ChemPubSoc Europe

DOI: 10.1002/ejoc.201600616

EurJOC European Journal of Organic Chemistry

Full Paper

Hydroquinone Synthesis

Biomass-Based and Oxidant-Free Preparation of Hydroquinone from Quinic Acid

Benedicta Assoah,[a] Luis F. Veiros,[b] Carlos A. M. Afonso,[c] and Nuno R. Candeias*[a]

Abstract: A biomass-based route to the preparation of hydroquinone starting from the renewable starting material quinic acid is described. Amberlyst-15 in the dry form promoted the one-step formation of hydroquinone from quinic acid in toluene without any oxidants or metal catalysts in 72 % yield. Several acidic polymer-based resins and organic acids as promoters as well as a variety of reaction conditions were screened including temperature, concentration and low- and high-boiling-point solvents. A 1:4 (w/w) ratio of quinic acid/Amberlyst-15 was determined to be optimal to promote hydroquinone formation with only traces of a dimeric side-product. A mechanism has been proposed based on the decarbonylation of protonated quino-1,5-lactone that is supported by experimental and computational calculation data.

Introduction

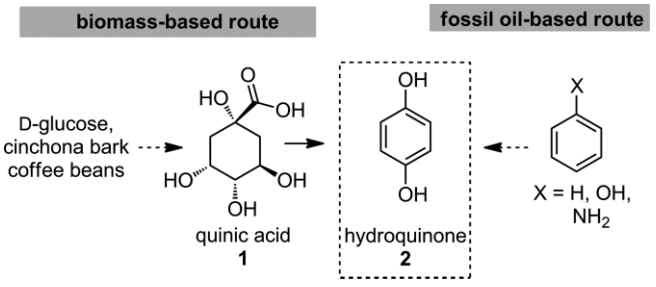
The chemical industry has made enormous efforts in the last decades to minimise waste and use less toxic and/or hazardous reagents to develop safer and greener processes. However, most of the raw materials used in the chemical industry are generally obtained from fossil resources totalling 10 % of the crude oil consumption.[1] To accomplish sustainable methods for the production of commodity chemicals and liquid fuels, non-renewable fossil resources (crude oil, coal and natural gas) should be replaced by sustainable feedstocks. Despite the intense interest and the methods developed for the large-scale industrial conversion of biomass into chemicals and materials in the second half of the 19th century, such investments declined in the 20th century due to the much cheaper products synthesised by the now conventional routes from abundantly available fossil resources.[2] Fossil raw materials are irrevocably decreasing and the environmental consciousness of the chemical industry and the regulatory authorities has led to enormous research activity in the last decade to progressively shift to renewable feedstocks.[3] The selective defunctionalisation of highly functionalised molecules derived from renewable feedstocks is probably the biggest challenge in such a shift, considering that sugars and polyol platforms can be highly exploited.[4] However, the production of aromatic compounds continues to be highly dependent on non-renewable fossil feedstocks. Despite the enormous achievements in the depolymerisation of lignin, the only renewable source of high-volume aromatic compounds,[5] the industrial application of any of the reported methods has not yet been achieved.

Hydroquinone is prepared industrially by the hydroperoxidation of *p*-diisopropylbenzene, the hydroxylation of phenol and the oxidation of aniline. The world production of hydroquinone is 40000–50000 tons a year and it is mainly used in the rubber industry, as monomer inhibitors, dyes and pigments and antioxidants as well as in agricultural and photographic applications.[6] It is mostly used as a water-soluble reducing agent in photography film development and in the rubber industry for the production of anti-oxidants and anti-ozonants. It is also used as an inhibitor of acrylic acid, methyl methacrylate, cyanoacrylate and other monomers commonly used in adhesives, glue and other types of bonding applications and in cosmetic applications in skin-whitening compositions.

The preparation of hydroquinone from non-fossil sources has been reported by Frost and co-workers since the seminal work of Woskresensky[7] on the isolation of hydroquinone by the dry distillation of quinic acid (**1**, Scheme 1). Frost reported the preparation of hydroquinone from glucose in two enzyme-catalysed steps and two chemical steps via 2-deoxy-*scyllo*-inosose synthase.[8] The construction of a transgenic *Escherichia coli* strain able to synthesise quinic acid from glucose under shake-flask conditions was coupled with the oxidation of the obtained quinic acid with stoichiometric amounts of MnO_2 to hydroquinone.[9] Other oxidative systems such as NaOCl, $(NH_4)_2Ce_2(SO_4)_3$, V_2O_5 and $K_2S_2O_8$ in the presence of catalytic amounts of Ag_3PO_4 have been reported to induce the same transformation in up to 91 % yield.[10] Quinic acid[11] is readily available from the bark of the cinchona tree[12] as a side-product during the extraction

