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Intramolecular Radical Substitution on the Sulfur of Thioester, Sulfide, Sulfoxide, and Sulfone

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Summary: Alkyl radicals having the sulfur functions such as thioester, sulfide, and sulfoxide at the γ-position gave five membered cyclic thiolactone, sulfide, and sulfoxide, while sulfone did not react with the alkyl radical. The product expected from the sulfuranyl radical intermediate, which can pseudo-rotate, was not obtained.

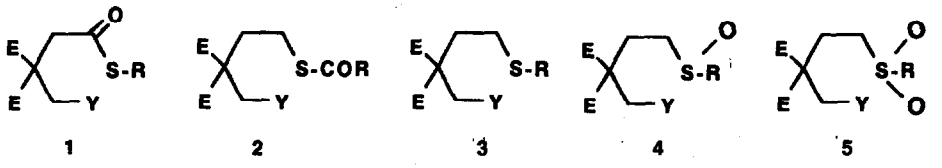
Radical substitutions on the sulfur of disulfide,[1] sulfoxide,[2] sulfinyl ester,[3] and S-sulfonate[4] have already been reported. Not known are many radical substitutions on sulfur functions in which both attacking and leaving groups are carbon-centered radicals. Moreover, reactions of this type are nearly limited to aryl radicals as attacking group.[5] A phenyl-coordinated sulfuranyl radical conceivably behaves in a different manner from an alkyl-coordinated sulfuranyl radical due to π-conjugation with a phenyl group[6] and electronegativity of a phenyl-carbon.[7] Kinetic and theoretical study on sulfide conducted by Franz *et. al.* [8] is the only example of this type with an aliphatic attacking radical. In previous studies we have conducted, we have found radical substitutions on the sulfur of thioesters during the model studies on the coenzyme-B_{12} mediated rearrangement of thioester group; the formation of thiolactone and sulfide (Eq. 1).[9]

(1)

Here, we would like to report radical substitutions on the sulfur functions; thioester, sulfide, sulfoxide, and sulfone. Alkyl-bis(dimethylglyoximato)pyridinecobalt(III), alkylcobaloxime R-Co(dmgH)$_2$Py, generates a pair of alkyl and cobaloxime(II) radicals.[10]

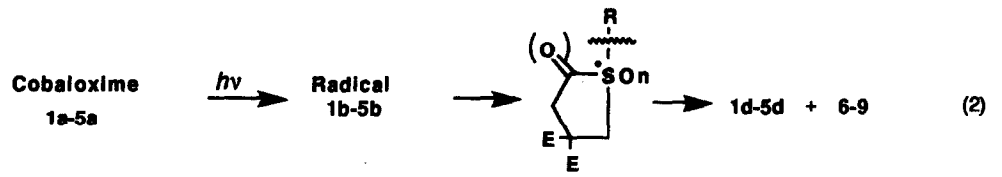
Photolyses of cobaloxime **1a-5a** in benzene or chloroform gave a mixture of hydrogen abstraction products **1d-5d** and intramolecular substitution products **6-9** in the ratio as shown in Eq. 2 and Table 1.

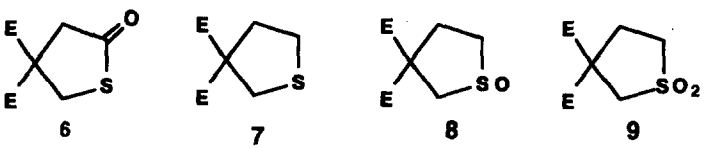
Intramolecular substitutions with radicals **1b-4b** to give thiolactone **6**, cyclic sulfide **7**, and sulfoxide **8** are



E=COOEt 1a-5a: Y = $Co(dmgH)_2Py$ 1b-5b: Y = • (radical)

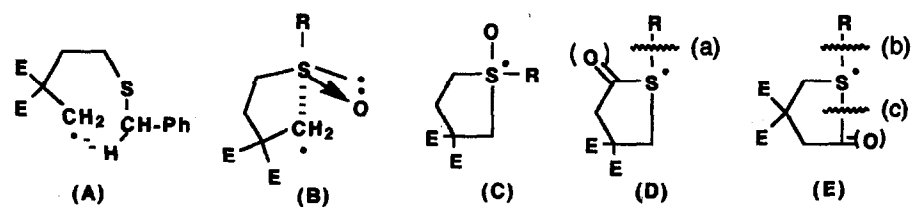
1c-5c: Y = Br 1d-5d: Y = H





facile in benzene. However, radical substitution on the sulfone **5b** to produce **9** very inefficient. In contrast, hydrogen abstraction is a major or comparable process in chloroform, a potent hydrogen donor. Appreciable formation of **3d** (R=benzyl) (19%) even in benzene (entry 6) is accounted for by the 1,6-hydrogen shift as shown in (A).[8]

Photolysis of organocobaloxime generates a cobaloxime(II) radical besides an organo-radical. The former radical may affect the reactivity of the sulfur function to the organo-radical since we have an ample evidence for the complex formation between cobaloxime(II) radical and sulfur functions, sulfide and thioester.[10b] Radicals **1b-5b** were generated in benzene from bromides **1c-5c** by the action of tributylstannyl radical, generated by photolysis of hexabutyldistannane. The products from radicals **1b-5b** are hydrogen abstraction products **1d-5d** and radical substitution products **6-9**, and the distribution between the two products are essentially the same as the photolyses of organocobaloxime **1a-5a** in benzene. Thus, the reactivities of radicals **1b-5b** are not affected by the coexistence of cobaloxime(II) radical in the present system.



