

## DITHIOCARBONATE GROUP TRANSFER IN RADICAL CHAIN REACTIONS

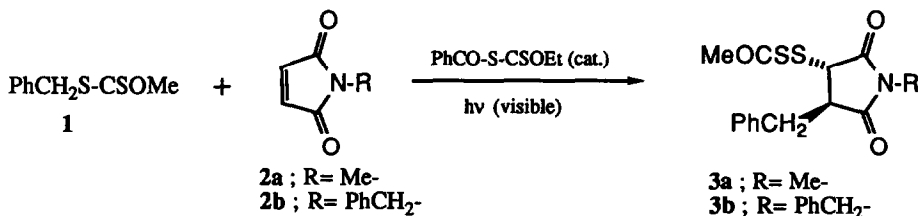
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*Summary: Alkyl and cycloalkyl xanthates can serve as a convenient source of carbon centered radicals in a chain process involving carbon-carbon bond formation, and initiated by a suitable peroxide.*

In the light of the tremendous progress in the use and application of radical methods in organic synthesis, the design and development of new radical processes acquires a special importance<sup>1</sup>. We have recently shown<sup>2</sup> that S-acyl dithiocarbonates (S-acyl xanthates) represented a convenient source of acyl, and in certain cases alkyl, radicals which could be captured in an inter- or intramolecular fashion by suitable olefins. The radical chain process was triggered by visible light and resulted in the formation of at least one new carbon-carbon bond.

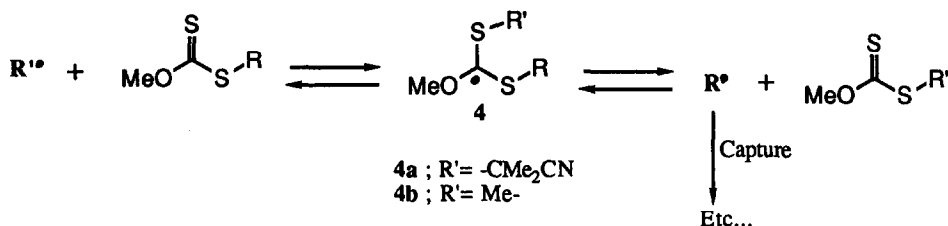
In a further extension, we had shown that S-benzoyl-O-ethyl xanthate in catalytic quantities could induce a radical chain reaction from S-alkyl xanthates using visible light<sup>2</sup>, as shown, for example, by the reaction displayed in scheme 1 which leads to 3a in 77% yield. Unfortunately, this contrivance is only successful in producing resonance stabilised radicals (e.g. a benzylic radical as in the example given), and this imposes some limitation on its synthetic utility.



Scheme 1

In this letter we wish to report a simple variant which circumvents most of the inherent limitations of the photolytic system and allows the obtention of stabilised as well as non-stabilised radicals. The key modification is simply to use di-*t*-butyl or dicumyl peroxide as the initiator.

Our early attempts with chemical initiators, before turning to a combination of visible light and an *S*-benzoyl xanthate, had met with failure. For instance, AIBN (azobisisobutyronitrile) did not induce any reaction leading to **3a**. Presumably, the tertiary isobutyronitrile radical ( $\text{Me}_2\text{C}^\bullet\text{-CN}$ ) produced by thermolysis of AIBN is itself too stabilised to trigger the chain reaction since the intermediate radical **4a** produced through addition to the thiocarbonyl group will have a stronger tendency to be cleaved back to starting materials, rather than to collapse in the desired direction to give radical  $\text{R}^\bullet$ . A combination of AIBN and tributylstannane did result in the production of the desired adduct **3a** but yields were low.

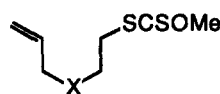


Scheme 2

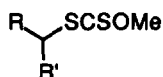
Di-*t*-butyl peroxide, in contrast, decomposes at high temperature (the half-life at 130° C is about 5 hrs) to give initially *t*-butoxy radicals which then fragment into the highly reactive methyl radicals and acetone<sup>3</sup>. In a similar way, di-cumyl peroxide, a nicely crystalline non volatile solid, produces methyl radicals and acetophenone<sup>3</sup>. With these initiators, the corresponding intermediate **3b**, resulting from the very fast addition of a methyl radical onto the xanthate will collapse to give radical  $\text{R}^\bullet$ , in view of the lower stability of a methyl radical as compared with other aliphatic radicals<sup>4</sup>. This should therefore allow access to essentially any aliphatic radical from xanthates, as indeed the following examples will demonstrate.

