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LETTERS

New Opportunities for α-Ketenyl Radicals in Ring Synthesis

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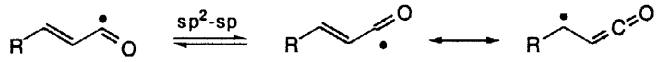
Abstract : Unsaturated acyl radicals are shown to be useful precursors to α-ketenyl radical intermediates which are then used in the synthesis of aromatic cyclic ketones. The behaviour of cyclopropyl acyl radicals is also described, in particular the 8-*endo*-trig cyclisation of 3-substituted cyclopropyl acyl radicals to give bicyclo[6.1.0]nonanones, and in the synthesis of cyclic enol lactones. © 1998 Published by Elsevier Science Ltd. All rights reserved.

In earlier studies[1,2] we have shown that α,β-unsaturated acyl radical intermediates take part in a variety of synthetically useful ring-forming reactions in which they react *via* their α-ketenyl radical counterparts *viz* **1**↔**2**.[3] In order to expand the scope of these novel reactions, we have now examined the chemistry of acyl radicals associated with aromatic and cyclopropane ring systems with a view to synthesising ring-fused aromatic and alicyclic ketones. These studies are now disclosed in this *Letter*.



1 **2**

Thus, we first examined the chemistry of the acyl radicals produced from the selenyl esters **3** and **9** which were easily prepared from their corresponding carboxylic acids following treatment with *N*-phenylselenylphthalimide-tributylphosphine.[4] When a solution of **3** in benzene was heated in the presence of Bu_3SnH - AIBN for 6 h, chromatography separated indanone **6** in 56 % yield. In a similar manner, under the same conditions, the cinnamyl selenyl ester **9** was converted into the unsaturated ketone **15** in 70 % yield.[5,6]

Interestingly, indanone **6** has been produced previously from flash vacuum pyrolysis of *o*-vinylbenzaldehyde[7,8] where the mechanism was thought to involve a 5-*endo* trig cyclisation from the intermediate acyl radical **4**, *viz* **4**→**7**. In the case of cyclisation of **3**, and in keeping with our earlier synthetic work with α,β-unsaturated acyl radicals,[1,2] we favour a mechanism which features the α-ketenyl radical **5** as a key intermediate and involving a 5-*exo* dig cyclisation, *ie* **5**→**8**, into the ketene carbonyl group as the key step. Likewise, we favour the 7-*exo* dig cyclisation from the ketene radical **11** produced from **10** as the most

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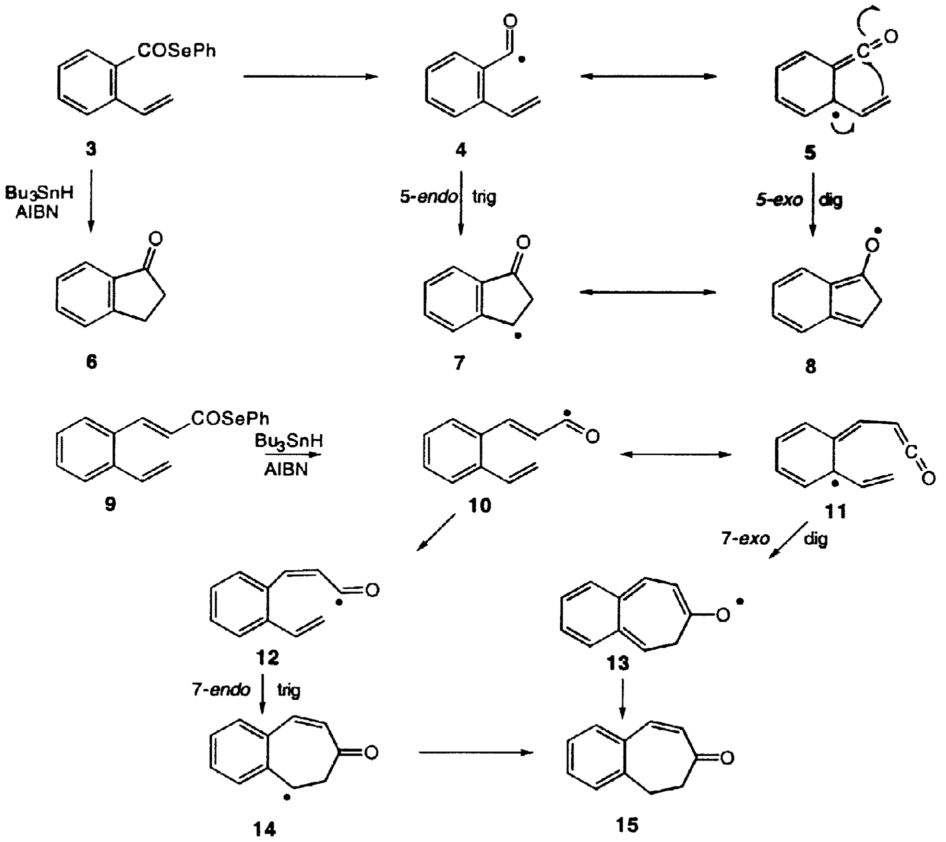
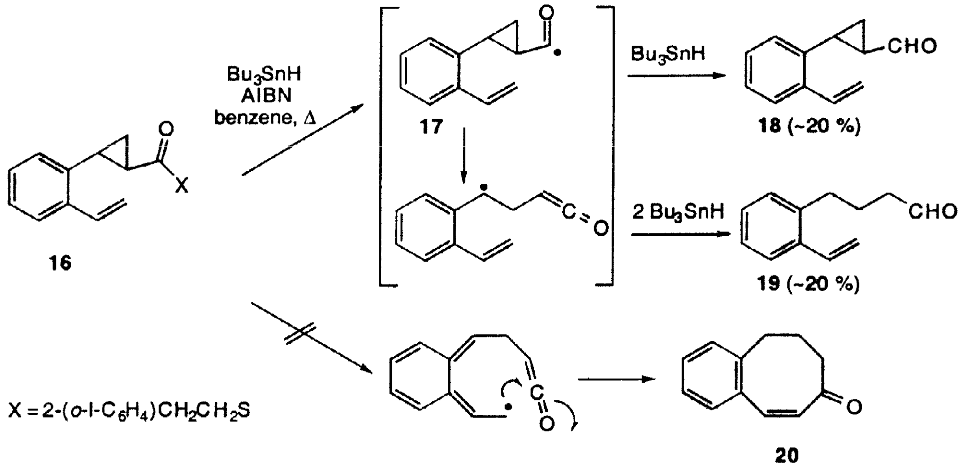
likely pathway leading to **15** from **9**, rather than an alternative route *via* the 7-*endo* trig process **10**→**12**→**14** involving prior isomerisation of the *E*-bond in **10**.

