Tetrahedron Letters, Vol. 33, No. 25, pp. 3687-3690, 1992
Printed in Great Britain

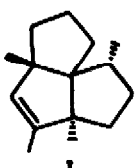
0040-4039/92 $5.00 + .00
Pergamon Press Ltd

AN EXPEDITIOUS APPROACH TO THE SYNTHESIS OF ANGULAR TRIQUINANE

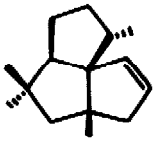
Yadav J.S*, Praveen Kumar T.K. and Gadgil V.R.
Indian Institute of Chemical Technology, Hyderabad 500007, India

ABSTRACT: A flexible approach for the synthesis of Angular Triquinane using free radical mediated reaction is described.

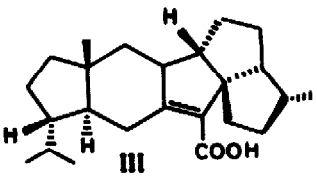
A variety of angular tricyclopentanoids have been isolated from natural products. Prominent among them are isocomene[1] (**I**), silphenene[2] (**II**), retigeranic acid[3] (**III**), pentalenene[4] (**IV**), and subergorgic acid[5] (**V**). The synthetically challenging decahydro-cyclopenta(C)-pentalene system of these compounds has attracted synthetic organic chemists over the past few years and lead to the development of many synthetic strategies involving sequential annulations[6] and tandem radical cyclisations[7].



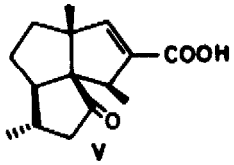
I



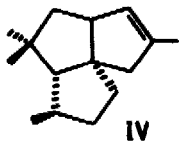
II



III



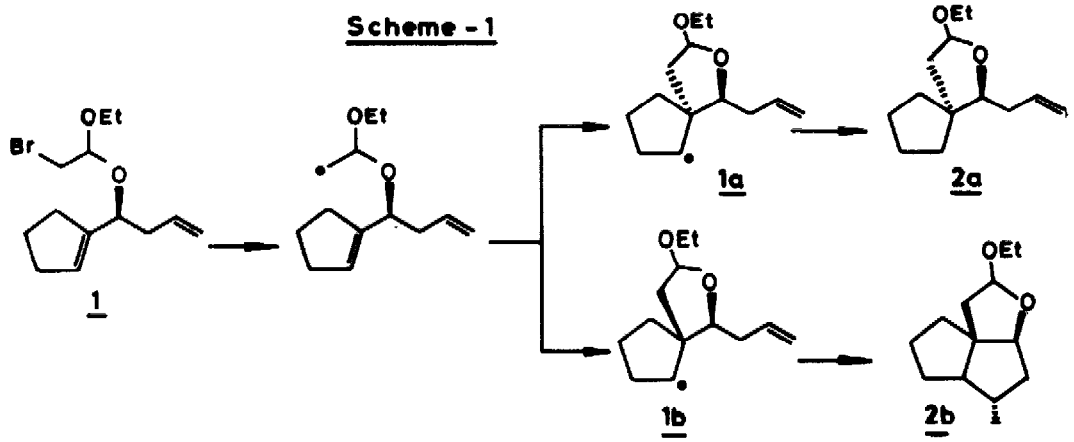
V



IV

We studied Stork's[8] and Ueno's[9] methods of radical cyclization of bromoacetals (**1**) for synthesis of the triquinane moiety. The initially generated radical from **1**

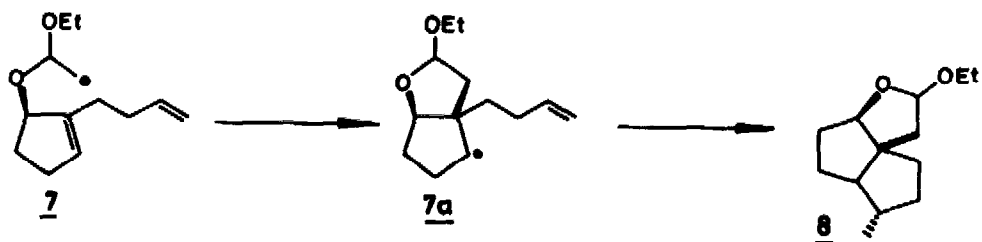
Scheme - 1



predominently attacks the olefin from the α-face, forming radical (**1a**) wherein substituents on the newly formed ring have "trans" geometry with respect to the carbon bearing radical thereby preventing further cyclisation. On the other hand, β-facial cyclisation gives rise to "cis" product (**1b**) which undergoes tandem cyclisation to produce oxa-triquinane moiety in 21% yield (Scheme 1). Thus, the cyclisation of bromoacetal (**1**) was found to be unsatisfactory owing to the nonselective bifacial attack of the radical on to the olefinic bond.

To overcome such a situation, we envisioned that if, the hydroxy group could be incorporated on the cyclopentene ring, the radical derived from the bromoacetal of such alcohol (**5**) would undergo cyclisation readily, where the face of the cyclisation would be governed by the stereochemistry of the hydroxyl group. The resultant carbon bearing radical (**7a**) will always be "syn" with the side chain enabling further cyclisation to give oxa-triquinane (Scheme 2).

