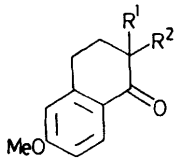
Stereoselective Synthesis of 3-Methoxy-*cis*- and -*trans*-6a,9a-dimethylhexahydrobenz[*e*]inden-8-one

By RICHARD A. PACKER and JOHN S. WHITEHURST*
(*Department of Chemistry, The University, Stocker Road, Exeter* EX4 4QD)

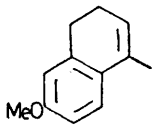
Summary Stereoselective syntheses of the title compounds have been achieved starting from 6-methoxy-1-tetralone.

3-METHOXY-*trans*-6a,9a-DIMETHYLHEXAHYDROBENZ[*e*]INDEN-8-ONE (**10**), a possible intermediate for the total synthesis of triterpenes of the lanostane–cycloartane group, has been synthesised as follows.

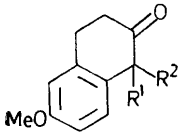
The 2-tetralone (**4**) was obtainable from 6-methoxy-2-tetralone,[1] or could equally conveniently be derived from 6-methoxy-1-tetralone (**1**) by addition of MeMgI followed by dehydration of the resulting alcohol to produce the dihydronaphthalene (**3**) and conversion of this into (**4**) either by epoxidation and rearrangement of the epoxide[2] or (better) by hydroboration and oxidation. Alkylation of (**4**) with 3-bromopropyne gave the propynyltetralone (**5**) which after hydration and cyclisation of the intermediary diketone furnished the racemic ketone (**6**).



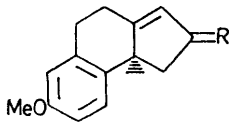
(1) $R^1 = R^2 = H$
(2) $R^1 = Me, R^2 = -CH_2-CCl{:}CH_2$



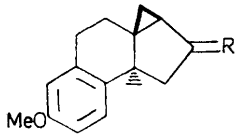
(3)



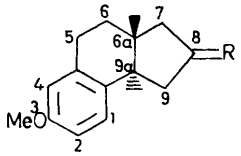
(4) $R^1 = Me, R^2 = H$
(5) $R^1 = Me, R^2 = -CH_2{\cdot}C{\equiv}CH$



(6) R = O
(7) R = α-H,β-OH



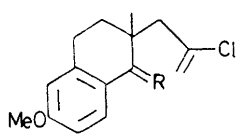
(8) R = α-H,β-OH
(9) R = O



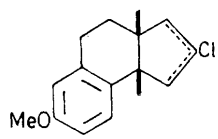
(10) R = O
(11) $R = SCH_2CH_2S$
(12) $R = H_2$

Reduction (AlH_3) of (**6**) in tetrahydrofuran solution produced as a single stereoisomer the alcohol (**7**) which on treatment with Simmons–Smith reagent[3] underwent cyclopropanation to yield (**8**). Chromic acid–acetone oxidation of (**8**) gave the corresponding ketone (**9**) which on reduction (Li–liq. NH_3) followed by gentle treatment of the product with chromic acid–acetone produced, as the sole isolated material, the desired *trans*-compound (**10**); τ ($CDCl_3$) 9·18 (6a-Me) and 8·82 (9a-Me).†

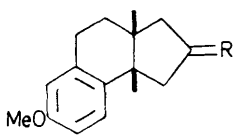
The *cis*-isomer (**17**) was also prepared from 6-methoxy-1-tetralone (**1**). Introduction of methyl and chloroallyl[4] groups (in that order) gave the chloroallylmethyl tetralone (**2**). Reaction of (**2**) with MeMgI furnished compound (**13a**) which underwent rapid dehydration to form (**14a**). By the action of hot formic acid both compounds underwent cyclisation stereospecifically to form the *cis*-hexahydrobenzindenone (**17**); τ ($CDCl_3$) 8·89 (6a-Me) and 8·67 (9a-Me).† Also formed in this reaction were the two isomeric chloroolefins (**16**) both of which were transformed into the required ketone (**17**) by treatment with H_2SO_4.



