Supplementary information for the paper

Oxidation of thiols to disulfides by dioxygen catalyzed by a bioinspired organocatalyst

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Experiments details

General

Instruments: Gas chromatographic (GC) analyses were carried out on an Agilent Technologies 7820A instrument with flame ionization detector equipped with an HP-5 capillary column. (carrier gas: dinitrogen, dihydrogen and air). Gas chromatographic – Mass Spectrometric (GC-MS) analyses were carried out on a GCMS-QP2010 SE instrument with secondary electron multiplier detector. NMR spectrum: ¹H and ¹³C NMR spectra were collected on 400 MHz NMR spectrometers (Bruker Avance) using D₂O as solvent. Chemical shifts are reported in parts per million (ppm). Chemical shifts for protons are reported in parts per million downfield and are referenced to residual protium in the NMR solvent (D₂O = δ 8.65).

General procedure of kinetic measurements

A thermostated vessel containing the described concentrations of 1,3,2oxazaphosphole and substrates in methanol or methanol and water (2:1) solution, fitted with septum and O_2 -filled gas buret was used for the kinetic measurements. The increasing disulfide was monitored by GC in the presence of an internal standard, naphthalene in the case of thiophenol. The resulting hydrogen-peroxide was determined by iodometric titration.¹ The oxidation reaction of cysteine and glutathione was followed by a gas burette. The product was precipitated during the oxidation reaction. The precipitate was collected, dryed under vacuum and analyzed by IR, m.p. mixed m.p., GC-MS, and ¹H- or ¹³C-NMR.

Materials and Methods: Methanol, thiophenol, cysteine and glutathione were obtained commercially and used without purification. We have prepared 2,3-dihydro-2,2,2-triphenylphenanatro[9,10-*d*]-1,3,2 λ ⁵-oxazaphosphole according to the literature. ^[2]

[1] J. Mendham, R. C. Denney, J. D. Barnes, M. J. K. Thomas, *Vogel's Quantitative Chemical Analysis*, 6th ed., New York, Prentice Hall, 2000.

[2] G. Speier, Z. Tyeklár, V. Fülöp, L. Párkányi, Chem. Ber. 1988, 121, 1685.



Figure S1 Catalytic oxidation of thiophenol followed by GC and gas-uptake. (• GC \blacksquare gas-uptake) [PhSH] = 30.00 × 10⁻³ M, [O₂] = 9.50 × 10⁻³ M, [1,3,2-oxazaphosphole] = 2.00 × 10⁻³ M, [naphtalene] = 4.00 × 10⁻³ M, V (MeOH) = 25 mL.



Figure S2 Autoxidation and catalytic oxidation of thiophenol. Autoxidation reaction: • [PhSH] = 100.00×10^{-3} M, [O₂] = 9.50×10^{-3} M, V (MeOH) = 25 mL. Catalytic reaction **=** [PhSH] = 100.00×10^{-3} M, [1,3,2-oxazaphosphole] = 2×10^{-3} M, [O₂] = 9.50×10^{-3} M, V (MeOH) = 25 mL.



Figure S3 Autoxidation and catalytic oxidation of cysteine. Autoxidation reaction: • [cysteine] = 3.00×10^{-2} M, [O₂] = 3.54×10^{-3} M, V (MeOH: H₂O) = 30 mL. Catalytic reaction: **•** [cysteine] = 3.00×10^{-2} M, [1,3,2-oxazaphosphole] = 0.60×10^{-3} M, [O₂] = 3.54×10^{-3} M, V (MeOH: H₂O) = 30 mL.



Figure S4 Autoxidation reaction and catalytic oxidation of glutathione. Autoxidation reaction: • [GSH] = 54.47×10^{-3} M, [O₂] = 3.54×10^{-3} M, V (MeOH: H₂O) = 30 mL. Catalytic reaction: **•** [GSH] = 54.47×10^{-3} M, [1,3,2-oxazaphosphole] = 0.60×10^{-3} M, [O₂] = 3.54×10^{-3} M, V (MeOH: H₂O) = 30 mL.



Mass spectrum of diphenyl-disulfide.

Figure S5 GC-MS of the product of the catalytic oxidation of thiophenol.



Figure S6 Infrared spectrum of diphenyl-disulphide.



Figure S7 Infrared spectrum of cystine.

(Roller J. Keller: The Sigma of library of FT-IR spectra, Vol 1., 1986, p121)



Figure S8 Infrared spectrum of glutathione disulfide.