Scheme-2



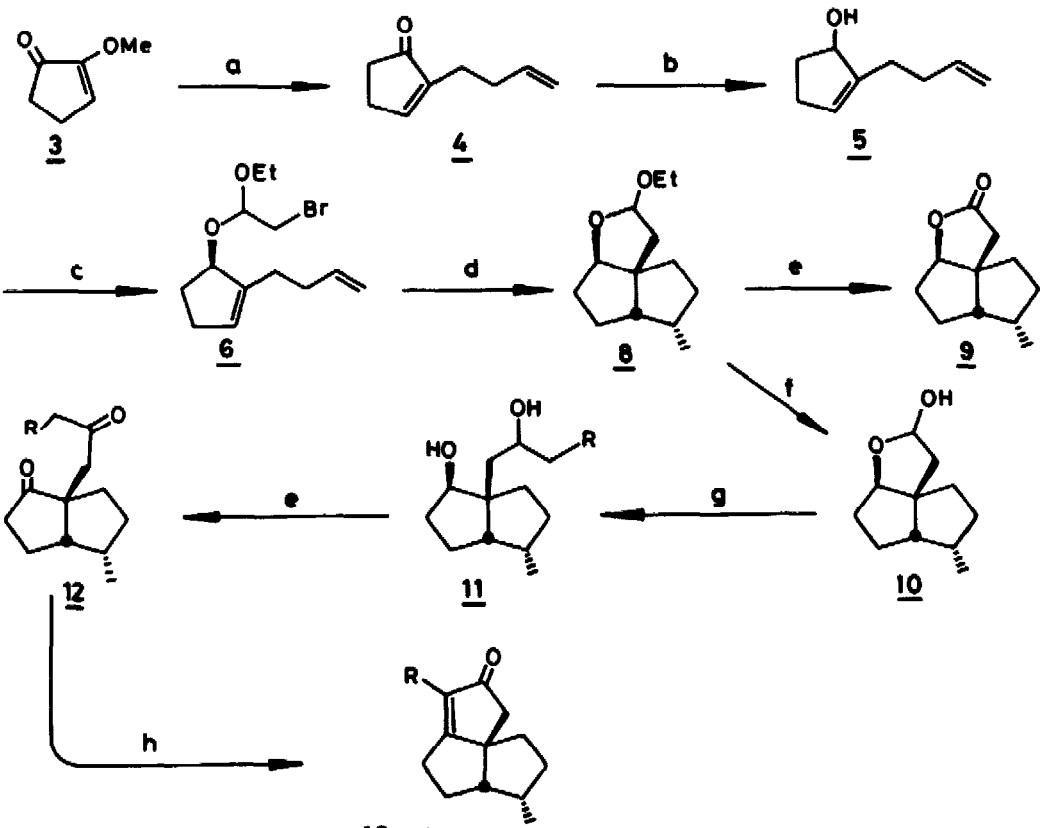
In the present communication, we describe the above new stratagem for the synthesis of triquinane which can also be extended to the optically active triquinane.

The required bromoacetal (**6**) was prepared starting from 2-methoxy cyclopent-2-enone[10]. The Grignard reagent from butenyl bromide was condensed with **3** to give 2(buta-4-enyl) cyclopenta-2-en 1-one according to the procedure of Ansell and Ducker[11]. Compound **4** on reduction with DIBAL-H in dichloromethane at -78°C produced dienol **5** which was further converted to bromoacetal **6** using standard procedure[9a]. The bromoacetal thus obtained, on treatment with one equivalent of sodium cyanoborohydride in t-butanol under reflux with catalytic quantity of tributyltinchloride and AIBN yielded the expected mixed cyclic acetal **8** in 77.5% yield. The tricyclic acetal was converted to the corresponding lactone using Jones' reagent for more ready characterisation[14]. At this stage, the stereochemistry of the methyl group present on C-9 carbon was confirmed as α- by correlating the value of methyl carbon from the ^{13}C NMR spectrum with those of reported values[12] which was also observed by several other workers[13]. Having secured the tricyclic acetal our next task was to construct the third ring and complete the synthesis of triquinane moiety. This was achieved by simple chemical transformations on the oxo-ring. First, the tricyclic acetal was hydrolysed with 90% TFA and the resulting hemiacetal was opened with three equivalents of methyl magnesium bromide to produce diol in 70% yield. The diol was oxidized with Jones' reagent to

obtain the diketone in 75% yield and finally the diketone on cyclodehydration with 20% ethanolic KOH, yielded the desired 9-methyl tricyclo (6.3.0.0.^{1,5}) unde-4-en-3-one in 55% yield **13a**. Similarly, compound **10** was also opened with 3 eq. of EtMgBr to give diol **11b** which was eventually converted to triquinane **13b** in 52% yield (Scheme 3).

Thus, we have presented a novel and operationally feasible approach for the stereospecific synthesis of triquinanes which would find widespread application in the preparation of optically active tricyclic natural products.