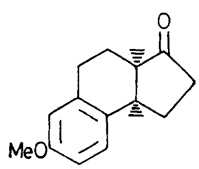
(13a) R = Me, OH
(13b) R = CD_3,OH
(14a) R = CH_2
(14b) R = CD_2
(15) R = Me, positive charge



(16)



(17) R = O
(18) $R = -SCH_2CH_2S-$
(19) $R = H_2$



(20)

That the formation of (**17**) from either (**13a**) or (**14a**) is not the result of a concerted process[5] was proved by the cyclisation of the deuteriated compounds (**13b**) and (**14b**) [prepared from the reaction of CD_3MgI with compound (**2**)] which occurred with complete loss of deuterium from the molecule. Other evidence to be presented later will demonstrate the relatively long life of carbonium ions of type (**15**).

Proof of the stereochemistry of the ring junctions in these compounds was first deduced by somewhat extensive n.m.r. studies. Chemical proof was obtained by conversion of the

† The individual methyl shifts were determined unambiguously by deuterium labelling. All compounds gave satisfactory spectral data.

ketones (**10**) and (**17**) into their diethylenethioacetal derivatives (**11**) and (**18**) and their subsequent Raney nickel desulphurisations to form the corresponding compounds (**12**) and (**19**). The ^{1}H n.m.r. spectrum of compound (**19**) was identical with that of material obtained by an analogous reaction sequence starting from the authentic (−)-*cis* hexahydrobenzindene (**20**), which has been obtained from dehydroabietic acid.[6] The stereochemistry[7] of the hydroxy-group in compound (**7**) follows from that of the subsequent cyclopropanation.

We thank the S.R.C. for financial support, and Dr. W. Graf for a gift of compound (**20**).

(*Received*, 17*th July* 1975; *Com.* 816.)

[1] J. H. Burckhalter and J. R. Campbell, *J. Org. Chem.*, 1961, **26**, 4232; J. J. Sims, L. H. Selman, and M. Cadogan, *Org. Synth.*, 1971, **51**, 109.
[2] W. Nagata and T. Teresawa, *Chem. Pharm. Bull* (*Japan*), 1961, **9**, 267; M. Fétizon and N. Moreau, *Bull. Soc. chim. France*, 1965, 3718.
[3] H. E. Simmons and R. D. Smith, *J. Amer. Chem. Soc.*, 1958, **80**, 5323; 1959, **81**, 4256; J. M. Denis and J. M. Conia, *Tetrahedron Letters*, 1972, 4593.
[4] P. T. Lansbury, F. R. Hilficker, and W. L. Armstrong, *J. Amer. Chem. Soc.*, 1968, **90**, 534; P. T. Lansbury, E. J. Nienhouse, D. J. Scharf, and F. R. Hilficker, *ibid.*, 1970, **92**, 5649; P. T. Lansbury and G. E. Du Bois, *Chem. Comm.*, 1971, 1107; P. T. Lansbury, *Accounts Chem. Res.*, 1972, **5**, 311.
[5] G. Stork and A. W. Burgstahler, *J. Amer. Chem. Soc.*, 1955, **77**, 5068; A. Eschenmoser, L. Ruzicka, O. Jeger, and D. Arigoni, *Helv. Chim. Acta*, 1955, **38**, 1890; W. S. Johnson, *Accounts Chem. Res.*, 1968, **1**, 1.
[6] T. Wirthlin, H. Wehrli, and O. Jeger, *Helv. Chim. Acta*, 1974, **57**, 351.
[7] S. Winstein and J. Sonnenberg, *J. Amer. Chem. Soc.*, 1961, **83**, 3235; W. G. Dauben, G. J. Fonken, and D. S. Noyce, *ibid.*, 1956, **78**, 2579; W. G. Dauben and G. H. Berezin, *ibid.*, 1963, **85**, 468; W. G. Dauben and A. C. Ashcraft, *ibid.*, p. 3673.