[a] *Department of Chemistry and Bioengineering, Tampere University of Technology,*
Korkeakoulunkatu 8, 33101 Tampere, Finland
E-mail: nuno.rafaelcandeias@tut.fi
http://www.tut.fi/en/about-tut/departments/chemistry-and-bioengineering/
[b] *Centro de Química Estrutural, Instituto Superior Técnico, Universidade de Lisboa,*
Av. Rovisco Pais No. 1, 1049-001 Lisboa, Portugal
[c] *The Research Institute for Medicines (iMed.ULisboa), Faculty of Pharmacy, University of Lisbon,*
Av. Prof. Gama Pinto, Lisboa, Portugal
Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under http://dx.doi.org/10.1002/ejoc.201600616.

of cinchona alkaloids and is the principal constituent in coffee beans and other plant products.[13]



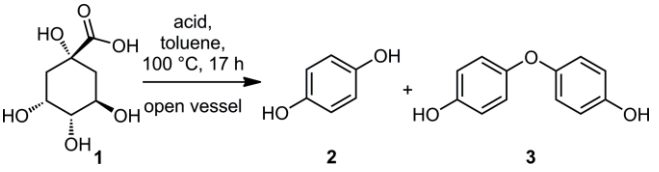
Scheme 1. Fossil-based route and the alternative biomass-based route to hydroquinone.

Taking the dry distillation of quinic acid for the preparation of hydroquinone,[7] it was hypothesised that the same transformation could be achieved under aerobic, strongly acidic conditions. Besides the formation of hydroquinone, other products expected in the acid-promoted decomposition of quinic acid are bicyclic quino-1,5-lactone,[14] benzoic acid[15] and quinone.[10]

Results and Discussion

Versatile and robust polymer-based resins were screened as promoters for the conversion of quinic acid (**1**) into hydroquinone (**2**).[16] Preliminary reactions of quinic acid were carried out with different forms of polystyrene macro-reticular Amberlyst resins: Amberlyst-15 (dry and wet), Amberlyst-16 and Amberlyst-36 in toluene at 100 °C (Table 1). Amberlyst-15 in the dry form resulted in the formation of hydroquinone (**2**) in 62 % yield accompanied by ether **3**, which results from the condensation of hydroquinone (entry 1). Despite the presence of quino-1,5-lactone in the reaction mixture, a likely reaction intermediate, benzoquinone formation was not observed. Amberlyst-15 has been reported in many instances as a mild and selective heterogeneous polymeric material for routine acid-catalysed transformations in organic synthesis.[17] Other Amberlyst resins tested showed inferior activity, leading to only traces of the desired hydroquinone (entries 2–4). Acidic ion-exchange resins Amberlite IRC86, IR120/H and Dowex 50WX4 also failed to provide hydroquinone (**2**) in decent yields (entries 5–7). Despite the high moisture content (64–72 %), Dowex 50WX4 proved to be superior to the other ion-exchange resins, providing 12 % of hydroquinone after 17 h (entry 7). After identification of Amberlyst-15 in the dry form as the best reaction promoter amongst those tested, and being a polymer-supported sulfonic acid resin, we tested *p*-toluenesulfonic acid (*p*TSA, entries 8 and 9) and sulfuric acid (entry 10) as reaction promoters. Although sulfuric acid and monohydrate *p*TSA resulted in traces of hydroquinone (entries 8 and 10), use of molecular sieves and anhydrous *p*TSA resulted in recovery of the starting materials after 17 h (entry 9). Better conversions of the starting quinic acid were achieved by employing ground Amberlyst-15, sieved through a 106 μm sieve. Previous studies on the acid-site accessibility of Amberlyst-15 showed similar strengths of acid sites for both the bead and powder forms of Amberlyst-15 and the higher activity of the powder resin should be associated with the exposed external surface of the resin.[18] Despite the 71 % yield of hydroquinone (**2**), use of the ground Amberlyst led to considerable formation of the ether side-product **3** (entry 13).

Table 1. Screening of acid promoters for the formation of hydroquinone from quinic acid.[a]



Entry	Acid	Yield [%][b]	
		2	**3**
1	Amberlyst-15 (dry)	62	3
2	Amberlyst-15 (wet)	6	n.d.[c]
3	Amberlyst-16 (wet)	4	n.d.
4	Amberlyst-36 (wet)	5	n.d.
5	Amberlite IRC86	n.d.	n.d.
6	Amberlite IR120/H	6	n.d.
7	Dowex 50WX4	12	<3
8	*p*TSA·H_2O[d]	<3	n.d.
9	*p*TSA, 4 Å MS[d]	n.r.[e]	
10	H_2SO_4[f]	<3	n.d.
11	Acetic acid[g]	n.d.	n.d.
12	none	n.r.	
13	Amberlyst-15 (dry), ground	71	7

[a] Reagents and conditions: Unless otherwise stated, the reaction was carried out with quinic acid (0.5 mmol), resin (0.3 g), and toluene (15 mL) at 100 °C for 17 h in an open vessel. [b] Determined by analysis of the ^{1}H NMR spectra of the reaction mixtures using bromobenzene as internal standard. [c] n.d.: not detected. [d] 0.5 mmol of *p*TSA in 7 mL of toluene heated for 24 h. [e] n.r.: no reaction. [f] 1.5 mL of H_2SO_4 in 15 mL of toluene. [g] 3 mL of AcOH as solvent.

