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CATALYTIC OXIDATION OF THIOLS BY COENZYME PQQ

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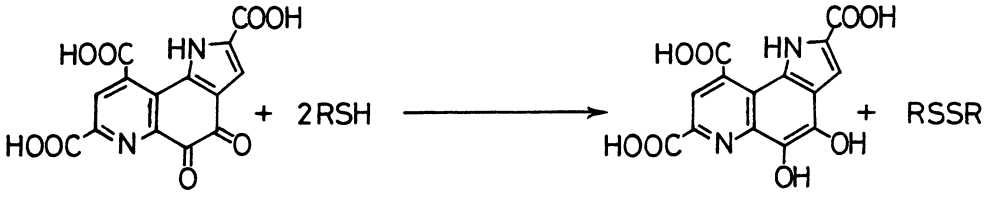
Oxidation of thiols by coenzyme PQQ as a new enzymatic oxidation-reduction model was found to proceed catalytically under aerobic conditions to give corresponding disulfides.

PQQ is a novel coenzyme playing an important role in alcohol and amine dehydrogenases and amine oxidases.[1—3] Recently, we reported that PQQ oxidizes amines and amino acids catalytically in the presence of a cationic micelle under aerobic conditions.[4] Meanwhile, oxidation of thiols to disulfides with electron deficient organic reagents such as flavins has been of much concern in connection with the enzymatic oxidation-reduction process. Duine and his coworker showed hitherto that the prosthetic group of methanol dehydrogenase is reduced by 2-mercaptoethanol.[5] In this communication, we wish to report the effective catalytic oxidation of thiols by coenzyme PQQ. The oxidation of thiols by quinonoid compounds has not been investigated so widely except for the oxidation of thiols catalyzed by hydroquinone derivatives.[6]



PQQ $\qquad$ $PQQH_2$

In the reaction of PQQ[7] (2.5×10 M) and benzenethiol (0.25 M) under anaerobic conditions, diphenyl disulfide was obtained in 99% yield based on PQQ.[8] When the reaction was carried out under aerobic conditions, effective catalytic systems were constructed to give the disulfide in 4270% yield which was only 152% in the absence of PQQ. Benzenemethanethiol and 1-propanethiol were also converted into the corresponding disulfides catalytically. 2-Methyl-2-propanethiol, on the other hand, was not oxidized under the same conditions, but in the presence of a cationic micelle (CTAB) it was oxidized efficiently to di-t-butyl disulfide (2320%).[10] The results are summarized in Table 1.

Interestingly, an asymmetric disulfide, t-butyl phenyl disulfide, was predominantly produced in 66% yield based on thiols (diphenyl disulfide : 8%, di-t-butyl disulfide : 0%) in the reaction of benzenethiol (0.12 M) and 2-methyl-

2-propanethiol (0.12 M) in the presence of CTAB under the same conditions. The asymmetric selectivity, however, reduced in the reaction of 1-propanethiol and benzenethiol (diphenyl disulfide : 24%, n-propyl phenyl disulfide : 51%, di-n-propyl disulfide : 12%). In order to clarify the mechanism of the present reaction, kinetic studies are in progress now.

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Table 1. Oxidation of Thiols by Coenzyme PQQ[a)]

Thiol	pH		Yield of disulphide / % [b)]
	Initial	Final	
PhSH	6.87	10.18	4270
	7.10	7.33	152 [c)]
$PhCH_2SH$	6.88	8.70	4169
	6.87	8.07	246 [c)]
n-PrSH	6.64	8.90	3042
	6.80	8.78	60 [c)]
t-BuSH	6.98	8.97	trace
	7.38	8.43	2320 [d)]

a) After quantitative hydrolysis of PQQTME[7)] (PQQ-trimethyl ester, 0.025 mmol) to PQQ in 0.05 M Na_2CO_3 aqueous solution (10 ml), thiol (2.5 mmol) was added. The initial pH was adjusted with 0.5 M HCl, and the reaction was carried out at 30 °C under aerobic conditions for 24 h.
b) Yields were determined by GLC based on PQQ.
c) Control experiments without PQQ : Yields were determined by GLC based on PQQ (0.025 mmol) which is assumed to be added.
d) CTAB (cetyltrimethylammonium bromide, 0.25 mmol) was added.

References

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8) When a 0.1M phosphate buffer solution (containing 20% acetonitrile, pH 6.2) of PQQ (4×10^{-5}M) was mixed with approx. 100-fold excess of benzenethiol (4×10^{-3}M) under anaerobic conditions (N_2), an increase in the absorption of $PQQH_2$ (quinol) at 310 nm was observed. After a few minutes, the spectrum changed completely to that of $PQQH_2$. The pseudo-first-order rate constant (k_{obsd}) was $1.3 \times 10^{-1}s^{-1}$ at 30 °C. The formation of $PQQH_2$ was also confirmed by HPLC analysis.[9)]
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