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A NOVEL RADICAL CHAIN REACTION OF XANTHIC ANHYDRIDES. FURTHER OBSERVATIONS ON THE INTERMEDIACY OF ALKOXY-THIOCARBONYL RADICALS IN THE BARTON-McCOMBIE REACTION.

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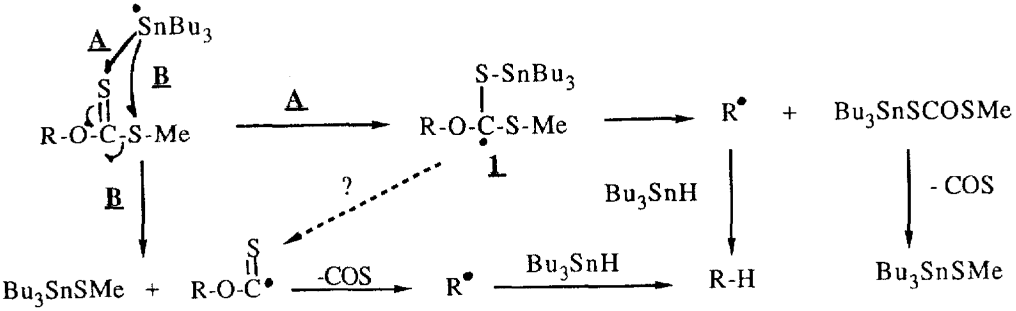
Summary . On irradiation with visible light, primary and secondary xanthic anhydrides undergo a radical chain reaction to give the corresponding xanthates with loss of carbon oxysulphide.

In their pioneering paper on the radical deoxygenation of secondary alcohols through their xanthate derivatives, Barton and McCombie[1] proposed the chain mechanism displayed in scheme 1 (path A). Recently however, Beckwith and Barker[2] put forward an alternative mechanistic pathway whereby attack of the stannyl radical takes place on the sulphide sulphur rather than on the thiocarbonyl group as shown in scheme 1 (path B). This proposal follows in the main from the observation of e.s.r. signals corresponding to an alkoxythiocarbonyl radical **2** on U.V. irradiation of a solution of xanthate and hexamethylditin.

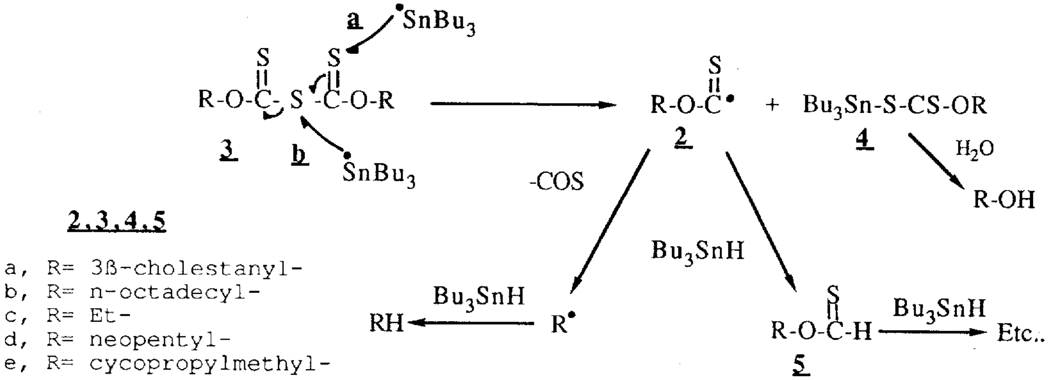


Scheme 1

Subsequent mechanistic studies by the Barton group provided strong, and in our view compelling, evidence for the original mechanism, which was slightly modified to include a reversible first step[3]. This was further corroborated by Bachi and Bosch[4] who succeeded in capturing intramolecularly the intermediate radical **1**.