In an attempt to optimise the reaction conditions and to allow the dissolution of quinic acid into the reaction solvent, other solvents were screened. Using Amberlyst-15 as the reaction promoter in THF, 1,4-dioxane, CH_2Cl_2, 1,2-dichloroethane, CCl_4, chlorobenzene and methanol at reflux temperature or in glycerol, sulfolane and poly(ethylene glycol) at 125 °C for 24 h did not improve the selectivity towards hydroquinone formation. Besides toluene, hydroquinone (**2**) was detected in the crude reaction mixtures of only chlorinated solvents. Of the above-mentioned solvents, chlorobenzene gave the highest formation of hydroquinone when the reaction was performed in a sealed tube, with **2** and **3** obtained in a 4:3 ratio (68 % conversion).

Taking toluene as the reaction solvent for this two-phase reaction, the influence of temperature on the reaction outcome was assessed (Figure 1). Very low conversions were achieved below 100 °C, hydroquinone was formed in higher yields in the range 100–110 °C, and higher temperatures induced the dimerisation of **2** into ether **3**. This process was verified by the exclusive formation of **3** in 48 % isolated yield after heating hydroquinone **2** in toluene in the presence of Amberlyst-15 for 6 days.

With these optimised conditions, we shifted our attention to the effect of the Amberlyst/quinic acid ratio on the reaction (Table 2). It was observed that the yield of hydroquinone

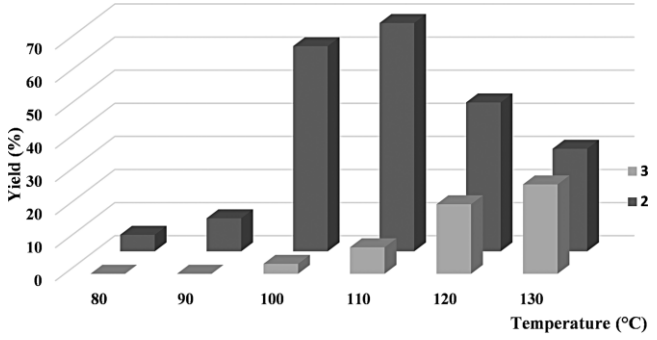
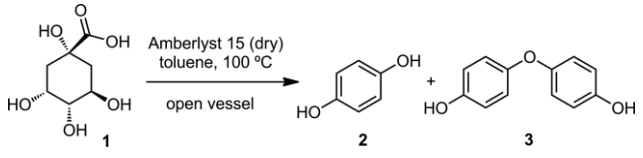


Figure 1. Effect of temperature on hydroquinone formation. Reagents and conditions: Quinic acid (0.5 mmol), Amberlyst-15 (0.3 g), toluene (15 mL), 100 °C, 17 h.

increased with only trace formation of ether **3**, or none at all, as the Amberlyst/quinic acid ratio (w/w) was increased from 0.5 to 4 (entries 1–7). Further increasing the amount of Amberlyst did not show any considerable improvement when performing the reaction at 100 °C for 17 h (entries 7–9). Tuning the reaction conditions further, namely the amount of solvent and reaction time (see the Supporting Information), resulted in the formation of the desired hydroquinone in a yield of 71 % together with 5 % of ether **3** after 25 h (entry 10) and isolation by chromatography. Extension of the reaction time to 48 h proved beneficial for ether **3** formation, but the yield of hydroquinone remained the same (entry 11).

Table 2. Effect of amberlyst/quinic acid ratio on reaction.[a]

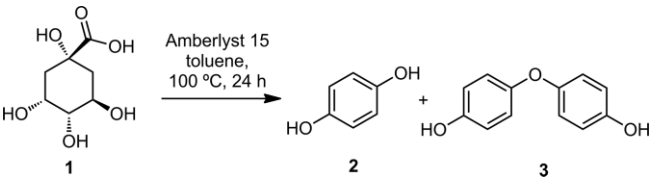


Entry	Amberlyst-15/**1** ratio (w/w)	Time [h]	Yield [%][b] **2**	**3**
1	0.5	17	9	n.d.[c]
2	1	17	17	n.d.
3	2	17	29	n.d.
4	3	17	43	<3
5	3.125	17	48	<3
6	3.5	17	56	<3
7	4	17	55	<3
8	5	17	55	<3
9	10	17	59	<3
10[d]	4	25	72 (71)[e]	5
11[d]	4	48	72	9

[a] Reagents and conditions: Unless otherwise stated, the reaction was carried out with quinic acid (0.5 mmol), Amberlyst-15 (dry) in toluene (15 mL) at 100 °C in an open vessel. [b] Yield calculated from the ^{1}H NMR spectra of reaction mixtures using bromobenzene as internal standard. [c] n.d.: not detected. [d] 10 mL of toluene as solvent. [e] Isolated yield after flash chromatography.

