Tetrahedron Letters, Vol. 34, No. 1, pp. 127-130, 1993
Printed in Great Britain

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

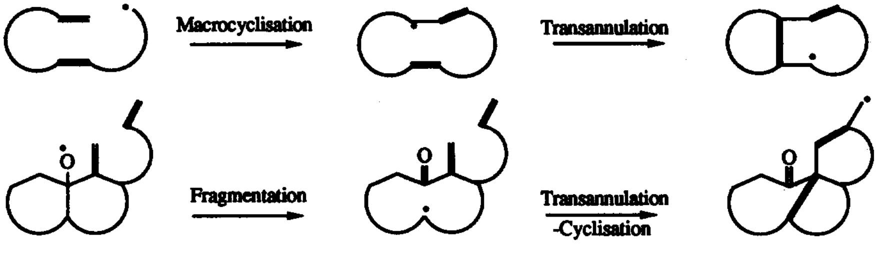
Polycycle Construction *via* Cascade Radical Fragmentation-Transannulation-Cyclisation Processes

Charles E. Mowbray and Gerald Pattenden*

Department of Chemistry, The University, Nottingham NG7 2RD

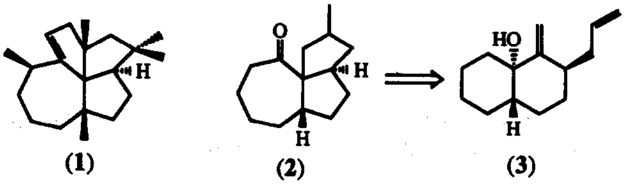
Abstract: *Treatment of the bicyclic dienol (8) with iodosylbenzene diacetate-iodine is shown to lead to the 7,5,5-tricycle (11, 81%) by way of a cascade radical fragmentation-transannulation-cyclisation sequence, cf. Scheme 1.*

The elaboration of polycyclic compounds by electrophilic polyolefin cyclisations,[1] together with a number of tandem transition metal catalysed reactions[2] and pericyclic cycloadditions[3] are well documented. Illustrations of the scope for a range of tandem radical mediated cyclisation reactions in the synthesis of carbo- and heterocyclic compounds have also come to the fore in the past few years.[4] We have now considered the feasibility of developing alternative new and powerful synthetic strategies for polycycle construction based on combinations of : (i) cascade radical macrocyclisation-transannulation processes, and (ii) cascade radical fragmentation-transannular-cyclisation reactions (see Scheme 1). In an earlier communication[5] we provided a succinct illustration of the first strategy with a cascade radical 12-*endo* macrocyclisation-8-*endo* transannulation sequence producing the novel tricyclo $[10.3.1.0^{4,6}]$ pentadecane ring system found in the taxane family of alkaloids. In this *Letter* we highlight the scope for cascade radical fragmentation-transannulation-cyclisation processes in polycycle construction with a concise, one-pot synthesis of the angular fused 7,5,5-tricyclic core unit (**2**) found in the natural product laurenene (**1**), from the substituted naphthalenol (**3**) in the presence of iodosylbenzene diacetate and iodine (Scheme 2).[6]



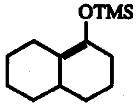
Scheme 1

Thus, treatment of the trimethylsilyl enol ether (**4**) derived from octahydro-1(2H)naphthalenone with *m*-chloroperbenzoic acid[7] first gave the 8a-hydroxyoctahydro-1(2*H*)-naphthalenone (**5**, 53%) and the corresponding *cis*-isomer (**6**, 13%), which could be easily separated by chromatography. Treatment of the

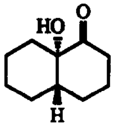


Scheme 2

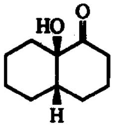
trans-hydroxy ketone (**5**) with lithium diisopropylamide at -78°C followed by the addition of propenyl bromide at -78°C next gave the allyl substituted derivative (**7**) as a single diastereoisomer in 54% yield.[8] A Wittig condensation between (**7**) and methylenetriphenylphosphoranylide (DMSO, 25°C) then led to the dienol (**8**, 68%) as a colourless oil; a small amount (~7%) of the diastereoisomeric dienol (**9**) was also separated by chromatography.



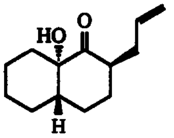
(**4**)



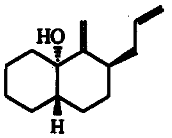
(**5**)



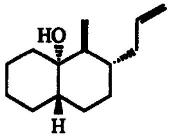
(**6**)



(**7**)

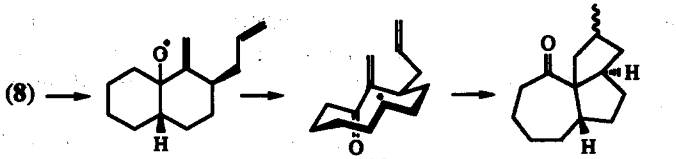


(**8**)

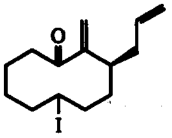


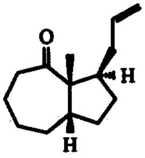
(**9**)

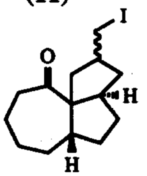
When a solution of the dienol (**8**) in dry degassed cyclohexane was irradiated under reflux in the presence of iodosylbenzene diacetate (10 equiv.) and iodine (1 equiv.),[9] using a sunlamp, it was converted in 'one-pot' into the angular fused 7,5,5-tricycle (**11**) in 58% yield (or 81% based on recovered starting material). When the same reaction was carried out under conditions of a large excess of iodine, *i.e.* dienol (**8**) (1 equiv.), iodosylbenzene diacetate (1 equiv.), iodine (10 equiv.), chromatography separated the intermediate iodides (**12**, 15%), (**13**, 44%) and (**14**, 14%) in the cascade fragmentation-transannulation-cyclisation sequence leading to (**11**). Furthermore, when a solution of this mixture of iodides, (**12**)-(**14**), in benzene was irradiated for a short period in the presence of catalytic hexabutyldistannane,[10] the tricyclic iodide (**14**) could be isolated in 61% preparative yield. Elimination of the elements of hydriodic acid from (**14**), using diazabicyclo[5.4.0]undec-7-ene then provided the corresponding alkene (**15**, 63%).

