Tetrahedron Letters, Vol. 34, No. 1, pp. 131-132, 1993
Printed in Great Britain

0040-4039/93 $5.00 + .00
Pergamon Press Ltd

A Route to Spiroketals using Radical Translocation

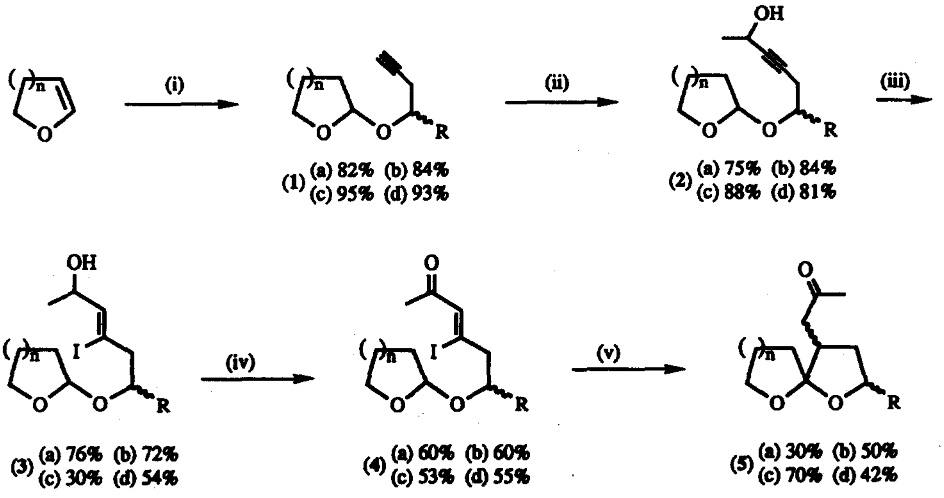
Christopher D. S. Brown and Nigel S. Simpkins*
Department of Chemistry, University of Nottingham, University Park, Nottingham NG7 2RD, UK

and Keith Clinch
ICI Agrochemicals, Jealott's Hill Research Station, Bracknell, Berkshire RG12 6EY, UK

Abstract: Reaction of β-iodoenones of general structure 4 with Bu_3SnH leads to formation of spiroketal products via 1,5-translocation of the initially formed radical.

The ability of reactive carbon-centred radicals to undergo intramolecular 1,5-hydrogen atom transfer has recently been developed into a useful way of translocating radicals.[1] Usually an initially formed vinyl or aryl radical abstracts a hydrogen atom from an appropriately positioned C–H bond of an sp^3 hybridised carbon centre to give a new radical, which then undergoes further reaction, usually cyclisation.[2] Our interest in the synthesis of spirocyclic ethers and amines using radical cyclisations[3] lead us to explore a route to spirocyclic ketals using radical translocations, which is described herein.

We employed a straightforward route to prepare a number of β-iodoenone systems having tetrahydrofuranyloxy or tetrahydropyranyloxy substitution suitable for our planned radical translocation reactions. This route, along with the results of the radical translocation–cyclisation reactions, leading to spiroketals, is shown in Scheme 1.



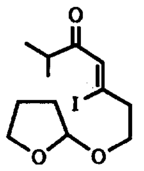
reagents:
(i) but-3-yn-1-ol or hex-1-yn-4-ol, pTSA (cat.), CH_2Cl_2
(ii) ^nBuLi, THF, -78°C; MeCHO (3 eq.) warm to RT
(iii) Red-Al® (1.6 eq.), Et_2O, RT (or reflux for c and d series); I_2, THF, -78°C
(iv) PCC (5 eq.), NaOAc, CH_2Cl_2
(v) Bu_3SnH (1.2 eq.), AIBN (0.2 eq.), benzene reflux, syringe pump addition

(a) R = H, n = 1
(b) R = H, n = 2
(c) R = Et, n = 1
(d) R = Et, n = 2

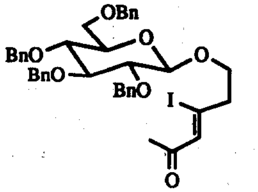
Scheme 1

Treatment of the THF or THP protected acetylenic alcohols **1** with butyllithium, followed by quenching with acetaldehyde, gave the secondary alcohol products **2**. These compounds were reacted with Red-Al® and then iodine to give the iodoalkenes **3**,[4] which were then oxidised in the dark, using PCC under buffered conditions, to give the rather sensitive iodoenones **4**. Cyclisation was then cleanly effected by slow addition of a mixture of Bu_3SnH and AIBN to a solution of **4** in benzene at reflux, the chemical yields being somewhat reduced due to the volatility of the products.

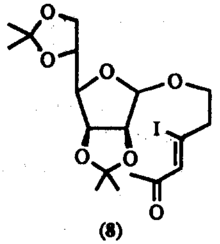
Each of the spiroketal products **5** was formed as a mixture of diastereoisomers, with one isomer predominating in the simpler systems (6:1 for **5a**, 9:1 for **5b**).[5] We attempted to further develop this novel route to spiroketals, and to probe the stereocontrol possible with more conformationally fixed substrates, by reacting the iodoenone **6**, and the carbohydrate-derived iodoenones **7** and **8** in the same way, but in these cases none of the desired product was observed.



(6)



(7)



(8)

These failures presumably reflect the more sterically encumbered nature of the substrates, and the consequent difficulty in attaining the required conformation for either the hydrogen atom abstraction or the subsequent cyclisation.[6]

In summary, we have shown for the first time that the Curran-type of radical translocation protocol can be used to convert a vinyl radical to an anomeric type radical,[7] and that subsequent cyclisation can produce spiroketals in moderate to good yield.

Acknowledgements

We thank the SERC and ICI Agrochemicals for a CASE award to CDSB (ICI Agrochemicals in the UK is part of Imperial Chemical Industries PLC). We would also like to thank Dr D. S. Middleton for preliminary studies in this area.

References

1. For key references in this area, see D. Denenmark, T. Winkler, A. Waldner, and A. De Mesmaeker, *Tetrahedron Lett.*, **1992**, *33*, 3613.
2. For an alternative use, see D. P. Curran and H. Yu, *Synthesis*, **1992**, 123.
3. D. S. Middleton, N. S. Simpkins, and N. K. Terrett, *Tetrahedron Lett.*, **1989**, *30*, 3865; D. S. Middleton, N. S. Simpkins, M. J. Begley, and N. K. Terrett, *Tetrahedron*, **1990**, *46*, 545.
4. S. E. Denmark and T. K. Jones, *J. Org. Chem.*, **1982**, *47*, 4595; K. D. Kim and P. Magriotis, *Tetrahedron Lett.*, **1990**, *31*, 6137.
5. For the more complex c and d series all four possible diastereoisomers were detected, although two compounds predominated in each case. The compounds described here have been characterised by IR, ^1H NMR, ^{13}C NMR and elemental analysis or high resolution MS.
6. Labelling studies, using Bu_3SnD have so far been inconclusive.
7. This type of abstraction has been proposed previously, see V. M. Girijavallabhan and A. K. Ganguly, *Heterocycles*, **1989**, *28*, 47. See also J. Griffiths and J. A. Murphy, *Tetrahedron*, **1992**, *48*, 5543.

(Received in UK 24 September 1992)