Being a formal oxidation, the influence of oxygen and other oxidative conditions were also investigated (Table 3). The absence of air or the presence of water had a detrimental effect on hydroquinone formation and neither oxygen nor copper salts[19] were effective catalysts in the putative aerobic oxidation process.

Table 3. Effect of oxidation conditions on the reaction.[a]



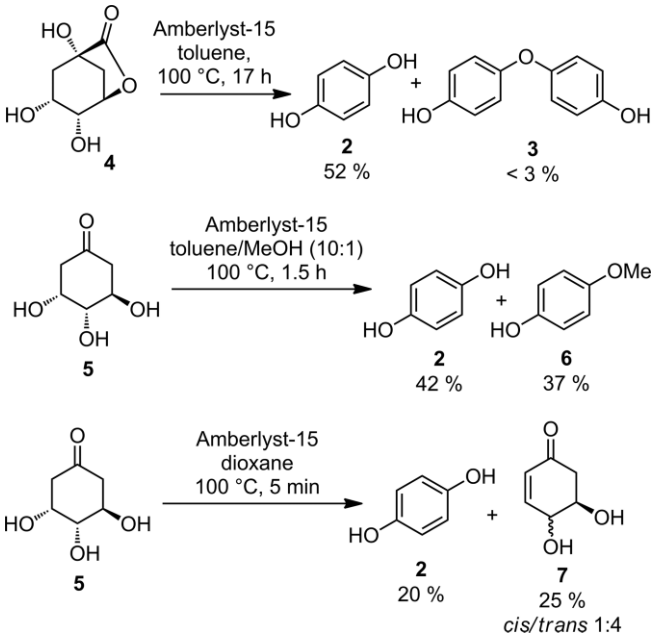
Entry	Reaction conditions	Yield [%][b] **2**	**3**
1	open vessel	72	5
2	O_2 atmosphere	64	6
3	argon atmosphere	46	<3
4	1.5 equiv. of H_2O	62	3
5	5 mol-% CuBr	58	4
6	5 mol-% CuI	51	4
7	5 mol-% $CuBr_2$	43	3
8	5 mol-% $CuCl_2 \cdot H_2O$	47	4

[a] Reagents and conditions: Quinic acid (0.5 mmol), Amberlyst-15 (1:4 ratio, w/w) in toluene (10 mL) at 100 °C for 24 h in an open vessel, except entries 2 and 3. [b] Determined by analysis of ^{1}H NMR spectra of the reaction mixtures using bromobenzene as internal standard.

To gain further insight into the reaction mechanism, two possible reaction intermediates, **4** and **5**, were prepared and allowed to react under similar reaction conditions (Scheme 2). Lactone **4** was converted into hydroquinone (**2**) in 52 % yield, as observed for the reaction of quinic acid. As previously demonstrated by Frost and co-workers,[10] ketone **5** was converted into the hydroquinone via the two possible enone intermediates. In such a strongly acidic medium, the dehydration of **5** is a very fast process and such intermediates are not visible in the NMR spectrum of the quinic acid dehydration reaction mixture. It was nevertheless possible to detect and isolate a mixture of the enones **7** in 25 % yield when the reaction was performed in dioxane.

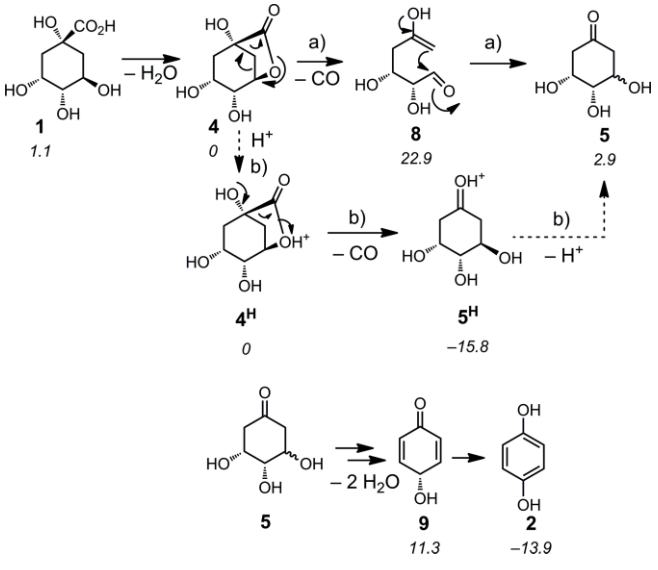
Adding (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO), butylated hydroxytoluene (BHT), styrene and azodicarboxylates to the reaction mixture did not allow the isolation of any intermediates derived from a single-electron-transfer pathway. Curiously, TEMPO inhibited the formation of the hydroquinone (**2**) and only starting material and lactone **4** were detected. Additionally, the use of *tert*-butyl peroxide as radical initiator did not improve hydroquinone formation or reduce the reaction rate. The carbon atom lost in the conversion of quinic acid (**1**) into hydroquinone (**2**) occurs through the liberation of carbon monoxide. Such an event was confirmed by the reduction of palladium chloride to palladium when a filter paper soaked in $PdCl_2$ aqueous solution (1:500, w/v) was placed on the top of the reaction condenser (see the Supporting Information).[20]

