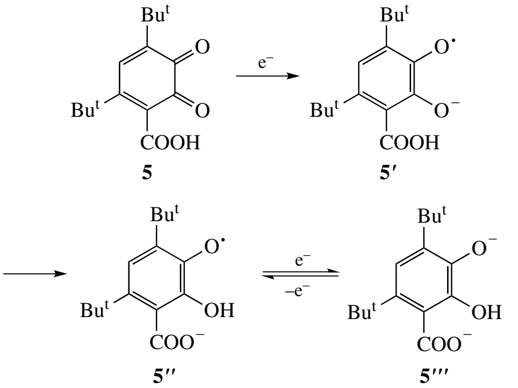


Figure 3 CV curve of compound **5** in the range from –1.0 to 0.8 V [100 mV s^{-1}, MeCN, $C = 5\times10^{-3}$ M, Ar, 0.1 M Bu$_4$NClO$_4$ relative to Ag/AgCl/KCl (sat.)].



Scheme 2

The cyclic voltammogram of compound **5** (Figure 3) is not typical for substituted 3,5-di-*tert*-butyl-*o*-benzoquinones. Typical CV curves of *o*-quinones are characterized by the first reversible reduction potential (Q/SQ$^-$ transition), while the second is an electrochemically irreversible process (the SQ$^-$/Cat^{2-} transition is accompanied by the protonation of the catecholate dianion).[33] As for compound **5**, the opposite picture is observed, namely, the first reduction wave ($E_{\text{red1}} = -0.24$ V) is irreversible, while the second stage is partially reversible ($E_{1/2,\text{ red2}} = -0.65$ V). The second oxidation wave is observed at $E_{\text{ox2}} = 0.44$ V. These facts can be explained by the proposed scheme of electrochemical transformations of quinone **5** (Scheme 2). In the first stage, radical anion **5′** is formed upon the reduction of quinone **5** (electrode stage) and transformed to phenoxyl radical **5″** by a rapid proton transfer (chemical stage). Further reduction of phenoxyl radical **5″** is reversible and leads to the stable di-reduced dianionic form **5‴**.

In conclusion, *o*-quinone carboxylic acid, an oxidized form of sterically hindered pyrocatechuic acid, was obtained in four simple steps from available 4,6-di-*tert*-butyl-2,3-dihydroxybenzaldehyde in 28% overall yield. This compound seems promising for coordination chemistry as redox-active ligand and for polymer chemistry as the photoinitiator of free radical polymerization.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.03.042.

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The intensity data were integrated by CrysAlisPro[34] program. SCALE3 ABSPACK [35] was used to perform area-detector scaling and absorption corrections. The structure was solved by direct method with a dual-space algorithm using SHELXT program[36] and was refined by the full-matrix technique on F^2 using SHELXTL[37] package. All non-hydrogen atoms were refined anisotropically. The H atoms were placed in the calculated positions and refined in the 'riding model' except for the H(4B) atom located and refined isotropically from the difference Fourier synthesis of the electron density.

CCDC 2050641 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

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