A Convenient Source of Alkyl and Acyl Radicals

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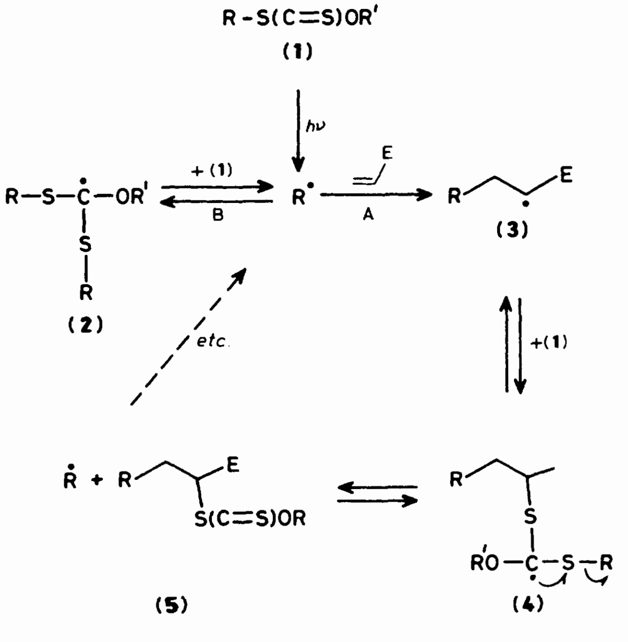
S-Alkyl and *S*-acyl xanthates are valuable sources of alkyl and acyl radicals which can be trapped inter- or intra-molecularly by various alkenes in a radical chain process.

The past few years have witnessed an explosive growth in the use of radical addition reactions for introducing new carbon–carbon bonds.[1] The most versatile procedures exploit an efficient chain process for generating a carbon radical which is then intercepted by an external or internal alkene. The presence of the alkene diverts the original sequence of steps present in the basic process as, for example, in a trialkylstannane-induced radical cyclisation. The cyclisation step, however, has to be faster than hydrogen abstraction by the uncyclised radical. Indeed, the high rate constant for the undesired pathway has effectively confined such cyclisations to the construction of five membered rings.[2]

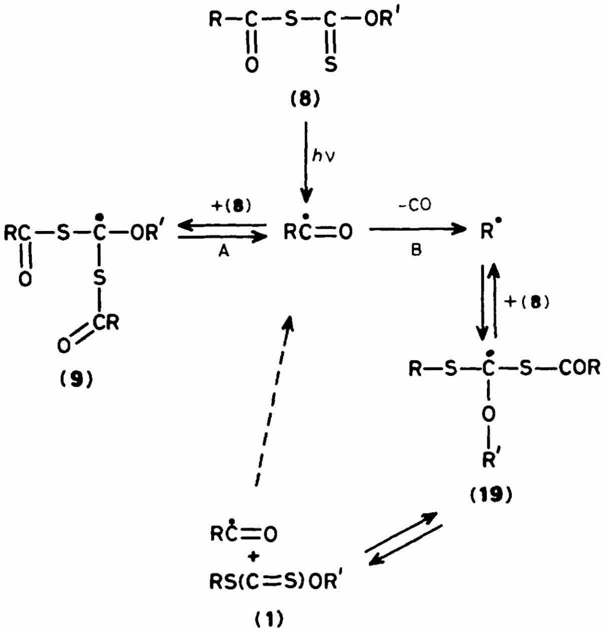
Other methods based on radical chain processes such as those involving organomercury derivatives[1] or Barton's thiohydroxamic esters[3] face the same predicament. A constant and sometimes unfavourable competition thus exists between the desired capture of the radical and its premature quenching by its precursor.

We now report our preliminary results concerning an alternative radical source where such an adverse competition is virtually by-passed. Moreover, the advantages of a chain process, namely a low steady state concentration of the intermediate radical species to avoid unwanted radical–radical interactions, are retained.



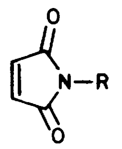
a; R = PhCH$_2$, R' = Me

Scheme 1. E = electron withdrawing group.

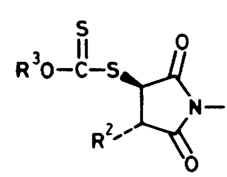


(**8a**), R = Ph, R' = Et
(**8b**), R = PhCH$_2$, R' = Et
(**8c**), R = Bu^t, R' = Et
(**8d**), R = Ph, R' = Me

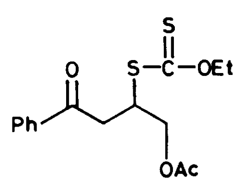
Scheme 2



(6a), R = Me
(6b), R = $PhCH_2$



(7), $R^1 = R^3 = Me$, $R^2 = PhCH_2$
(16), $R^1 = R^2 = PhCH_2$, $R^3 = Et$
(17), $R^1 = PhCH_2$, $R^2 = Bu^t$, $R^3 = Et$



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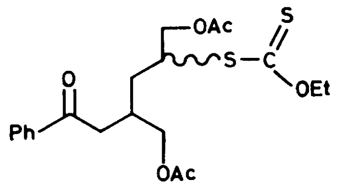

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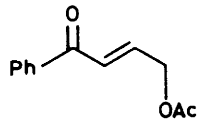

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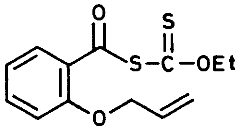

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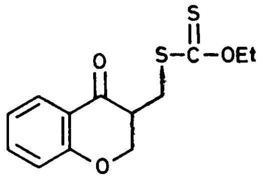

