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Dichotomy in The Addition of Carbon-Centred Radicals to Ketenedithioacetals.

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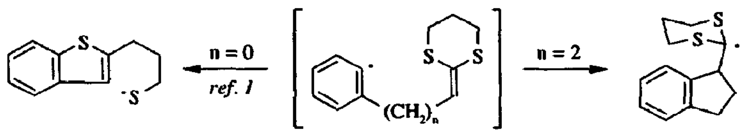
Abstract : Further studies on the addition of carbon centred radicals to ketenedithioacetals have shown that cyclisation may occur to either the sulfur atom or the alkene moiety and that the outcome is governed by the availability of a 5-exo cyclisation process.

We recently disclosed a versatile new route to condensed thiophenes in which the heterocyclic ring was created by the addition of a carbon centred radical to the sulfur of a ketenedithioacetal, *e.g.* **2** to **1**.[1] The success of this transformation encouraged us to investigate further aspects of this chemistry. In particular, we were intrigued as to whether the mode of cyclisation would be altered if the alkene moiety, rather than the sulfur atom, was most favourably disposed towards the radical centre, *e.g.* **2** to **3**. In this *letter* we report the results of our initial investigations that clearly demonstrate this dichotomy.[2, 3]

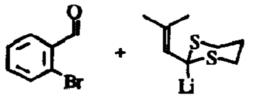
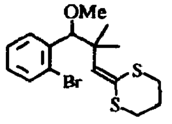
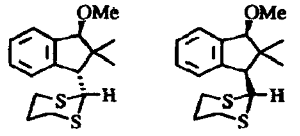
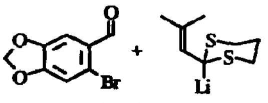
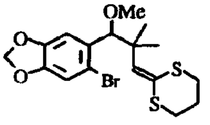
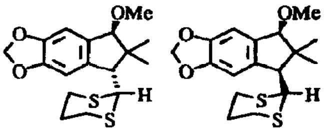
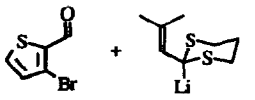
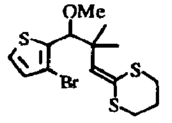
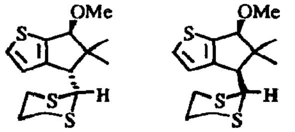
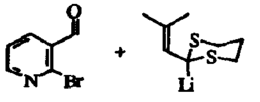
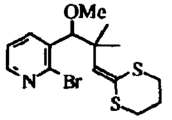
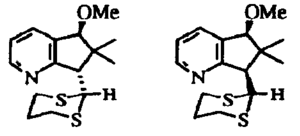
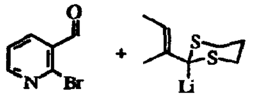
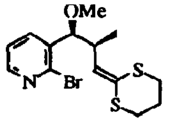
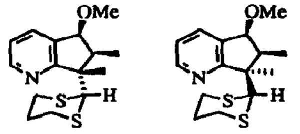


1 2 3

Thus, we prepared a series of ω-bromoketenedithioacetals from which a 5-*exo*-trig cyclisation to the alkene moiety was available to the radical intermediate. On exposure of these materials to standard tin mediated radical forming conditions (Bu_3SnH, AIBN, PhH, reflux, N_2, 24h; $KF_{(aq)}$, 16h) we were pleased to observe that, in each case, a diastereomeric mixture of the anticipated carbocycles was furnished in good yield (Table).[4] Indeed, we were unable to detect any products arising from sequential radical addition and fragmentation at the sulfur atom.

The clear preference exhibited for the formation of the *trans*-isomer in entries A to D is similarly noteworthy. However, whilst to the best of our knowledge this is established during the cyclisation step, in the light of some early experimental difficulties we feel obliged to add a note of caution. For when we used commercial $CDCl_3$ as solvent for N.M.R. analysis we observed equilibration of the *cis*- and *trans*- products. By pre treatment of this solvent with anhydrous potassium carbonate we were able to circumvent this problem, but the extent to which equilibration might occur during reaction remains uncertain.

Table: Preparation and Tin Mediated Radical Cyclisation of ω-Ketenedithioacetals

Entry	Preparation of Substrate [a]	Substrate	Products [b]	Yield (ratio)
A	 then MeI			62% (3:1)
B	 then MeI			53% (3:1)
C	 then MeI			59% (>5:1)
D	 then MeI			85% (4:1)
E	 then MeI	 + *ca.* 20% of isomer		68% (2:1)

a. The 2-lithio-2-vinyl-1,3-dithianes were prepared as solutions in THF by deprotonation of the parent 2-vinyl-1,3-dithianes with BuLi at -30°C. These solutions were sequentially treated with the requisite aldehyde then MeI giving, after purification by column chromatography, the precursors as viscous oils in greater than 80% isolated yield.[5] b. The determination of relative configuration followed from some initial n.O.e. studies and latterly by simple ^{1}H N.M.R. The trans-isomers (entries A-D) exhibit two singlets at ~δ 1.4 and 0.9 p.p.m. for the geminal dimethyls compared to ~δ 1.2 and 1.1 p.p.m. for the cis-isomers.

References and Notes:

1. Harrowven, D.C.; *Tetrahedron Lett.*, **1993**, *34*, 5653.
2. For two excellent reviews of the chemistry of ketenedithioacetals see: **a.** Kolb, M.; *Synthesis*, **1990**, 171; **b.** Kolb, M. Ketene Thioacetals. In *The Chemistry of Ketenes, Allenes and Related Compounds*, Patai, S. Ed., Wiley: Chichester, 1980, pp. 669.
3. For an overview of radical cyclisation reactions see: Curran, D.P. Radical Cyclisation and Sequential Radical Reactions. In *Comprehensive Organic Synthesis*, Trost, B.M.; Fleming, I. Eds., Pergamon: Oxford, 1991, pp. 779.
4. All new compounds exhibited satisfactory spectral and analytical characteristics and are racemic.
5. Harrowven, D.C.; *Tetrahedron Lett.*, **1992**, *33*, 2879.

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