Catalytic aerobic oxidation of phenols to *ortho*-quinones with air-stable copper precatalysts

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1. General Experimental

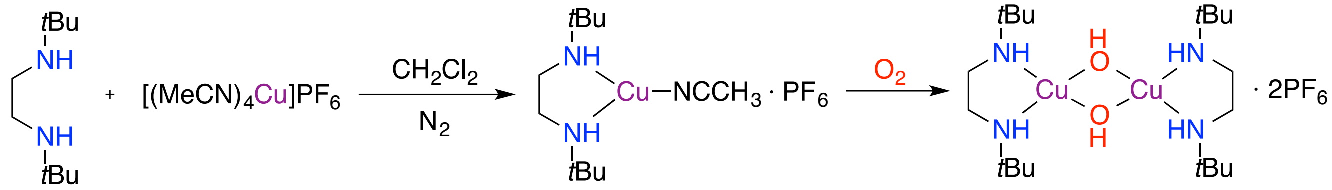
Chemicals and solvents were purchased from Sigma Aldrich, Alfa Aesar or Strem Chemicals. Inhibitor-free solvents were dried using a MBraun SPS 800, transferred to an inert-atmosphere glove box (MBraun Labmaster, <1 ppm O_2 and H_2O, filled with a dry N_2 atmosphere), further degassed under vacuum and stored over activated molecular sieves (4 Å). *tert*-Butylphenol **1** was purified by double recrystallization from CH_2Cl_2/hexanes. *N*,*N'*-di-*tert*-butylethylenediamine (DBED) was distilled over CaH_2 under N_2 and stored in an inert atmosphere glove box. The copper(I) salt $[Cu(CH_3CN)_4](PF_6)$, abbreviated $CuPF_6$, was made via a literature procedure.[1] $Cu^{II}(TfO)_2·4H_2O$,[2] anhydrous $Cu^{II}(TfO)_2$,[2] and $[Cu(MeCN)_{3.5}](MsO)$[3] were prepared according to literature procedures. $Cu^{II}(OAc)_2·MeCN$ was prepared by reacting $Cu^{II}O$ with acetic acid and acetic anhydride (1:1) in dry acetonitrile then extracted by Soxhlet (48h). All copper(I) complexes were stored inside the glovebox.

Unless otherwise noted, reactions were performed in oven-dried glassware under a positive pressure of nitrogen using standard synthetic inert-atmosphere techniques. Bulk oxidation reactions were set-up in the glovebox in 25 mL, oven-dried Radley tubes equipped with a Teflon-coated stir bar. The reaction vessels were then connected to a cylinder of O_2, purged three times with O_2 and then overpressurized to +1.0 atm.

UV-visible spectra were recorded on a B&W Tek iTrometer equipped with fiber-optic cables connected to a Hellma full-quartz dip-probe having a 1.0 mm pathlength. The probe was immersed in the solution inside a custom-made Schlenk flask.

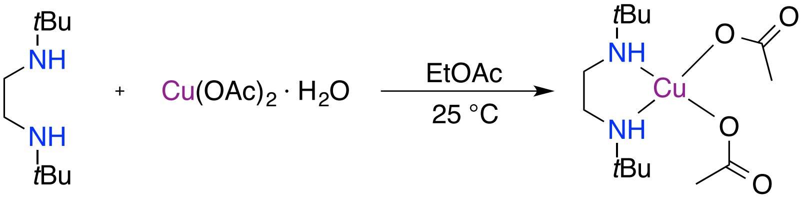
2. Syntheses and Characterizations

a) Synthesis of 3



3:[4] In the glovebox, solid $[Cu(MeCN)_4]PF_6$ (370 mg, 0.99 mmol) was added to a solution of DBED (172 mg, 1.0 mmol) in 5 mL of CH_2Cl_2. The resulting pink solution was stirred until all the copper dissolved. The solution was then exposed to oxygen or air upon which the color changed to deep green. Diethyl ether was added to the mixture to precipitate the complex. The solid was filtered off, washed with Et_2O, and dried in vacuo. Crystals suitable for x-ray diffraction were grown by slow evaporation of a concentrated solution in CH_2Cl_2.

b) Synthesis of 4



4: To a solution of DBED (1.9 g, 11 mmol) in 10 mL ethyl acetate was added solid $Cu^{II}(OAc)_2 \cdot H_2O$ (2.0 g, 10 mmol). The blue solution was left stirring until all the copper was dissolved. The solution was then filtered and solvent was removed in vacuo to give a blue solid residue. The solid was triturated in Et_2O, filtered off, and dried in vacuo to give a blue powder. Yield: 82%. Elemental analysis (mol%): expected for $C_{14}H_{30}N_2O_4Cu$: C, 47.51; H, 8.54; N, 7.81; found: C, 47.67; H, 8.58; N, 7.85. Crystals suitable for X-ray diffraction were grown by slow evaporation of a concentrated solution of **4** in ethyl acetate.