However the validity of this latter experiment was very recently questioned by Crich who invoked, without adducing any experimental or theoretical evidence, the possibility of a cage mechanism [5]

The formulation of Beckwith and Barker hinges on the assumption that a secondary alkoxythiocarbonyl radical readily looses carbon oxysulphide (COS) under the usual reaction conditions. In order to find out whether this was indeed the case, an unambiguous source of alkoxythiocarbonyl radicals is required. Symmetrical xanthic anhydrides **3** appeared to be ideal candidates since, as portrayed in scheme 2, attack by tributylstannyl radicals from tributylstannane either at the thiocarbonyl group or at the sulpide sulphur would give the same products, namely an alkoxythiocarbonyl radical **2** and the tin xanthate **4**. This approach should therefore provide alkoxythiocarbonyl radicals irrespective of the mechanism actually operating. Expulsion of COS would give an alkyl radical R. and thence the corresponding alkane RH by hydrogen abstraction from the stannane. If loss of COS is difficult, the reaction would lead to thioformate **5** or to products derived therefrom. The tin xanthate **4** can also be further converted into RH by the stannane[3] but, if only equimolar amounts of the latter are used, quantitative analysis of the products should still lead to valid conclusions.



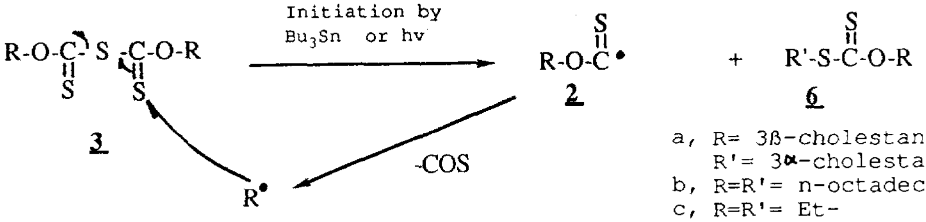
2,3,4,5

a, R= 3ß-cholestanyl-
b, R= n-octadecyl-
c, R= Et-
d, R= neopentyl-
e, R= cycopropylmethyl-

Scheme 2

This conjecture was tested using xanthic anhydride **3a** which is easily prepared by treating sodium or lithium O-cholestanyl xanthate with methyl chloroformate by analogy with the method described by Barany and co-workers[6]. Heating **3a** with one equivalent of tributylstannane and 5 mol% of azo- bis-isobutyronitrile (AIBN) in refluxing toluene for 5 minutes resulted in the formation of cholestane in a crude yield of 33% along with the corresponding amount of cholestanol, formed by hydrolysis of **4a**. The major compound, isolated in 57% yield, was identified as xanthate **6a**. The formation of this side product most logically arises through the chain mechanism depicted in scheme 3, in which the stannyl radicals act simply as initiators. Indeed, **3a** could be completely transformed into **6a** by using only 5% tributylstannane and AIBN. The 3-cholestanyl radicals produced by COS extrusion from **2a** react preferentially with either of the thiocarbonyl groups in the starting anhydride **3a** from the less hindered α- side to give the observed stereochemistry.

The same xanthate could be obtained in high yield by mere irradiation with visible light of a refluxing toluene solution of **3a** alone ; the yellow colour was discharged within minutes. This novel photochemical conversion, which took place rapidly even at 0°C, did not occur thermally when light and oxygen were rigorously excluded. Mechanistically, the process is akin to the photo-decarbonylation of acyl xanthates[7].



a, R= 3β-cholestanyl-;
R'= 3α-cholestanyl-
b, R=R'= n-octadecyl-
c, R=R'= Et-
d, R=R'= neopentyl-
e, R= Et-; R'= neopentyl-
f, R= neopentyl-; R'=Et-
g, R= 3-butenyl-;
R'= cyclopropylmethyl-

Scheme 3

It is clear from these results that secondary alkoxythiocarbonyl radicals readily extrude carbon oxysulphide in contrast to their alkoxycarbonyl counterparts which require much higher temperatures[8]. In fact, loss of COS is facile even from primary alkoxythiocarbonyl radicals as evidenced by the rapid (ca.5 min.) photochemical conversion of xanthic anhydride **3b** into the known xanthate **6b** in refluxing toluene or even benzene. It is worthy of note that, in this case, hardly any reaction was observed when the irradiation was carried out at or below room temperature. As with acyl radicals derived from acyl xanthates[7], the reaction of the alkoxythiocarbonyl radical **2** with its precursor **3** is degenerate; hence an apparent lack of reactivity at low temperature when expulsion of carbon oxysulphide is slow. In the same manner, the corresponding diethyl and di-neopentyl derivatives **3c** and **3d** afforded **6c** and **6d** respectively in essentially quantitative yield.