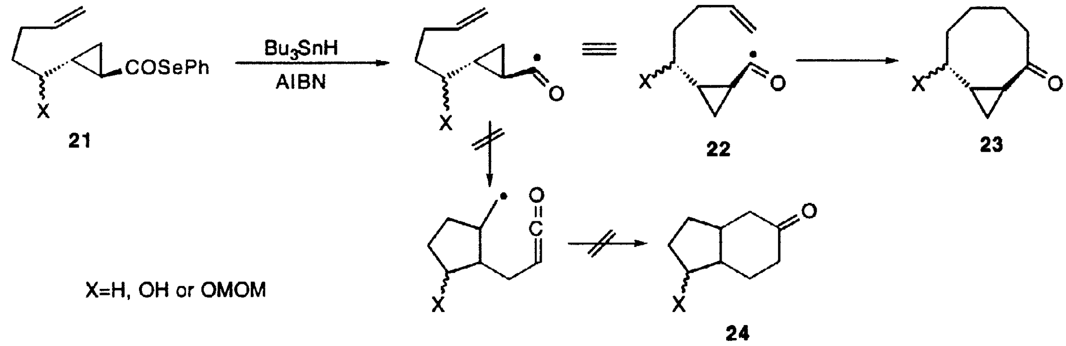


In an extension of this study, we next produced the cyclopropane acyl radical **17** (analogous to **10**) from the ester **16**, using the novel method described by Crich and Yao,[9] with a view to the synthesis of the 6,8-fused system **20**. Unfortunately, this reaction led only to the product **18** of reduction, together with the aldehyde **19** which results from cyclopropane ring opening in **17** without cyclisation.[10]

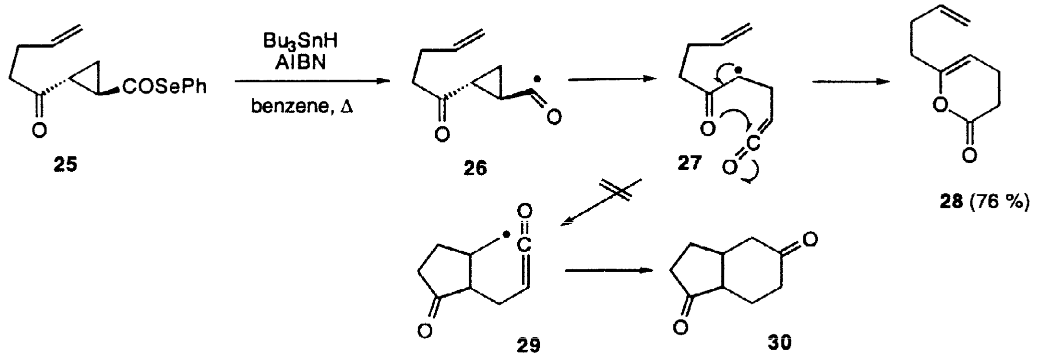
With the intention of synthesizing the bicyclo[4.3.0]nonanone **24** from a tandem 5-*exo* trig, 6-*exo* dig acyl radical cyclisation, we also synthesised the cyclopropane selenyl ester **21** and then treated it under the usual conditions with Bu_3SnH-AIBN. To our surprise, instead of leading to the bicyclononanone **24**, the only product isolated was the unusual *trans*-cyclopropane ring-fused eight-membered ring ketone **23** which was obtained in 80-95 % yield. The structure **23**, which results from a straightforward 8-*endo* trig cyclisation of the acyl radical intermediate **22**, was established by X-ray crystallography of the 4-hydroxy bicyclo[6.1.0]nonanone **23** (X=OH).[11]



