Radical Substitution on the Sulphur of Thioester Group

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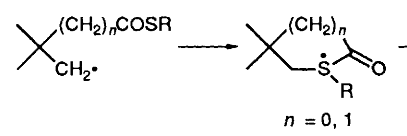
Intermolecular reaction of an organo-radical with thioester gives the sulphide, which is formed by the sulphur centred substitution of acyl groups with a nucleophilic organo-radical, but no displacement of *S*-alkyl groups with the organo-radical takes place.

Radical substitution on the sulphur atom of disulphide[1–3] and sulphinyl ester[4,5] has been well studied. However, only a limited number of examples have been reported for the radical substitution in which attacking and leaving groups are both carbon-centred radicals, and this type of radical substitution has been known to occur only intramolecularly, and the entering group is mostly an aryl radical.[6–9] In these reactions a sulphuranyl radical is believed to be an intermediate.[10]

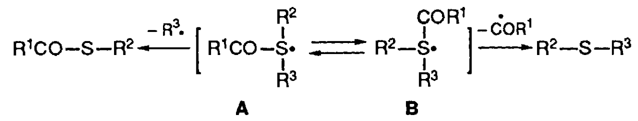
In the studies of the coenzyme-B_{12} model, we have found that 2- and 3-(alkylthiocarbonyl)alkyl radicals undergo intramolecular radical substitution to afford β- and γ-thiolactones (Scheme 1).[11,12] In these thiolactonisations the attacking radical ($\cdot R^3$) and the leaving radical ($\cdot R^2$) can take a co-linear alignment in the sulphuranyl radical intermediate **A** (Scheme 2), but the acyl group cannot be co-linear with the entering radical as in **B**. This stereocontrol seems to be the reason for the preferential formation of thiolactones by *S*-alkyl fission instead of *S*-acyl fission.

In this communication we report the first example of the intermolecular reaction of an organo-radical with thioesters, in which the attacking radical can take co-linear geometry with either the *S*-alkyl **A** or the *S*-acyl group **B** (Scheme 2). Electronic control, therefore, must overcome the stereocontrol observed in the thiolactonisation by radical substitution.

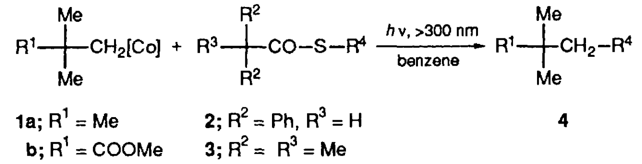
Photolysis of organocobaloxime, $(dmgH)_2PyCoR$, has been well characterised to give an alkyl and cobaloxime radical



Scheme 1



Scheme 2



Scheme 3

pair.[13-16] Thus, the photolysis of neopentylcobaloxime **1a** or (2-methoxycarbonyl-2-methyl)propylcobaloxime **1b** in the presence of thioester **2** or **3** gave sulphide **4** in the yields shown in Table 1 (Scheme 3). The photolyses were continued until the starting cobaloxime **1a** or **1b** had disappeared. The reaction with **2** gave triphenylmethane as a by-product which was formed by the reaction between the solvent (benzene) and the diphenylmethyl radical, formed by the decarbonylation of the primarily formed diphenylacetyl radical. We could not detect the ketonic product that was anticipated to form by the direct attack of the organo-radical on the carbonyl carbon of the thioester group. Further, we detected no product formed by the *S*-alkyl or *S*-aryl (S–R^4) fission as observed in the intramolecular radical substitution (Scheme 1), which seemed to proceed under stereocontrol.†

These results indicate that electronic control operates in these reactions and that the polar acyl group rather than the less polar alkyl group takes an apical geometry for the ready radical fission as shown in Scheme 2.[10]

Among the reactions of arylthioesters with an organo-radical, 4-chlorobenzenethioesters **2** and **3**, (R^4 = 4-Cl–C_6H_4) gave higher yields of **4** than did benzenethio- and 4-methoxybenzenethio-esters. 4-Methoxybenzenethioesters **2** and **3** (R^4 = 4-$MeOC_6H_4$) gave the lowest yield among the arylthioesters. This feature indicates that the radical substitution on the sulphur of thioester groups proceeds by the attack of organo-radical in nucleophilic manner and the attacking organo-radical interacts with a σ^*-orbital of the *S*-acyl bond.

These results suggest that the rate-determining step is the formation of the sulphuranyl radical. We do not know the exact nature of the decay process of the sulphuranyl radical, kinetically or thermodynamically controlled. The discussions in this communication, however, emphasise the rate-determining formation step of the sulphuranyl radical and should be valid whatever the nature of the decay process of the intermediate.

The radical derived from *N*-(3-methoxycarbonyl-3-methylbutyroxy)-pyridine-2-thione **5**[17] gave the product **4** (R^1 = CO_2Me, R^4 = Ph) when reacted with **2**. Thus, the radical substitution on the sulphur of the thioester group does not require the coexistence of the cobalt(II) species, cobaloxime(II).

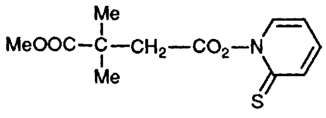


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Table 1 Photoreaction[a] of organocobaloximes with thioesters

		Product 4		
Cobaloxime	Thioester	R^1	R^4	Yield (%)[b]
1a	**2**	Me	4-MeO-C_6H_4	56
1a	**2**	Me	Ph	81
1a	**2**	Me	4-Cl-C_6H_4	84
1a	**2**	Me	$PhCH_2CH_2$	70
1b	**3**	CO_2Me	4-MeO-C_6H_4	43
1b	**3**	CO_2Me	Ph	64
1b	**3**	CO_2Me	4-Cl-C_6H_4	78
1b	**3**	CO_2Me	$PhCH_2CH_2$	77

[a] Photolysis conditions: Internal irradiation by a 100 W high-pressure mercury lamp mounted in a Pyrex water-cooling jacket. **1a** (1×10^{-4} mol) and **2** (1×10^{-3} mol) in 50 ml of benzene; irradiation, 7 h **1b** (8.4×10^{-5} mol) and **3** (2.0×10^{-3} mol) in 50 ml of benzene; irradiation, 50 h. [b] Isolated yield from the chromatography on a silica-gel plate developed by hexane–benzene (9 : 1)

In conclusion, the substitution of the thioester with an organo-radical proceeds by the rupture of *S*-acyl bond under electronic control.

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† Photolysis of **1a** was completed in a shorter irradiation time and the formation of by-products by the direct photolysis of **2** was negligible. Photolysis of **1b**, however, required longer irradiation than **1a** owing to the deterioration of the reaction mixture, and **3** was photolysed in part to give the by-products, mainly t-butyl aryl sulphide, which were confirmed by the direct photolysis.