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MILD AND CATALYTIC OXIDATIVE CLEAVAGE OF C-S BOND OF SULFIDES WITH Co(II)(BZACEN) UNDER OXYGEN ATMOSPHERE

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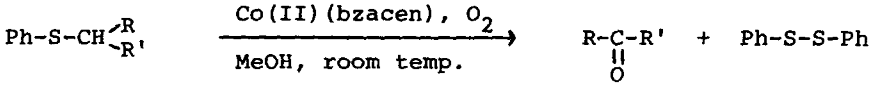
There are many examples of dealkylation of N-alkylamines in biological systems in which monooxygenase enzymes such as cytochrome P-450,[1] and horse radish peroxidase[2] take part in the dealkylation, while S-dealkylation of sulfides is also known but only with non-purified oxygenase systems.[3] In searching an enzymatic model reaction for the oxidative C-S bond cleavage (dealkylation) of sulfides, we have carried out the reaction of sulfides with Co(II)(bzacen) under oxygen atmosphere, and found that oxidative C-S bond cleavage of sulfides took place under mild conditions.

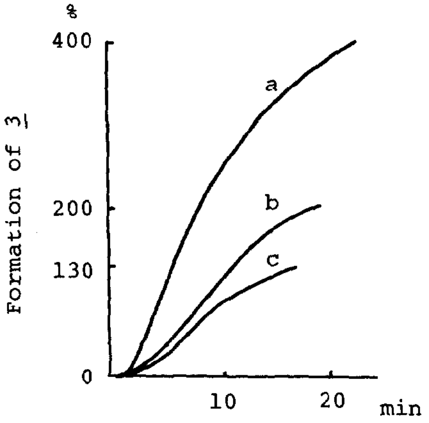
When oxygen gas was bubbled into a methanol solution of either one of the alkyl phenyl sulfides (1) having an acidic α-hydrogen and a catalytic amount of Co(II)(bzacen)[4] (molar ratio to sulfide : 1/8 - 1) at room temperature, oxidative cleavage of C-S bond of the sulfide took place, eventually yielding the corresponding carbonyl compound (2) and diphenyl disulfide (3) generally in high yields.



$$\text{Ph-S-CH}\begin{smallmatrix}R\\R'\end{smallmatrix} \xrightarrow[\text{MeOH, room temp.}]{\text{Co(II)(bzacen), O}_2} \text{R-}\underset{\underset{\text{O}}{\|}}{\text{C}}\text{-R'} + \text{Ph-S-S-Ph}$$

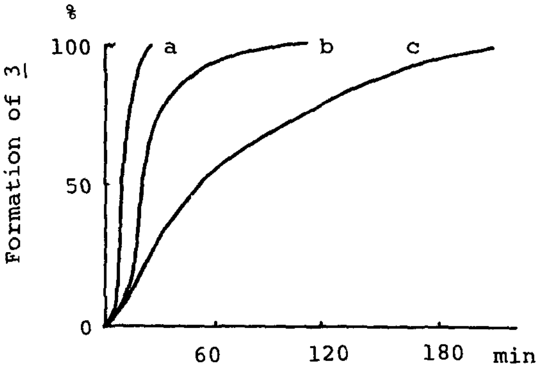
1 2 3

a) R = H, R'= COPh b) R = H, R'= CN c) R = H, R'= COOEt
d) R = H, R'= C_6H_4-NO_2-p e) R = R'= Ph f) R = Me, R'=COOEt



PhSCH$_2$COPh + Co(II)(bzacen)
4, 2, 1.3 eq.
a: Co/1a = 1/4 b: Co/1a = 1/2
c: Co/1a = 1/1.3
Co = 7.2 x 10^{-3} mole/l

Figure 1



PhSCH$_2$COPh + Co(II)(bzacen)
1/2, 1/4, 1/8 eq.
a: Co/1a = 1/2 b: Co/1a = 1/4
c: Co/1a = 1/8
1a = 2.5 x 10^{-2} mole/l

Figure 2

In the presence of 1/4 molar equivalent of the catalyst, oxidative cleavage of the β-keto sulfide (1a) took place quantitatively at room temperature in methanol within 30 min during which an equimolar amount of oxygen was absorbed. After removing the catalyst by adsorption through an ion exchange resin [Dowex 50W-8 (H$^+$ form)], and replacing methanol by methylene chloride, treatment of the mixture with excess diazomethane gave finally the product mixture which was analyzed by glc. Thus 2a and 3 were found to be formed in 81% and quantitative yields, respectively, together with small amounts of methyl benzoylformate (13%) and methyl benzoate (5%).