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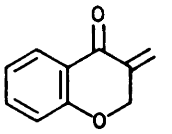

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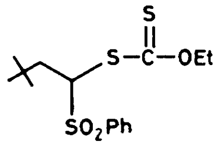

(18)

Our approach becomes clear on considering the fate of a carbon radical R•, generated from xanthate[5] (**1**) by photochemical (or chemical) means, in the presence of an external (or internal) alkene. As outlined in Scheme 1, R• may either add to the alkene (path A) or to the thiocarbonyl group of the starting xanthate to give the symmetrical intermediate (**2**) (path B). If R′ is primary or aromatic (to render β-cleavage through the oxygen difficult),[4] radical (**2**) can only fragment to give back R• and xanthate (**1**). Overall, therefore, the reaction of R• with its xanthate precursor is degenerate.

The feasibility of the process was tested using xanthate (**1a**) and *N*-methylmaleimide (**6a**) as the trap. On irradiation with a u.v. lamp, a reaction occurred to give the expected adduct (**7**) but in only 40% yield. This positive but nevertheless poor performance was ascribed to the fact that the end product was also a xanthate that absorbs in the same wavelength region.

To circumvent this difficulty, we modified slightly our approach and turned to a hitherto little known class of xanthate derivatives, the *S*-acyl xanthates (**8**). These are yellow substances that can act in a similar way as a source of acyl radicals. Indeed, a pioneering investigation by Barton and co-workers[6] revealed that irradiation with visible or u.v. light triggered a decarboxylative rearrangement to give an alkyl xanthate when R was benzylic, tertiary, or even secondary: R-COS(C=S)OR′ → R-S-(C=S)OR′ + CO. The reaction of the acyl radical with its xanthate precursor (**8**) is degenerate [*cf.* intermediates (**2**) and (**9**)], resulting in an apparent lack of reactivity in the case of aromatic, and to a lesser extent primary, derivatives. When decarbonylation of the acyl radical is favoured[7] (R being tertiary or benzylic), an alkyl radical is produced irreversibly. The system can now evolve to the alkyl xanthate (**1**) by a series of *reversible* steps, liberating in the process an acyl radical to propagate the chain (Scheme 2). If this mechanistic view is correct, it should be possible to alter the basic scheme by incorporating an alkene trap as for the simple alkyl xanthates. The advantage in this case is that the reaction can be induced with visible light instead of the less selective u.v. radiation. Moreover, the products will be ordinary alkyl xanthates which do not absorb in the same region of the spectrum.

The benzoyl derivative (**8a**) was first prepared from benzoyl chloride and potassium *O*-ethyl xanthate following the published procedure.[6] When this compound was irradiated with a 250 W tungsten lamp in a refluxing mixture of toluene and allyl acetate, a smooth reaction occurred to give the expected adduct (**10**) in 60% yield. A small amount of what appears to be the double addition product (**11**) was also observed. By way of contrast, no reaction took place in the absence of allyl acetate. A chain process could therefore be established whereby the acyl radical is cleanly captured by a rather unreactive alkene in accord with our initial objective. Treatment of (**10**) with triethylamine–methyl iodide furnished the somewhat sensitive enone (**12**) in 40% yield. A better yield of (**12**) (87% crude, 50% purified) was obtained by heating (**11**) *in vacuo* over Cu powder and collecting the distillate.

The intramolecular version of the novel radical addition also proceeded satisfactorily. The rearrangement of the salicylic acid derivative (**13**) was complete within minutes of irradiation, furnishing the chromanone (**14**) in 70% yield. The readiness with which a six-membered ring is obtained is noteworthy. As above, the xanthate group could be eliminated either with base or by dry distillation from Cu powder to give the reactive enone (**15**) in *ca.* 40% yield. Interestingly, such enones are reported to have appreciable antimicrobial activity.[8]

For cases where the decarbonylation of the acyl radical is fast, the system becomes a useful source of tertiary and benzylic alkyl radicals. Thus, from *S*-acyl xanthates (**8a**) and (**8c**) the corresponding adducts (**16**) and (**17**) were obtained in 70 and 63% yield, respectively, using *N*-benzylmaleimide as the radical trap. Similarly, irradiation of (**8c**) in the presence of phenyl vinyl sulphone gave (**18**) in 45% yield. This sequence therefore constitutes a valuable decarboxylative radical addition.[3]

One interesting feature of this method with potentially far-reaching mechanistic and synthetic implications is the possibility of exploiting the series of reversible steps depicted in Scheme 2 to induce, with visible light, a radical chain reaction from an ordinary alkyl xanthate. Thus irradiation with a tungsten lamp of a mixture of xanthate (**1a**) and *N*-methylmaleimide (**6a**) in the presence of 10 mol % of the benzoyl xanthate (**8a**) increased the yield of (**7**) from the previous figure of 40 to 77%. In the absence of the *S*-acyl xanthate no reaction is observed under these conditions. The benzoyl radicals produced by photochemical scission of (**8a**) react reversibly with (**1a**) to give benzyl radicals *via* an analogue of intermediate (**19**) in Scheme 2. The other product in this reaction is the methyl congener (**8d**) of the original catalyst (**8a**). The catalytic activity is thus regenerated. Finally, addition of the benzyl radicals onto *N*-methylmaleimide propagates the chain.

A mild and convenient source of alkyl and especially acyl radicals is now in hand. Although the present preliminary study is confined to xanthates, other analogous thiocarbonyl derivatives should exhibit a similar behaviour.

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