c) Crystallographic details

3: A rhomb-like specimen of $C_{20}H_{50}Cu_2F_6N_4O_2P_2$, approximate dimensions 0.367 mm x 0.469 mm x 0.503 mm, was used for the X-ray crystallographic analysis. The integration of the data using a monoclinic unit cell yielded a total of 12237 reflections to a maximum θ angle of 27.55° (0.77 Å resolution), of which 12237 were independent (average redundancy 1.000, completeness = 94.9%, R_{sig} = 3.62%) and 8327 (68.05%) were greater than 2σ(F^2). Unit cell The final cell constants of $\underline{a}$ = 24.870(3) Å, $\underline{b}$ = 16.8713(18) Å, $\underline{c}$ = 18.708(2) Å, β = 120.7840(10)°, volume = 6743.7(13) $Å^3$, are based upon the refinement of the XYZ-centroids of reflections above 20 σ(I). Scaling The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6216 and 0.7456. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group C 1 2/c 1, with Z = 8 for the formula unit, $C_{20}H_{50}Cu_2F_6N_4O_2P_2$. Structure refinement The final anisotropic full-matrix least-squares refinement on F^2 with 393 variables converged at R1 = 6.33%, for the observed data and wR2 = 16.59% for all data. The goodness-of-fit was 1.115. The largest peak in the final difference electron density synthesis was 0.895 $e^-/Å^3$ and the largest hole was -0.651 $e^-/Å^3$ with an RMS deviation of 0.112 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.567 g/cm^3 and F(000), 3280 e^-.

4: A light blue rhomb-like specimen of $C_{14}H_{30}CuN_2O_4$, approximate dimensions 0.422 mm x 0.558 mm x 1.140 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on measured on Mo Kα radiation (λ = 0.71073 Å) of Bruker APEX DUO. A total of 1464 frames were collected. The total exposure time was 4.07 hours. Integration The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 9419 reflections to a maximum θ angle of 27.98° (0.76 Å resolution), of which 2002 were independent (average redundancy 4.705, completeness = 93.9%, R_{int} = 2.07%, R_{sig} = 1.52%) and 1867 (93.26%) were greater than

$2\sigma(F^2)$. Unit cell The final cell constants of a = 15.876(4) Å, b = 11.938(3) Å, c = 12.088(6) Å, β = 129.534(3)°, volume = 1766.9(11) Å^3, are based upon the refinement of the XYZ-centroids of 6748 reflections above 20 $\sigma(I)$ with 4.765° < 2θ < 55.95°. Scaling Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.697. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.3295 and 0.6202. The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group C 1 2/c 1, with Z = 4 for the formula unit, $C_{14}H_{30}CuN_2O_4$. Structure refinement The final anisotropic full-matrix least-squares refinement on F^2 with 100 variables converged at R1 = 2.35%, for the observed data and wR2 = 6.66% for all data. The goodness-of-fit was 1.103. The largest peak in the final difference electron density synthesis was 0.283 e$^-$/Å^3 and the largest hole was -0.440 e$^-$/Å^3 with an RMS deviation of 0.065 e$^-$/Å^3. On the basis of the final model, the calculated density was 1.331 g/cm^3 and F(000), 756 e$^-$.