DFT calculations[21] were performed to compare ionic and radical mechanisms through the optimisation of likely intermediates. The free-energy values obtained for the diradical intermediates considered in single-electron-transfer processes clearly preclude a radical pathway for the reaction (ΔG = 80–84 kcal/mol, see the Supporting Information for details). Furthermore, the high acidity of Amberlyst should favour an ionic



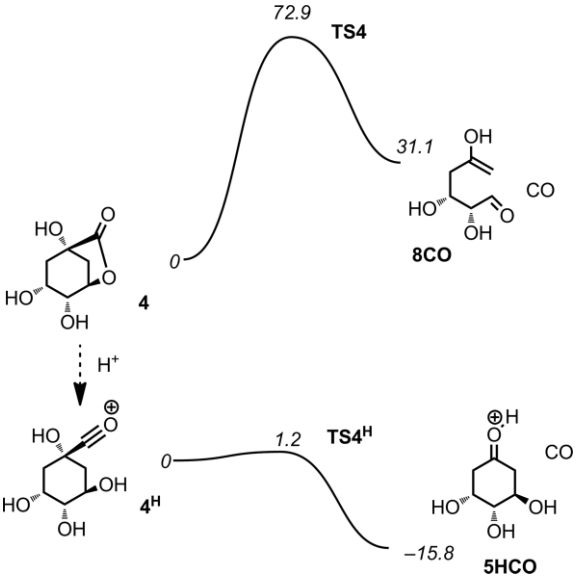
Scheme 2. Reactivity of reaction intermediates **4** and **5**.

mechanism by the favourable protonation of the starting material and reaction intermediates. Two ionic mechanisms were considered for the decarbonylation step, both having lactone **4** as the starting point: 1) Pericyclic decarbonylation of the lactone with concomitant formation of the enol aldehyde **8** and b) ring-opening of protonated lactone $\mathbf{4^H}$ (Scheme 3). From a thermodynamic point of view, the formation of enol aldehyde **8** seems to be unlikely due to its high free energy (ΔG = 22.9 kcal/mol) whereas the decarbonylation of protonated lactone $\mathbf{4^H}$ should be a spontaneous process towards the formation of protonated ketone $\mathbf{5^H}$ (ΔG = –15.8 kcal/mol). This is further confirmed by the energy barriers calculated for both processes, which clearly indicate a preference for the ring-opening of the



Scheme 3. Proposed ionic reaction mechanisms. Calculated free energies of the intermediates are indicated in italics [kcal/mol].

protonated lactone over the pericyclic process (Scheme 4): A large energy barrier of 72.9 kcal/mol needs to be overcome for the pericyclic process, whereas the energy barrier for the decarbonylation of $\mathbf{4^H}$ is only 1.2 kcal/mol. Under the highly acidic reaction conditions, **9** should be formed after the double protonation and dehydration of **5** to form the more stable hydroquinone. The overall reaction from quinic acid (**1**) to hydroquinone (**2**) is a thermodynamically favourable process with ΔG = –15 kcal/mol.



Scheme 4. Energy profiles calculated for two alternative decarbonylation steps. The free energies of the intermediates and transition states are indicated in italics [kcal/mol].

Conclusions

A mild and efficient method for the conversion of naturally available quinic acid (**1**) into hydroquinone (**2**) has been disclosed herein. By using Amberlyst-15 in its dry form as an acid promoter it is possible to obtain the hydroquinone in up to 72 % yield with only small amounts of the dimeric ether compound formed after 24 h. This method does not rely on the use of any oxidants or high temperatures unlike the previously reported methods. An ionic decarbonylation mechanism has been proposed, supported by experimental and computational calculation data.