The oxidative cleavage of other alkyl sulfides (1b, 1c and 1d) were also found to proceed catalytically in methanol solution at room temperature but required longer reaction times to complete. Namely, 1b gave 3 (1.5%, 37 hr, Co/1b = 1/123; quant. yield, 15 hr, Co/1b = 1), 1c gave 3 (52%, 78 hr, Co/1c = 1/4; quant. yield, 20 hr, Co/1c = 1), and 1d gave 2d (50%) and 3 (98%) (48 hr, Co/1d = 1). Meanwhile, the secondary alkyl sulfides (1e and 1f) were found to react with oxygen surprisingly slowly, e.g., 1e gave 2e (13%) and 3 (12%) [5 days

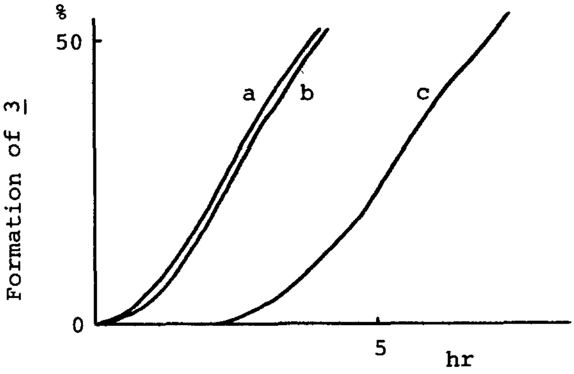


Figure 3

(13% conversion), Co/1e = 1], and 1f gave 3 (2%) [5 days (2% conversion)], Co/1f = 1].

Thus the reactivity of the reaction appears to be strongly dependent on both the acidity of α-hydrogen and the bulkiness of alkyl group attached to the sulfur atom.

In order to draw a rough mechanistic picture of this reaction, several experiments have been conducted. In the kinetic experiments of 1a in methanol, the rate of the reaction was found to be of first-order dependence on both the concentrations of the substrate 1a and that of the catalyst, while a sigmoidal curve was obtained for the formation of 3 against time as shown in Figure 1 and Figure 2. The effect of p-substituent on benzene ring of 1b was observed substantially large as shown in Figure 3. The effect of solvent was quite substantial; e.g., the reaction in methanol was markedly faster than that in methylene chloride or pyridine, in which the reaction proceeded only 2% during when the reaction of 1a in methanol was completed.

When the reaction of 1b was carried out in methanol-d_1, the recovered sulfide was found to have incorporated 70% of deuterium at α-methylene carbon after 50% conversion (4 hr, room temp., Co/1b = 1). The H-D exchange reaction was also found to be somewhat sluggish when the sulfide was treated with Co(II)(bzacen) under argon atmosphere (40% H-D exchange, 4 hr, room temp., Co/1b = 1). Meanwhile, oxidative cleavage reaction of the sulfides (1a and 1b) was found to take place rather slowly without the catalyst in strongly basic media under oxygen atmosphere; e.g., 1a gave 2a (10%), 3 (10%) and 1a (90%, recovered) by the treatment of 1a with NaH in THF under oxygen atmosphere at room temperature for 30 min.

These observations seem to suggest that the reaction proceeds through an initial equilibrium formation of the α-carbanion of the sulfide formed by α-proton abstraction from the complex formed between the sulfide and the cobalt, followed by recombination with molecular oxygen to give the unstable α-hydroperoxysulfide intermediate, which easily decomposes to the carbonyl compound (2) and diphenyl disulfide.

Since no sulfoxide was found to be formed during the reaction of these sulfides while cyanomethyl phenyl sulfoxide did not react at all under the present oxidation system, any sulfoxide or S-peroxygenated intermediate is considered not to be involved in this reaction, although such a S-peroxygenated intermediate was suggested in the reactions of alkyl sulfide with singlet oxygen5) and with ozone6), in which both the S-monooxygenation and the oxidative C-S bond cleavage reactions are known to take place concurrently.

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