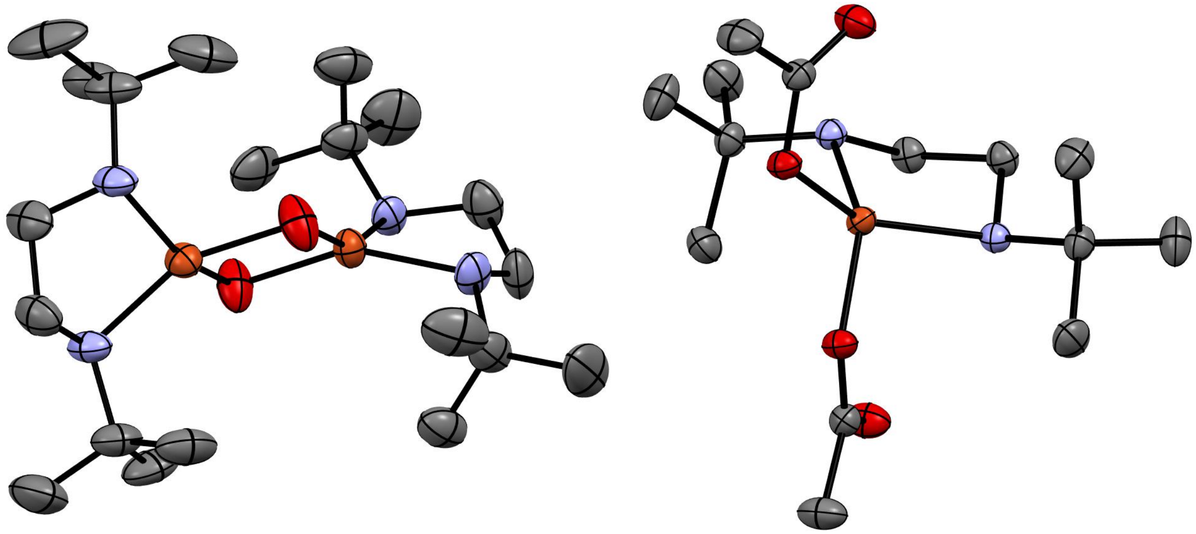


Figure S1. ORTEP representation at 50% ellipsoid probability of **3** (left, one cation only) and **4** (right). Hydrogen atoms removed for clarity. Selected bond lengths and angles for **4**: Cu–O = 1.9272(11) Å, Cu–N = 2.0282(13) Å. O1–Cu1–O1 = 87.19(6)°, O1–Cu1–N1 = 146.62(5)°, N1–Cu1–N1 = 87.18(8)°.

Table S1: Crystal data and structure refinement for **3** and **4**.

CCDC deposition number	1051251	1051252
Empirical formula	$C_{20}H_{50}N_4O_2F_6P_2Cu_2$	$C_{14}H_{30}N_2O_4Cu$
Formula weight	795.66	353.94
Temperature	150(2)	293(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system	Monoclinic	Monoclinic
Space group	C2/c	C2/c
Unit cell dimensions	*a* = 24.870(3) Å	*a* = 15.876(4) Å
	b = 16.8713(18) Å	*b* = 11.938(3) Å
	c = 18.708(2) Å	*c* = 12.088(6) Å
	α = 90.00°	α = 90.00°
	β = 120.7840(10)°	β = 129.534(3)°
	γ = 90.00°	γ = 90.00°
Volume	6743.8(13)	1766.9(11) $Å^3$
Z	8	4
Density (calculated)	1.567 g/cm^3	1.331 g/cm^3
Absorption coefficient	1.448 mm^{-1}	1.252 mm^{-1}
F(000)	3280	756
Crystal size	0.503 × 0.469 × 0.367 mm	1.14 × 0.558 × 0.422 mm
Theta range for data collection	2.26 – 27.44°	2.38 – 27.98°
Index ranges	*h* = −32→27	*h* = −19→20
	k = 0→21	*k* = −15→14
	l = 0→24	*l* = −15→15
Reflections collected	12237	9419
Independent reflections	12237	2002 (R_{int} = 2.07%)
Completeness	94.9%	93.9%
Absorption correction	Multiscan	Multiscan
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	12237 / 0 / 393	2002 / 0 / 100
Goodness of fit on F^2	1.115	1.103
Final R indices [I > 2σ(I)]	R_1 = 6.33%, wR_2 = 14.17%	R_1 = 2.35%, wR_2 = 6.49%
R indices (all data)	R_1 = 10.43%, wR_2 = 16.59%	R_1 = 2.62%, wR_2 = 6.66%
Largest diff. peak and hole	0.895 and −0.651 e $Å^{-3}$	0.283 and −0.440 e $Å^{-3}$

3. Typical Reaction Procedure

For reproducibility of the yield measurements, solutions were prepared in the glovebox prior to oxygenation. A solution containing DBED (0.1 mol), $Cu^{II}(OAc)_2 \cdot H_2O$ (0.05 mol), and phenol (1 mmol) in 10 mL CH_2Cl_2 was placed in a Radley tube equipped with a stir bar, then sealed with a Radley cap. Outside the glovebox, the tube was then pressurized with 2 atmospheres of dry O_2 (after 5 purges) and left stirring for 4 hours. The reaction mixture was then transferred to a separatory funnel and hexamethylbenzene (0.15 equiv.) was added. The organic layer was washed twice with aqueous 10% $NaHSO_4$, dried over Na_2SO_4, and filtered. Evaporation of the solvent under reduced pressure afforded the quinone which was analyzed by NMR in $CDCl_3$.