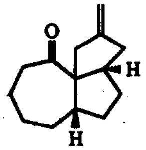


(10) (11)

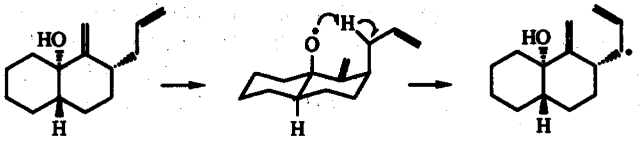

(12)


(13)

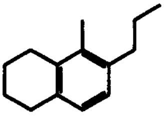

(14)

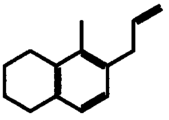

(15)

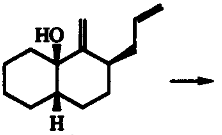
In order to gain further insight into the stereochemical requirements demanded by the reacting centres involved in the cascade radical sequence leading to (11) from (8), we also examined the outcome of the reactions between iodosylbenzene diacetate-iodine and the diastereoisomeric dienols (9) and (20) corresponding to (8). Thus, treatment of the axial propenyl substituted dienol (9), produced in the Wittig reaction (7) → (8)/(9), with iodosylbenzene diacetate-iodine did not lead to any tricyclic product corresponding to (11). Instead, the only products isolated were the aromatic materials (18, 26%) and (19, 26%). This observation no doubt reflects the importance of having an equatorial-orientated propenyl side chain in (8) to facilitate the final 5-*exo*-trig ring closure leading to (11), *cf.* intermediate (10). It also indicates that γ-hydrogen abstraction, involving the oxy-centred radical intermediate (16) and the side chain allylic hydrogen atoms, is facile with the diastereoisomer (9), *viz* (16) → (17), so as to completely preclude the cascade radical sequence observed with (8).



(9) (16) (17)


(18)


(19)


(14) + (18) / (19)

(20)

In a similar manner, the all-*cis*-(*syn*) diastereoisomeric dienol (**20**), prepared from (**6**), was treated with iodosylbenzene diacetate-iodine. Interestingly, this substrate gave rise to the tricyclic iodide (**14**), albeit in only 16% yield, and also to similar amounts of the same aromatic compounds (**18**) and (**19**) produced from the diastereoisomer (**9**).

Further studies are now in progress to develop this new cascade radical sequence to other ring fused carbo- and heterocycles.

Acknowledgements

We thank I.C.I. for financial support through their Strategic Funding Programme.

References and Notes

1. Johnson, W.S.; Telfer, S.J.; Cheng, S.; Schubert, U. *J. Am. Chem. Soc.*, **1987**, *109*, 2517; Sutherland, J.K. *Comp. Org. Synth.*, **1991**, *3*, 341, Pergamon Press.
2. Grigg, R.; Dorrity, M.J.; Malone, J.F. ; Sridharan, V.; Sukirthalingham, S. *Tetrahedron Lett.*, **1990**, *31*, 1343; Meyer, F.E.; Parsons, P.J.; de Meijere, A. *J. Org. Chem.*, **1991**, *56*, 6487; Carpenter, N.E.; Kucera, D.J.; Overman, L.E. *J. Org. Chem*, **1989**, *54*, 5846; Trost, B.M. ; Shi, Y. *J. Am. Chem. Soc.*, **1992**, *114*, 741.
3. See for example: Deslongchamps. P. *Aldrichimica Acta*, **1991**, *24*, 43.
4. See: Ali, A.; Harrowven, D.C.; Pattenden, G. *Tetrahedron Lett.*, **1992**, *33*, 2851 and selected bibliography contained therein.
5. Hitchcock, S.A.; Pattenden, G. *Tetrahedron Lett.*, **1992**, *33*, 4843.
6. For preliminary studies of the scope for alkyoxy radical fragementation transannulation reactions in synthesis, see Ellwood, C.W.; Pattenden, G. *Tetrahedron Lett.*, **1991**, *31*, 1591, and other references contained therein.
7. See: Hassner, A.; Reus, R.H.; Pinnick, H.W. *J. Org. Chem.* **1975**, *40*, 3427.
8. Satisfactory spectroscopic data together with microanalytical and/or mass spectrometry data were obtained for all new compounds.
9. Fransisco, C.G.; Freire, R.; Rodriguez, M.S.; Suarez, E. *Tetrahedron Lett.*, **1987**, *28*, 3397.
10. *cf.* Curran, D.P; Tamine, J. *J. Org. Chem.*, **1991**, *56*, 2746; Curran, D.P.; Chang, C.-T. *Tetrahedron Lett.*, **1987**, *28*, 2477; Curran, D.P.; Chang, C.-T., *J. Org. Chem.* **1989**, *54*, 3140; Curran, D.P.; Chen. M.-H.; Kim, D. *J. Am. Chem. Soc.*, **1989**, *111*, 6285; Curran, D.P. Chen, M.-H. *J. Am. Chem. Soc.*, **1987**, *109*, 6558.

(Received in UK 14 September 1992)