The reactivity of sulfide and sulfoxide for the radical substitution seems comparable since the product ratios **7/3d** (R=^{t}Bu, 99/1 in benzene (entry 4) and 56/44 in chloroform (entry 5)) and **8/4d** (R=^{t}Bu, 92/8 in benzene (entry 8) and 54/46 in chloroform (entry 9)) are almost the same and the rates of hydrogen

abstraction must be essentially the same for sulfide and sulfoxide.

The attack of alkyl radical on sulfur proceeds in a nucleophilic manner,[11] and the sulfur of sulfoxide and sulfone is considered to be more electronegative than that of sulfide. This feature predicts the higher reactivity for sulfoxide- and sulfone-sulfur over sulfide-sulfur. The experimental finding, however, can not be rationalized by this principle.

One explanation for this discrepancy is steric hindrance of sulfoxide and sulfone (**B**). As a probe (phenylthio)methyl phenyl sulfoxide, $PhSCH_2SOPh$, was reacted in benzene with the radical, $(EtOOC)_2(Me)CCH_2$, from the corresponding organocobaloxime. This preliminary experiment gave sulfide and sulfoxide in a ratio of 10:1. Steric hindrance must be more crucial in intermolecular reaction than in intramolecular reaction since the two reaction centers in the latter are already in a close relation. Another presumably more decisive factor is the formation of the unproductive sulfuranyl radical intermediate of the type **C** from sulfoxide and sulfone. In a three - five coordinated sulfuranyl radical of T-shape, the two most electronegative ligands take apical sites and possess elongated bond distances.[12] These elongated apical groups are expected to be entering and leaving groups at the transition state of the substitution. Sulfoxide and sulfone, therefore, are expected to form the sulfuranyl radical intermediate in which oxygen occupies one of the apical sites. This sulfuranyl radical, however, is unproductive and regenerates the attacking organo-radical. Sulfone is the least reactive function to an organo-radical as deduced from these considerations and the experimental findings.

Table 1. Reaction of the Radicals Generated from Cobaloximes **1a-5a** by Photolyses.[a)]

Entry	Cobaloxime	R	Solvent	Reaction Time/h	Product/ Composition(%)[d)]		Total Yeld(%)
1[9b]	**1a**	^{t}Bu	benzene	8	**6** / 100	--	81
2	**2a**	^{t}Bu	benzene	10	**7** / 97	**2d** / 3	53
3	**2a**	^{t}Bu	chloroform	10	**7** / 18	**2d** / 82	86
4	**3a**	^{t}Bu	benzene	10	**7** / 99	**3d** / 1	84
5	**3a**	^{t}Bu	chloroform	10	**7** / 56	**3d** / 44	74
6	**3a**	Bn[b)]	benzene	10	**7** / 81	**3d** / 19	52
7	**3a**	Bn[b)]	chloroform	10	**7** / 85	**3d** / 15	70
8	**4a**	^{t}Bu	benzene	15	**8** / 92	**4d** / 8	74
9	**4a**	^{t}Bu	chloroform	15	**8** / 54	**4d** / 46	51
10	**4a**	Bn[b)]	benzene	15	**8** / 96	**4d** / 4	45
11	**4a**	Bn[b)]	chloroform	15	**8** / 85	**4d** / 15	53
12	**5a**	^{t}Bu	benzene[c)]	18	**9** / 1	**5d** / 99	e)
13	**5a**	^{t}Bu	chloroform	18	--	**5d** / 100	74
14	**5a**	Bn[b)]	benzene[c)]	18	--	**5d** / 100	e)
15	**5a**	Bn[b)]	chloroform	18	--	**5d** / 100	70

a) Solutions containing cobaloximes **1a-5a**(3.0×10^{-3} mol/l) were externally irradiated with a 400 w high pressure mercury lamp through Pyrex reaction vessels.
b) Bn denotes benzyl group.
c) Containing 6% of ethanol to make the cobaloximes soluble.
d) Yields and compositions were determined by *vpc*-analyses using internal reference, benzophenone or phenyl tosylate for the thioester and sulfides, phenyl tosylate or triphenylmethane for sulfoxides and sulfones.
e) The solutions became nontransparent while a part of the starting materials remain intact.

Experimental and theoretical studies[8,12,13] showed that the sulfuranyl radical having an electronegative ligand is an observable species but a trialkyl sulfuranyl radical has no energy minimum. Hypothetical T-shaped sulfuranyl radical intermediate can give the products by an "*a-fission*" in D or conceivably by a "*b-fission*" in E, a pseudo-rotational isomer of D, but no "*c-fission*" (E) was observed experimentally.

The results described here as well as those reported in literatures[2,6] favor a concerted S_Hi mechanism with inversion rather than a stepwise mechanism through a sulfuranyl radical intermediate.

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