Heating *S*-5-hexenyl-*O*-methyl xanthate **5** in refluxing chlorobenzene in the presence of 5% di-*t*-butyl peroxide for 6 hrs afforded the cyclopentylmethyl isomer **6** in 61% yield. In a similar manner, the tetrahydrofuranyl derivative **8** was obtained in 57 % yield from the open-chain precursor **7** using 5% di-cumyl peroxide as the initiator. In both these examples, an intermediate unstabilised primary carbon radical is involved.

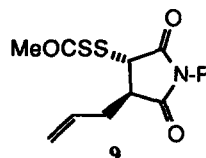
These new conditions were also applicable to cases where the initial radical produced is stabilised. As would be expected, the chain reaction was much faster, taking minutes instead of hours to go to completion. Thus heating a mixture of benzyl xanthate **1**, N-benzyl maleimide **2b** and a catalytic amount of di-*t*-butyl peroxide in chlorobenzene for 30 min. afforded the corresponding adduct **3b** in a yield (78%) comparable to that obtained using the photochemical process<sup>2</sup> displayed in scheme 1. Addition of allyl radicals produced using S-allyl-O-methyl xanthate also took place to give **9** in 53% yield. In the same way, xanthates **10** and **11** gave derivatives **12** and **13**, resulting from capture of the intermediate electrophilic phenacyl and malonyl radicals with allyl acetate, in 72 and 64% yield respectively.



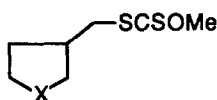
**5**; X = -CH<sub>2</sub>-  
**7**; X = -O-



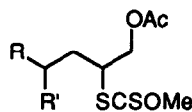
**10**, R = PhCO-; R' = H  
**11**, R = R' = CO<sub>2</sub>Et



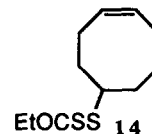
**9**



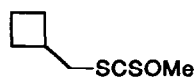
**6**; X = -CH<sub>2</sub>-  
**8**; X = -O-



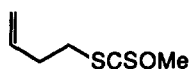
**12**, R = PhCO-; R' = H  
**13**, R = R' = CO<sub>2</sub>Et



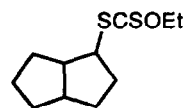
**14**



**16**



**17**



**15**

The fact that the reaction of R<sup>•</sup> with its xanthate precursor is reversible and degenerate (intermediate **4** in scheme 2, with R' = R, is symmetrical; it can only fragment to give back R<sup>•</sup> and starting xanthate) essentially removes what otherwise would have been a serious competing pathway<sup>2a,5</sup>. It is therefore not necessary to work under high dilution conditions or to add the reagents slowly. Moreover, even comparatively slow radical processes can be made to take place. For example, exposure of cyclooctenyl xanthate **14** to the reaction conditions causes smooth conversion into the bicyclic derivative **15** in 60% yield. The unsubstituted 5-cyclooctenyl radical is reputed to cyclise rather slowly<sup>6</sup>. Even the well known reluctance of unsubstituted cyclobutylmethyl radicals towards ring opening<sup>7</sup> can be overcome, as shown by the transformation of xanthate **16** into its open chain isomer **17** (41%).

The present approach for generating carbon radicals allies the advantages of cheapness, ready accessibility of starting materials, and an extremely simple experimental procedure.

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### References and notes.

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3. Walling, C. *Tetrahedron* **1985**, *41*, 3887 and references therein. Direct measurement of the rate constant for  $\beta$ -scission of the cumyloxyl radical has recently been reported: Neville, A. G.; Brown, C. E.; Rayner, D. M.; Luszyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1989**, *111*, 9269.

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5. A similar situation also obtains in atom transfer reactions (Kharasch reactions). For an excellent discussion of this point see reference 1b.

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7. (a) Beckwith, A. L. J.; Moad, G. *J. Chem. Soc., Perkin Trans. 1.* **1980**, 1083 and references there cited. (b) Beckwith, A. L. J.; Bowry, V. W.; Moad, G. *J. Org. Chem.* **1988**, *53*, 1632. (c) For a synthetic example where opening of a four-membered ring proved troublesome with conventional stannane chemistry see: Crimmins, M. T.; Mascarella, S. W. *Tetrahedron Lett.* **1987**, *28*, 5063.

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