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SYNTHESIS OF (±)-PENTALENENE

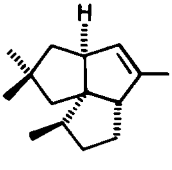
Gerald Pattenden* and Simon J. Teague

Department of Chemistry, The University,
Nottingham, NG7 2RD

Summary: A total synthesis of (±)-pentalenene (1), based on transannulation of the bicyclo[6.3.0]undecadiene (15) in the presence of boron trifluoride etherate, is described.

Pentalenene (1) is the parent hydrocarbon[1] of the pentalenolactone family of antibiotic fungal metabolites, e.g. (2)[2], found in Streptomyces.[3] The hydrocarbon is related structurally to the naturally occurring tricyclo $[6.3.0.0^{4,8}]$ undecanes isocomene (3)[4], silphinene (4)[5], and senoxydene (5).[6] In continuation of our studies of transannular cyclisation as a strategem in the synthesis of triquinane natural products[7], we now describe a stereocontrolled approach to (±)-pentalenene based on transannulation of the bicyclo[6.3.0]undecadiene (15) in the presence of boron trifluoride etherate.

The unsaturated carboxylic acid (7), which was readily available from the Meldrum's acid derivative (6), was first converted into the corresponding vinyl ketone (8) (CH_2=CHLi,glyme, 40-50°C, 12h; 66%).[8] Michael addition of dimethyl malonate to (8) followed by demethoxycarbonylation (NaCl, H_2O, DMSO, 150°C) then produced the δ-keto ester (9 ; 80%) which underwent smooth intramolecular acylation (KOBu^t, Et_2O, 0°C, 0.5h) leading to the cyclohexane-1,3-dione (10; 98%)[9] as a white solid m.p. 102-4°C, ν_{max} ($CHCl_3$) 3500-3100, 1695,



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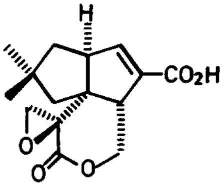

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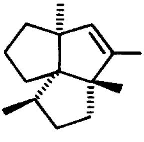

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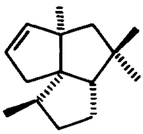

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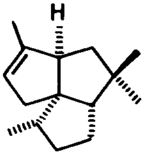

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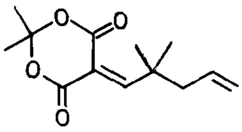
1660-1600cm.$^{-1}$, δ_{carbon} 188.8, 136.5(d), 116.2(t), 114.2, 47.3(t), 35.7, 33.2, 33.0(t), 26.9(t), 26.6(q), and 20.6(t)p.p.m. After conversion to the corresponding t-butyldimethylsilyl enol ether, irradiation in heptane through Pyrex using a 450W medium pressure mercury lamp resulting in regioselective intramolecular [2+2] photocycloaddition producing the tricyclic ketone (11; 81%)[10] as an oil, ν_{max} (film) 1695 cm.$^{-1}$, δ_{carbon} 212.2, 74.8, 69.2, 49.7(t), 43.5(t), 43.3(t), 40.4(t), 37.8(t), 37.4(t), 37.4(d), 30.7(q), 30.4(q), 25.6(q), 18.3(t), 17.9, and -2.8(q) p.p.m.

Addition of the tricyclic ketone (11) to a cold (-68°C) solution of Me_3CuLi_2 in diethyl ether[11] resulted in stereoselective formation of the crystalline tertiary alcohol (12; 82%), m.p. 70-1°C, which on treatment with hydrofluoric acid in aqueous tetrahydrofuran[12] at 25°C for 3h produced the enone (13; 75%) as colourless needles m.p. 40-1°C, ν_{max} 1700cm.$^{-1}$, δ_{carbon} 214.3, 139.5, 126.1, 55.6(t), 48.8(dd), 45.1(t), 39.4(t), 37.6, 57.4(d), 32.6(t), 29.1(q), 27.7(q), 21.3(t), and 19.4(q) p.p.m.