(Shayani-Jam, H.; Nematollahi, D. Chem. Com, 2010, 46, 409)



Figure S9 ¹H NMR spectrum of cystine.

(C. J. Pouchert, J. Behnke The Aldrich Library of ¹³C and ¹H FT NMR Spectra, Vol. 1., 484B, USA, 1993)



Figure S10 ¹³C NMR spetrum of cystine.

(C. J. Pouchert, J. Behnke The Aldrich Library of ¹³C and ¹H FT NMR Spectra, Vol. 1., 484B, USA, 1993)



Figure S11 ¹H NMR spectrum of glutathione disulfide.

(C. J. Pouchert, J. Behnke The Aldrich Library of ¹³C and ¹H FT NMR Spectra, Vol. 1., 484C, USA, 1993)



Figure S12 ¹³C NMR spectrum of glutathione disulfide.

(C. J. Pouchert, J. Behnke The Aldrich Library of ¹³C and ¹H FT NMR Spectra, Vol. 1., 484C, USA, 1993)



Figure S13 Dependence of formation rate of [PhSSPh] on the starting concentration of PhSH in the oxidation of PhSH. [1,3,2-oxazaphosphole]₀ = 2.00×10^{-3} M, [O₂] = 9.50×10^{-3} M, 25 mL MeOH, T = 298 K.



Figure S14 Rate dependence of the oxidation of cysteine on the initial concentration of cysteine. [1,3,2-oxazaphosphole]₀ = 6.00 × 10⁻³ M, $[O_2]$ = 3.54 × 10⁻³ M, 30 mL MeOH:H₂O (2:1), T = 298 K.



Figure S15 Rate dependence of the oxidation of GSH on the initial concentration of GSH. $[1,3,2-xaconstandowsphole]_0 = 0.60 \times 10^{-3} \text{ M}$, $[O_2]= 3.54 \times 10^{-3} \text{ M}$, 30 mL MeOH: H₂O (2:1), T=298 K.



Figure S16 The dependence of [PhSSPh] formation rate on the starting catalyst concentration in the oxidation of PhSH. [PhSH]₀ = 45.00×10^{-3} M, [O₂] = 9.50×10^{-3} M, 25 mL MeOH, T = 298 K.



Figure S17 The dependence of reaction rate of the oxidation of cysteine on the initial catalyst concentration. [cysteine]₀ = 3.00×10^{-2} M, [O₂] = 3.54×10^{-3} M, 30 mL MeOH:H₂O (2:1), T = 298 K.



Figure S18 The dependence of reaction rate of the oxidation of GSH on the initial catalyst concentration. [GSH]₀ = 47.50 ×10⁻³ M, [O₂] = 3.54×10^{-3} M, 30 mL MeOH:H₂O (2:1), T=298 K.



Figure S19 Plot of 2d[PhSSPh]/dt in the oxidation of PhSH versus dioxygen concentration. [PhSH]₀ = 45.00×10^{-3} M, [1,3,2-oxazaphosphole]₀ = 2.00×10^{-3} M, 25 mL MeOH, T = 298 K.



Figure S20 Plot of oxidation rate of cysteine versus dioxygen concentration. [cysteine]₀ = 3.00×10^{-2} M, [1,3,2-oxazaphosphole]₀ = 6.00×10^{-4} M, 30 mL MeOH:H₂O (2:1), T = 298 K.



Figure S21 Plot of oxidation rate of GSH versus dioxygen concentration. [GSH]₀ = 47.50×10^{-3} M, [1,3,2-oxazaphosphole]₀ = 0.60×10^{-3} M, 30 mL MeOH: H₂O (2:1), T = 298 K.



Figure S22 The Arrhenius plot of the oxidation of PhSH.



Figure S23 The Eyring plot of the oxidation of PhSH.



Figure S24 The Arrhenius plot of the oxidation of cysteine.



Figure S25 The Eyring plot of the oxidation of cysteine.



Figure S26 The Arrhenius plot of the oxidation of glutathione.



Figure S27 The Eyring plot of the oxidation of glutathione.