Experimental Section

General Methods: Polymer-based resins were used as received from suppliers: Amberlyst-15 (dry), 20–50 mesh from Fluka (06423) and Aldrich (216380), Amberlyst-15 (wet) from Aldrich (216399), Amberlyst-16 (wet) from Aldrich (86317), Amberlyst-36 (wet) from Fluka (06455), Amberlite IRC86 from Aldrich (10322), Amberlite IR120/H from Aldrich (216534) and Dowex 50WX4 from Aldrich (422096). Quinic acid was obtained from Sigma–Aldrich and sieved through a 106 μm sieve prior to use. Retsch ZM200 and Retsch AS200 were used as grinder and sieve, respectively. Other reagents were used as obtained from the suppliers (Sigma–Aldrich and

Fluka). The reactions were monitored by TLC carried out on precoated (Merck TLC silica gel 60 F254) aluminium plates by using UV light as visualising agent and cerium molybdate solution as developing agent. Flash column chromatography was performed on silica gel 60 (Merck, 0.040–0.063 mm). NMR spectra were recorded with a Varian Mercury 300 MHz spectrometer using $CDCl_3$, [D_6]DMSO or D_2O as solvent and calibrated by using tetramethylsilane as internal standard. Chemical shifts are reported in ppm relative to TMS and coupling constants are reported in Hz. ^1H NMR yields were determined by adding a known amount of bromobenzene to the reaction mixture after work-up.

Hydroquinone (2): Quinic acid (0.5 mmol) was added to a suspension of Amberlyst-15 (dry, 0.38 g) in toluene (10 mL) in a round-bottomed flask equipped with a magnetic stirrer bar and condenser open to the air. The mixture was heated at 100 °C for 24 h. After cooling to room temperature methanol (5 mL) was added and the mixture stirred vigorously for 5 min. The mixture was filtered and the solid residue re-suspended in methanol (20 mL) and stirred for an additional 5 min. After filtration and washing with more methanol (10 mL), the solvents were removed under reduced pressure. The residue was either dissolved in [D_6]DMSO for ^1H NMR yield determination (72 %) or purified by flash chromatography with toluene/ethyl acetate (3:1) to afford pure hydroquinone (39 mg, 71 % yield) with similar spectroscopic data as commercial samples. ^1H NMR ([D_6]DMSO, 300 MHz): δ = 8.64 (s, 2 H), 6.55 (s, 4 H) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 149.8, 115.8 ppm.

Bis(4-hydroxyphenyl) Ether (3): Hydroquinone (1.0 mmol) was added to a suspension of Amberlyst-15 (dry, 0.77 g) in toluene (20 mL) in a round-bottomed flask equipped with a magnetic stirrer bar and condenser. The mixture was heated at 100 °C for 6 d. After cooling to room temperature, methanol (10 mL) was added and the mixture stirred vigorously for 5 min. The mixture was filtered and the solid residue re-suspended in methanol (40 mL) and stirred for an additional 5 min. After filtration and washing with more methanol (20 mL), the solvents were removed under reduced pressure. The residue was purified by preparative TLC with toluene/ethyl acetate (3:1) to afford pure **3** (49 mg, 48 %) with similar spectroscopic data as previously reported.[22] ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.70–6.83 (m, 8 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 151.9, 150.8, 120.1, 119.4, 115.9 ppm.

Quino-1,5-lactone (4): Amberlyst-15 (dry, 0.69 g) was added to a suspension of quinic acid (3 mmol) in acetonitrile (150 mL) and the mixture stirred at 50 °C for 24 h. After cooling, the reaction mixture was filtered through Celite and washed with methanol. Solvent removal under reduced pressure yielded the desired lactone **4** in quantitative yield (0.52 g) with similar spectroscopic data as previously reported.[23] ^1H NMR ([D_6]DMSO, 300 MHz): δ = 5.90 (s, 1 H), 5.24 (d, J = 3.8 Hz, 1 H), 4.84 (d, J = 6.7 Hz, 1 H), 4.61 (t, J = 5.3 Hz, 1 H), 3.81 (d, J = 4.1 Hz, 1 H), 3.49 (dd, J = 11.0, 4.8 Hz, 1 H), 2.27–2.24 (m, 1 H), 2.13–2.07 (m, 1 H), 1.87–1.82 (m, 1 H), 1.75–1.66 (m, 1 H) ppm. ^{13}C NMR ([D_6]DMSO, 75 MHz): δ = 177.8, 76.0, 71.6, 65.6, 65.3, 39.4, 36.8 ppm.