Scheme - 3



Reagents : a) Mg,  , HCl, H_2SO_4 ; b) DIBAL-H, DCM, -78°C ; c) NBS,  , DCM, 0°—RT ; d) $NaBH_3CN$ (1eq), AIBN (cat), Bu_3SnCl (cat), t-Butanol, reflux ; e) Jones' oxidation, 0°C ; f) 90% TFA ; g) Mg, RCH_2Br, Ether, RT ; h) 20% KOH, ethanol, reflux.

REFERENCES:

1. (a) Zalkow, L.H.; Harris, R.N.; Vanderveer, D.; Bertrand, J.A. J. Chem. Soc. Chem. Comm. **1977**, 452. (b) Zalkow, L.H.; Harris, R.N.; Burke, N.I. J. Nat. Prod, **1979**, 42, 96.

2. Crimmins, M.T.; Mascrarella, S.W. J. Am. Chem. Soc, **1986**, 108, 3435 and references cited therein.

3. Kaneda, M.; Takahashi, R.; Litata, Y.; Shibata, S. Tetrahedron Lett, **1972**, 13, 4609.

4. (a) Seto, H.; Uanehara, Y. J. Antibiot, **1980**, 33, 92. (b) Cane, D.E.; Rossi, T.; Pachlatko, J.P. Tetrahedron Lett, **1985**, 26, 3639.

5. Groweiss, A.; Fanicol, W., Clardy, J.; Cunheng, H.; Zhonde, W.; Zhongnian, Y.; Kanghou, L. Tetrahedron Lett, **1985**, 26, 2379.

6. (a) Jager, V.; Dorsch, M.; Sooniein, W. Angew Chem. Int. Ed. (Eng), **1984**, 23, 7981. (b) Khudson, M.J.; Shore, N.E. J. Org. Chem., **1984**, 49, 5025. (c) Mehta, G.; Rao, K.S. Tetrahedron Lett, **1984**, 25, 3481.

7. Curran, D.P.; Schen Chun Kuo, J. Am. Chem. Soc., **1986**, 108, 1106.

8. (a) Stork, G.; Mook, R. Jr, J. Am. Chem. Soc., **1983**, 105, 3741. (b) Stork, G. in "Selectivity - A Goal for Synthetic Efficiency, Bartmann, VCH, Weinheim, **1984**, pp. 281-298.

9. (a) Ueno, Y.; Chino, K. J. Chem. Soc.,Perkin Trans. 1, **1986**, 1351. (b) Ueno, Y.; Chino, K. J. Am. Chem. Soc, **1982**, 104, 5564.

10. Acheson, R.M. J. Chem. Soc, **1956**, 4232.

11. Ansell, M.; Ducker, J.W. J. Chem. Soc, **1959**, 329.

12. (a) Curran, D.P.; Schen Chun Kuo, Tetrahedron **1987**, 43, 5653. (b) "Studies in Natural Products Chemistry", Vol.3 by Atta-ur-Rahaman, Elsevier Publishing Company, Inc, NY, **1989**.

13. (a) Koteswar Rao, Y.; Nagarajan, M. Tetrahedron Lett, **1988**, 29, 107. (b) Beckwith, A.L.J.; Schiesser, C.H.; Tetrahedron, **1985**, 41, 3925.

14. All the compounds gave expected spectral data and Exact Mass (HRMS). ^{1}H NMR ($CDCl_3$), ^{13}C NMR of some selected compounds.
(**8**) δ 0.95 (d,3H,J=7 Hz, -CHMe), 1.1 (t,3H,J=7 Hz, $OCH_2\underline{CH_3}$), 1.8-2.2 (m,12H), 3.5-3.9 (m,2H), 4.1 (b s,1H,C_1), 5.05 (m,1H,C_3).
(**9**) δ 0.9 (d,3H,J=7 Hz, -CH$\underline{Me}$), 1.0-2.0 (m,10H), 2.6 (s,2H,-C-$\underline{CH_2}$), 4.5 (m,1H, -O-$\underline{CH}$).
(**9**) ^{13}C NMR: δ 177.2 (C-3), 93.5 (C-5), 57.2 (C-1), 54.0 (C-2), 42.2 (C-8), 37.8 (C-9), 37.0 (C-6), 34.0 (C-11), 29.5 (C-7), 25.0 (C-10), 15.7 (C-12).
(**13a**) δ 1.0 (d,3H,J=7 Hz,-HC-$\underline{Me}$), 1.5-2.2 (m,8H), 2.4-2.6 (m,4H), 5.7 (s,1H, C=$\underline{CH}$).
(**13b**) δ 1.0 (d,3H,J=7 Hz,-HC-$\underline{Me}$), 1.4 (q,1H,Me-$\underline{CH}$), 1.67 (s,3H,C=C-$\underline{CH_3}$), 1.5-2.1 (m,7H), 2.42 (s,2H,-C-$\underline{CH_2}$-), 2.3-2.5 (m,2H,C=C-$\underline{CH_2}$).

15. IICT Communication No.2784

(Received in UK 8 April 1992)