Alternatively, the reaction can be set up in the air as follow: the 1:1 mixture of DBED and $Cu^{II}(OAc)_2 \cdot H_2O$ in 5 mL CH_2Cl_2 was placed in the Radley tube and solubilized. Then a solution of the phenol in 5 mL CH_2Cl_2 was added and the vessel was closed, purged and pressurized with O_2.

4. Solvent Screening

Table S2 Solvent screening of the $Cu^{II}(OAc)_2 \cdot H_2O$-precatalyzed reaction [a]

Entry	Solvent	Yield (%) [b]
1	Dichloromethane	98
2	Chloroform	<30
3	Tetrahydrofuran	31
4	Acetone	31
5	Ethyl acetate	65
6	Toluene	60
7	Hexanes	3
8	Dimethylsulfoxide	32
9	Acetonitrile	93
10	Methanol	17
11	Ethanol	0

[a] Conditions: 0.666 mmol **1**, 5% Cu, 10% DBED, 6 mL solvent (0.1 M), 2 atm O_2, 4 h, 25°C. [b] NMR yield calculated based on relative peak areas of **1** and **2**.

5. UV-Visible Spectroscopic Monitoring of the Reactions

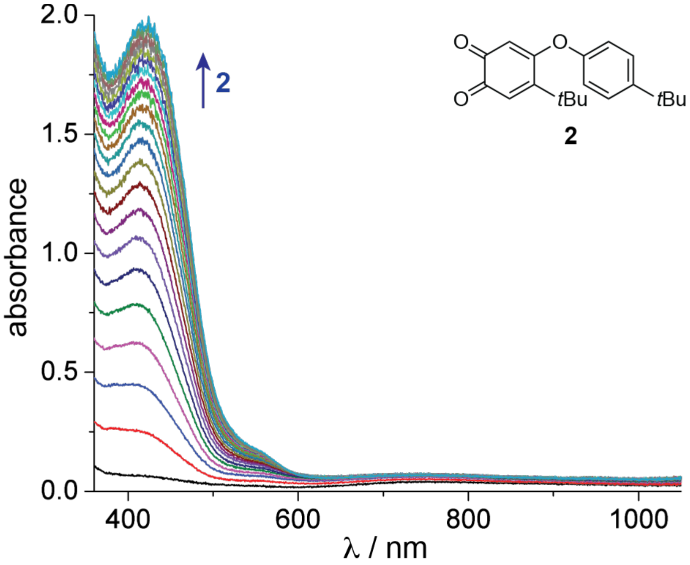


Figure S2. In-situ UV-visible monitoring of the reaction of **1** (50 mM) with 5% $Cu^{II}(OAc)_2 \cdot H_2O$ and 10% DBED, CH_2Cl_2 under 1.1 atm O_2 at 25°C. One spectrum every 2 min. The reaction was stopped after 4h, at which time, the final yield of **2** was 82% (reaction was not complete at this Cu concentration and under this lower O_2 pressure than in the bulk).

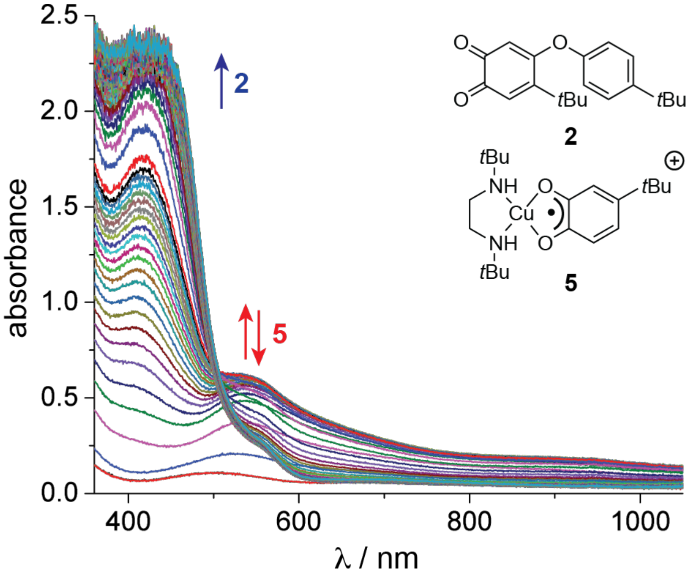


Figure S3. In-situ UV-visible monitoring of the reaction of **1** (50 mM) with 5% $Cu^{II}(OTf)_2 \cdot 4\ H_2O$ and 10% DBED, CH_2Cl_2 under 1.1 atm O_2 at 25°C. First part of the growth (until $A_{416} \approx 1.75$): one spectrum every 10s, then one spectrum every 1 min, at which point the absorbance of **2** saturates. Final yield of **2** was 98%.

6. References

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