Perhaps even more surprisingly, treatment of the ketone **25** analogous to **21** produced the enol lactone **28** in 76% yield rather than the anticipated bicyclononanedione **30** resulting from a tandem 5-*exo* trig, 6-*exo* dig process *via* **29**; the enol lactone results from cyclopropane ring opening of the acyl radical intermediate **26**, leading to the ketene radical **27** which then undergoes 6-*exo* trig cyclisation *via* its enolate oxy radical into the ketene electrophore.



The aforementioned cyclisations demonstrate the novel and unusual reactivity profiles of unsaturated and cyclopropyl acyl radical intermediates and the considerable scope for ketenes as electrophores in synthesis.



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References and notes:

1 Hayes, C. J.; Pattenden, G.; *Tetrahedron Lett.*, **1996**, *37*, 271-274.

2 Herbert, N.; Pattenden, G.; *Synlett*, **1997**, 69-70.

3 The α-ketenyl radical counterpart **2** to the α, β-unsaturated acyl radical **1** is related as a delocalised form of an intermediate resulting from sp^2-sp rehybridisation of the acyl radical centre in **1**.

4 a) Grieco, P. A.; Yaw, J. Y.; Claremon, D. A.; Nicolaou, K. C.; *J. Org. Chem.*, **1981**, *46*, 1215-1217. b) Nicolaou, K. C.; Petasis, N. A.; Claremon, D. A.; *Tetrahedron* ,**1985**, *41*, 4835-4841.

5 An attempt to cyclise phenyl *o*-ethynylbenzoselenoate under similar conditions led only to decomposition of the starting material without formation of any identifiable product.

6 All new compounds showed satisfactory spectroscopic data together with mass spectrometry or microanalytical data.

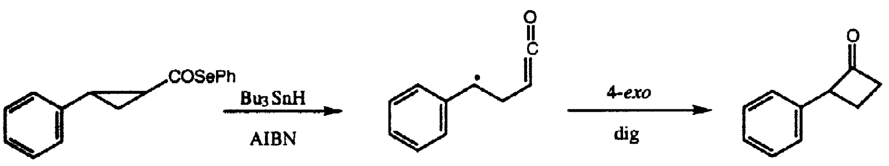
7 Brown, R. F. C.; Butcher, M.; *Aust. J. Chem.* , **1970**, *23*, 1901-1905.

8 For related *o*-formyl benzoyl radical cyclisations, see :a) Harrison, D. A.; Schwartz, R. N.; Kagan, J.; *J. Am. Chem. Soc.*,**1970**, *92*, 5793-5795.; b) Kende, A. S.; Belletire, J. L.; *Tetrahedron Lett.*, **1972**, 2145-2148.; c) Praefcke, K.; *Tetrahedron Lett.*, **1973**, 973-976.; d) Scaiano, J. C.; Encinas, M. V.; George, M. V.; *J. Chem. Soc., Perkin Trans. II*, **1980**, 724-730.; e) Mendenhall, G. D.; Protasiewicz, J. D.; Brown, C. E.; Ingold, K. U.; Lusztyk, J.; *J. Am. Chem. Soc.*,**1994**, *116*, 1718-1724.; f) Yamamoto, Y.; Ohno, M.; Eguchi, S.; *J. Org. Chem.*, **1996**, *61*, 9264-9271.

9 Crich, D.; Yao, Q.; *J. Org. Chem.*, **1996**, *61*, 3566-3570.

10 Compound **19** arises from reduction of the β-ketenyl radical formed by ring-opening of the cyclopropane in **17**, in the presence of excess Bu_3SnH.

Treatment of phenyl 3-phenylcyclopropaneselenoate **31** with Bu_3SnH-AIBN gave similar results although 2-phenylcyclobutanone **33** was also obtained in 37% yield. This compound is probably the result of a 4-*exo*-dig cyclisation of the intermediate benzylic radical **32** onto the ketene moiety present after opening of the cyclopropane ring.



31 **32** **33**

11 We thank Dr A. J. Blake at this department for determining this X-ray structure which will be published separately in a full paper.