Exp. No	Т (К)	[O ₂] (10 ⁻³ mol dm ⁻³)	[1,3,2- oxazaphosphole] (10 ⁻³ mol dm ⁻³)	[PhSH] (10 ⁻³ mol dm ⁻³)	2d[PhSSPh]/dt (10 ⁻⁶ Ms ⁻¹)	k₂ ^{₽hSH} (mol⁻¹dm³s⁻¹)
1.	298	9.50	2.00	20.00	10.60 ± 0.35	0.56±0.06
2.	298	9.50	2.00	30.00	10.67 ± 0.47	0.56±0.06
3.	298	9.50	2.00	45.00	10.70 ± 0.50	0.56±0.06
4.	298	9.50	2.00	50.00	10.79 ± 0.65	0.57±0.06
5.	298	9.50	2.00	100.00	10.70 ± 0.52	0.56±0.06
6.	298	9.50	1.00	45.00	4.58 ± 1.81	0.48±0.08
7.	298	9.50	1.50	45.00	7.18 ± 1.20	0.50±0.02
8.•	298	2.00	2.00	45.00	2.14 ± 0.19	0.54±0.14
9.	298	4.35	2.00	45.00	4.69 ± 0.72	0.57±0.07
						avg.: 0.55±0.03
10.	303	9.48	2.00	45.00	13.54 ± 1.86	0.69±0.13
11.	308	9.46	2.00	45.00	15.13 ± 2.56	0.80±0.17
12.	313	9.44	2.00	45.00	17.04 ± 3.84	0.90±0.22

Table S1 Summary of kinetic date for PhSH oxidation.

under air

Exp. No.	Temp. (K)	[O ₂] (10 ⁻³ mol dm ⁻³)	[1,3,2- oxazaphosphole] (10⁴ mol dm³)	[cysteine] (10 ⁻² mol dm ⁻³)	2d[cystine]/d <i>t</i> (10 ⁻⁶ Ms ⁻¹)	t k ₂ ^{cysteine} (mol ⁻¹ dm³s ⁻¹)
1.	298	3.538	3.00	3.00	1.15 ± 0.44	1.08±0.23
2.	298	3.538	4.50	3.00	1.73 ± 0.22	1.08±0.31
4.	298	3.538	7.50	3.00	3.21 ± 0.36	1.21±0.45
5.	298	3.538	9.00	3.00	3.74 ± 0.58	1.17±0.65
6.	298	3.538	6.00	2.00	2.67 ± 0.14	1.25±0.27
7.	298	3.538	6.00	2.50	2.52 ± 0.20	1.18±0.30
8.	298	3.538	6.00	3.00	2.76 ± 0.20	1.29±0.25
9.	298	3.538	6.00	3.50	2.40 ± 0.20	1.12±0.30
10.	298	3.538	6.00	5.50	2.45 ± 0.19	1.15±0.30
11.•	298	0.743	6.00	3.00	0.76 ±0.64	1.70±0.55
12.	298	2.436	6.00	3.00	2.17± 0.14	1.48±0.23
						avg.:1.25±0.18
13.	303	3.456	6.00	3.00	2.84 ± 0.24	1.37 ±0.27
14.	308	3.455	6.00	3.00	2.99 ± 0.31	1.44 ±0.24
15.	313	3.454	6.00	3.00	3.15 ± 0.38	1.52 ±0.33

 Table S2
 Summary of kinetic date for cysteine oxidation.

•under air

Exp. No.	Temp .(K)	[O ₂] (10 ⁻³ mol dm ⁻³)	[1,3,2- oxazaphosphole] (10 ⁻³ mol dm ⁻³)	[GSH]₀ (10 ⁻³ mol dm ⁻³)	2d[GSSG]/d <i>t</i> (10 ⁻⁶ Ms ⁻¹)	k ₂ glutathione (mol ⁻¹ dm ³ s ⁻¹)
1.	298	3.538	0.60	27.40	0.9011 ± 015	0.42±0.10
2.	298	3.538	0.60	40.48	0.8941 ± 0.15	0.42±0.06
3.	298	3.538	0.60	47.46	0.8780 ± 0.14	0.41±0.03
4.	298	3.538	0.60	54.43	0.8500 ±0.14	0.40±0.10
5.	298	3.538	0.30	47.46	0.4310 ±0.01	0.41±0.01
6.	298	3.538	1.00	47.46	1.8457 ±0.46	0.52±0.20
7.•	298	0.743	0.60	47.46	0.1508 ± 0.08	0.34±0.01
8.	298	1.982	0.60	47.46	0.4745 ±0.04	0.40±0.01
						avg.: 0.42±0.05
9.	303	3.456	0.60	47.46	0.9245 ± 0.17	0.45±0.03
10.	308	3.455	0.60	47.46	0.9561 ± 0.18	0.46±0.03
11.	313	3.454	0.60	47.46	1.0308 ± 0.20	0.49±0.04

Table S3 Summary	y of kinetic date for	glutathione oxidation.
	/	

• under air