(3*R*,5*R*)-3,4,5-Trihydroxycyclohexanone (5): Prepared according to a previously reported procedure.[10] A 14 % aqueous NaOCl solution (30 mmol) and H_2SO_4 (8 mmol) were added dropwise to a stirred solution of quinic acid (10 mmol) in water (7 mL) over 30 min. The reaction was stirred at room temperature for 2.5 h. The reaction was then quenched with isopropanol (30 mmol) and stirred for 30 min. After pH neutralisation with an aqueous saturated solution of Na_2CO_3, the solvent was removed under reduced pressure. The obtained residue was re-suspended in acetone (55 mL) and left to stir overnight at room temperature. After filtration and solvent removal under reduced pressure, the residue obtained was purified by flash chromatography with an eluent gradient from ethyl acetate/hexane (9:1) to methanol/ethyl acetate (1:9). The desired ketone **5** was obtained in 75 % yield (1.03 g) with similar spectroscopic data as previously reported.[10] ^1H NMR (D_2O, 300 MHz): δ = 4.83 (s, 3 H), 4.29 (ddd, J = 6.3, 3.7, 2.9 Hz, 1 H), 4.15 (td, J = 8.2, 5.3 Hz, 1 H), 3.97 (dd, J = 7.8, 2.8 Hz, 1 H), 2.83–2.80 (m, 1 H), 2.78–2.75 (m, 1 H), 2.65–2.50 (m, 2 H) ppm. ^{13}C NMR (D_2O, 75 MHz): δ = 212.8, 73.0, 68.7, 45.7 ppm.

4-Methoxyphenol (6): Ketone **5** (0.5 mmol) was dissolved in methanol (1 mL) and dispersed in toluene (10 mL) in a round-bottomed flask equipped with a magnetic stirrer bar. Amberlyst 15 (dry, 384 mg) was added and the mixture stirred at 100 °C until disappearance of the starting material, as judged by TLC (1.5 h). After cooling to room temperature, methanol (5 mL) was added, the mixture filtered and the solvent removed under reduced pressure. The residue was purified by flash chromatography with gradient elution with ethyl acetate/hexane (1:9 to 1:1), to afford 42 % (23 mg) of hydroquinone (**2**) and 37 % (23 mg) of **6** with similar spectroscopic data as previously reported.[24] ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.78 (d, J = 1.8 Hz, 4 H), 4.93 (br. s., 1 H), 3.77 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 153.6, 149.4, 116.0, 114.8, 55.8 ppm.

4,5-Dihydroxycyclohex-2-en-1-one (7): Amberlyst-15 (dry, 0.38 g) was added to a solution of ketone **5** (1 mmol) in 1,4-dioxane (10 mL) and the mixture stirred at 100 °C for 5 min. After cooling to room temperature the mixture was filtered and the solvent removed under reduced pressure. The residue was purified by flash chromatography with eluent gradient from ethyl acetate/hexane (4:1) to methanol/ethyl acetate (1:9) to afford 20 % (20 mg) of hydroquinone (**2**) and 25 % (31 mg) of **7** in a *cis*/*trans* ratio of 1:4, as determined by ^1H NMR spectroscopy and comparison with previous reports.[10] ^1H NMR (D_2O, 300 MHz): δ = 6.96 (dd, J = 10.1, 2.2 Hz, 1 H), 6.92–6.87 (m, 0.2 H), 6.73–6.72 (m, 0.2 H), 6.06 (dd, J = 2.2, 1.0 Hz, 0.2 H), 6.03–5.98 (m, 1 H), 4.64–4.61 (m, 0.2 H), 4.39–4.30 (m, 1.2 H), 3.99–3.91 (m, 1 H), 2.78–2.76 (m, 0.5 H), 2.73–2.71 (m, 1 H), 2.68 (dd, J = 5.1, 1.0 Hz, 0.2 H), 2.55–2.46 (m, 1.3 H) ppm. ^{13}C NMR (D_2O, 75 MHz): δ = 204.8, 204.4, 156.2, 154.2, 151.8, 131.6, 131.5, 119.2, 74.4, 74.3, 72.5, 70.3, 68.8, 63.3, 57.8, 46.5, 45.7 ppm.

Acknowledgments

N. R. C. acknowledges the Academy of Finland for an academy research fellowship (decision number 287954). Dr. Alexandre Efimov is acknowledged for valuable discussions of the NMR spectra and Dr. Henrik Tolvanen for facilitating the use of the grinder and sieve.

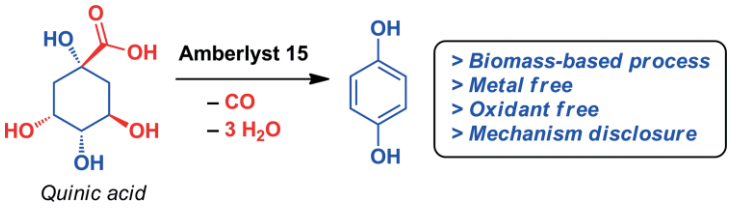
Keywords: Sustainable chemistry · Heterogeneous catalysis · Natural products · Cyclitols

[1] C. H. Christensen, J. Rass-Hansen, C. C. Marsden, E. Taarning, K. Egeblad, *ChemSusChem* **2008**, *1*, 283–289.
[2] P. Gallezot, *Chem. Soc. Rev.* **2012**, *41*, 1538–1558.
[3] F. W. Lichtenthaler, *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, Germany, **2000**.
[4] J. ten Dam, U. Hanefeld, *ChemSusChem* **2011**, *4*, 1017–1034.
[5] F. Cherubini, A. H. Strømman, *Biofuels Bioprod. Bioref.* **2011**, *5*, 548–561.
[6] a) L. Krumenacker, M. Costantini, P. Pontal, J. Sentenac, in *Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed., John Wiley & Sons, Inc., Hoboken, New Jersey, **2000**; b) P. M. Hudnall, *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, Germany, **2000**.
[7] A. Woskresensky, *Ann. Pharm.* **1838**, *27*, 257–270.