That these transformations were indeed radical chain processes could be easily demonstrated by a crossover experiment, carried out by irradiating an equimolar mixture of **3c** and **3d**. The expected four products **6c**, **6d**, **6e**, and **6f** were produced in comparable amounts as shown by chromatographic (capillary GC) and spectroscopic comparison with authenthic specimens, prepared by standard methods. Further confirmation of the radical nature of the intermediates was obtained by examining the behaviour of the cyclopropylmethyl derivative **2e** under the same reaction conditions. This compound was cleanly converted into **6g** (93%) with opening of one of the cyclopropyl rings, as would be expected from a cyclopropyl radical[9].

Xanthates of primary alcohols do not undergo significant deoxygenation (i.e. no cleavage of the R-O bond) in refluxing toluene[1,10] let alone at 80°C, even when the concentration of tin hydride is small (inverse addition). It seems therefore that alkoxythiocarbonyl radicals, although clearly present under the experimental conditions of Beckwith and Barker, cannot be major intermediates in the Barton-McCombie reaction. It must be pointed out that their conditions were very different from those normally used for the deoxygenation, since they were carried out *in the absence of a hydrogen atom source*. The alkoxy- thiocarbonyl radicals observed by e.s.r. could in principle arise from the intermediate radical **1** (which now have a longer lifetime in the non-chain situation of Barker and Beckwith), as indicated by the dashed arrow[11] in scheme 1. Our present observations are more in accord with the the (slightly modified) original proposal of Barton and McCombie, as outlined in scheme 1, path A.

Apart from providing an unambiguous and useful source of alkoxythiocarbonyl radicals, this novel photochemical reaction of xanthic anhydrides has far reaching mechanistic and synthetic implications. It constitutes a convenient and mild method for generating carbon radicals from primary and secondary alcohols. These various aspects are currently being examined.

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References:

1. Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1*, **1975**, 1574. For a recent review, see: Hartwig, W. *Tetrahedron*, **1983**, *39*, 2609.
2. Barker P. J.; Beckwith, A. L. J. *J. Chem. Soc., Chem. Commun.*, **1984**, 683.
3. Barton, D. H. R.; Crich, D.; Löbberding, A.; Zard, S. Z. *J. Chem. Soc., Chem. Commun.*, **1985**, 646; idem, *Tetrahedron*, **1986**, *42*, 2329.
4. Bachi, M. D.; Bosch, E. *J. Chem. Soc., Perkin Trans. 1*, **1988**, 1517.
5. Crich, D.; *Tetrahedron Lett.*, **1988**, ***29***, 5805.
6. Barany, G.; Fulpius, B. W.; King, T. P. *J. Org. Chem.*, **1978**, *43*, 2930.
7. Barton, D. H. R.; George, M. V.; Tomoeda, M. *J. Chem. Soc.*, **1962**, 1967. Delduc, P.; Tailhan, C.; Zard, S. Z. *J. Chem. Soc., Chem. Commun.*, **1988**, 308.
8. Kuivila, H. G.; Walsh, E. J. *J. Amer. Chem. Soc.*, **1966**, *88*, 571, 577. Beak, P.; Mojé, S.W. *J. Org. Chem.*, **1974**, *39*, 1320. Pfenninger, J.; Heuberger, C; Graf, W. *Helv. Chim. Acta*, **1980**, 63, 2328. Barton, D. H. R.; Crich, D. *J. Chem. Soc., Chem. Commun.*, **1984**, 774.
9. Maillard, B.; Forrest, D.; Ingold, K. U. *J.Amer. Chem. Soc.*, **1976**, *98*, 7024.
10. Barton, D. H. R.; Motherwell, W. B.; Stange, A. S. *Synthesis*, **1982**, 743. Tulshian, D. B.; Fraser-Reid, B. *Tetrahedron Lett.*, **1980**, *21*, 4549.
11. Similar transformations have been reported for related (but non radical) derivatives; see Bloodworth, A. J.; Davies, A. G.; Vasishtha, S. C. *J. Chem. Soc. (C)*, **1967**, 1309. Reichle, W. T. Inorg. Chem., **1962**, *1*, 650.

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