[8] C. A. Hansen, J. W. Frost, *J. Am. Chem. Soc.* **2002**, *124*, 5926–5927.
[9] K. M. Draths, T. L. Ward, J. W. Frost, *J. Am. Chem. Soc.* **1992**, *114*, 9725–9726.
[10] N. Ran, D. R. Knop, K. M. Draths, J. W. Frost, *J. Am. Chem. Soc.* **2001**, *123*, 10927–10934.
[11] a) J. Mulzer, M. Drescher, V. S. Enev, *Curr. Org. Chem.* **2008**, *12*, 1613–1630; b) A. Barco, S. Benetti, C. D. Risi, P. Marchetti, G. P. Pollini, V. Zanirato, *Tetrahedron: Asymmetry* **1997**, *8*, 3515–3545.
[12] E. Haslam, *Shikimic acid: metabolism and metabolites*, Wiley, New York, **1993**.
[13] a) C. Åkesson, H. Lindgren, R. W. Pero, T. Leanderson, F. Ivars, *Int. Immunopharmacol.* **2005**, *5*, 219–229; b) Y. Sato, S. Itagaki, T. Kurokawa, J. Ogura, M. Kobayashi, T. Hirano, M. Sugawara, K. Iseki, *Int. J. Pharm.* **2011**, *403*, 136–138.
[14] V. Sinisi, K. Boronov, S. Colomban, L. Navarini, F. Berti, C. Forzato, *Eur. J. Org. Chem.* **2014**, 1321–1326.
[15] E. Arceo, J. A. Ellman, R. G. Bergman, *ChemSusChem* **2010**, *3*, 811–813.
[16] G. Gelbard, *Ind. Eng. Chem. Res.* **2005**, *44*, 8468–8498.
[17] a) R. Pal, T. Sarkar, S. Khasnobis, *ARKIVOC (Gainesville, FL, U.S.)* **2012**, 570–609; b) L. M. T. Frija, C. A. M. Afonso, *Tetrahedron* **2012**, *68*, 7414–7421.
[18] a) P. F. Siril, H. E. Cross, D. R. Brown, *J. Mol. Catal. A* **2008**, *279*, 63–68; b) P. F. Siril, D. R. Brown, *J. Mol. Catal. A* **2006**, *252*, 125–131.
[19] S. D. McCann, S. S. Stahl, *Acc. Chem. Res.* **2015**, *48*, 1756–1766.
[20] a) H.-K. Hund, J. Breuer, F. Lingens, J. Hüttermann, R. Kappl, S. Fetzner, *Eur. J. Biochem.* **1999**, *263*, 871–878; b) F. Feigl, *Spot Tests, in: Organic Analysis*, Elsevier, Amsterdam, **1966**, p. 401–566.
[21] a) R. G. Parr, W. Yang, *Density Functional Theory of Atoms and Molecules*, Oxford University Press, New York, **1989**; b) DFT calculations at the M06–2X/6–31+G(d,p) level were performed by using the Gaussian 09 package. Full computational details, the corresponding list of references are provided in the Supporting Information.
[22] M. V. Gomez, A. Moreno, E. Vazquez, A. de la Hoz, A. I. Aranda, A. Diaz-Ortiz, *ARKIVOC (Gainesville, FL, U.S.)* **2010**, 264–273.
[23] a) K. S. Raheem, N. P. Botting, G. Williamson, D. Barron, *Tetrahedron Lett.* **2011**, *52*, 7175–7177; b) J. D. White, J. H. Cammack, K. Sakuma, G. W. Rewcastle, R. K. Widener, *J. Org. Chem.* **1995**, *60*, 3600–3611.
[24] E. J. Rayment, N. Summerhill, E. A. Anderson, *J. Org. Chem.* **2012**, *77*, 7052–7060.

Received: May 19, 2016
Published Online: ■

Hydroquinone Synthesis



Hydroquinone from a non-fossil source: Hydroquinone has been prepared from a biomass-based starting material by a metal- and oxidant-free process. Polymer-based Amberlyst-15 in the dry form promoted the conversion of quinic acid into hydroquinone under mild conditions, whereas uncatalysed processes demanded unpractical reaction conditions.

DOI: 10.1002/ejoc.201600616