The enone (13) was next converted into the cycloocta-1,5-diene (15)[δ5.2-5.4 (m, :CH), 1.72 (:CMe), 1.59 (:CMe), 1.1-3.3 (m, 11H), 1.05 (Me), 0.92 (Me)] following Wittig reaction with methylenetriphenylphosphoranylide (to 14) and isomerisation with rhodium chloride trihydrate (hot EtOH, 1h).[7] Treatment of the 1,5-diene (15) with boron trifluoride etherate in methylene chloride (25°C, 5 min) resulted in stereospecific transannulation *via* the carbocation (16) producing (±)-pentalenene (1) (35%) whose spectral data [δ0.9 (d,*J* 7, CH*Me*), 0.98 (.CMe_2), 1.2-1.5(m, 6H), 1.61(:CMe), 1.7-1.9(m, 6H), 2.54(d, $J\sim9$, C*H*), 2.66(br,C*H*), 5.2(:C*H*); δ_{carbon} 140.6, 129.6, 64.9, 62.2, 59.5, 49.0, 47.0, 44.7, 40.6, 33.7, 30.1, 29.2, 27.7, 17.1, and 15.6 p.p.m.], were superimposable on those of an authentic sample.[13] Although we found no evidence for the co-formation of the C-9-methyl epimer[13] of pentalenene from transannulation of (15)[14], a minor isomeric hydrocarbon was produced concurrently which, from its spectral data [δ 0.97(Me), 0.99(Me), 1.01(Me), 1.05-1.52(m, 4H), 1.56(:CMe), 1.6-1.9(m,5H), 2.62(t, $J\sim2$,1H), 5.18(:CH); δ_{carbon} 143.4, 128.3, 68.4, 58.5, 58.3, 50.4, 48.9, 45.4, 40.9, 39.5, 30.0, 29.0, 23.9, 23.5, and 13.3 p.p.m.], was assigned the structure (18).[15] This hydrocarbon , which we believe arises *via* initial transannulation from the alternative carbocation (17), *cf* (16), derived from (15), was the sole product obtained (72%) when the positional isomer (14) of (15) was treated in a similar manner with boron trifluoride etherate.

We thank the S.E.R.C. for a studentship (to S. J. T.), and Professor David Cane for providing ^{1}H and ^{13}C n.m.r. spectra of authentic pentalenene.



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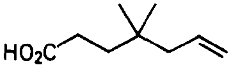

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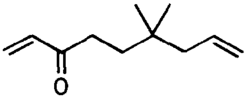

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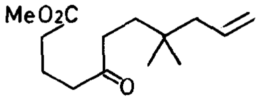

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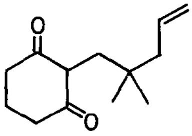

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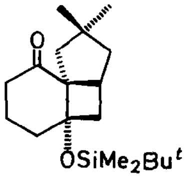

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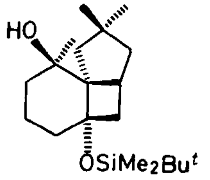

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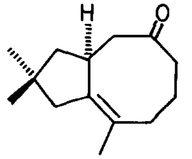

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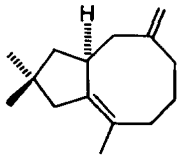

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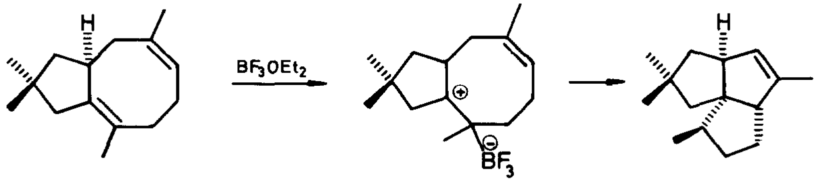

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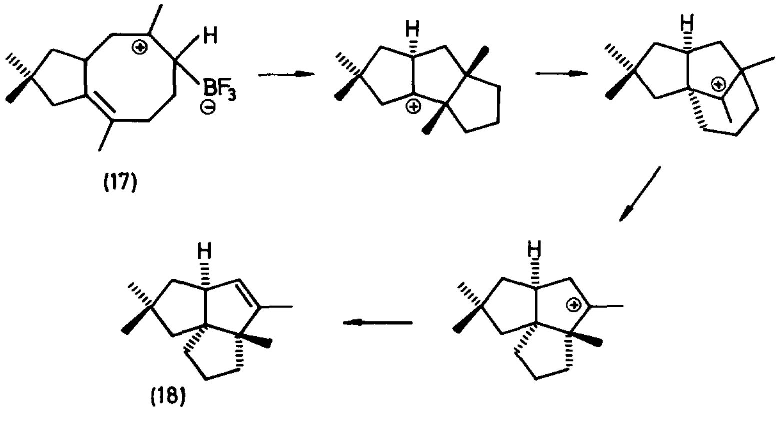

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7. A. M. Birch and G. Pattenden, Tetrahedron Lett., 1982, 23, 991; J. Chem. Soc., Perkin Trans. I., 1983, 1913.

8. Satisfactory microanalytical and/or mass spectral data were obtained for all new compounds.

9. A number of alternative routes to this deceptively simple molecule were developed. These will be described in the full paper.

10. For other studies of this intramolecular [2+2] photocycloaddition see (a) A. M. Birch and G. Pattenden, J. Chem. Soc., Chem. Commun., 1980, 1195; (b) ref. 7, and references cited therein.

11. cf. T. L. Macdonald and W. C. Still, J. Am. Chem. Soc., 1975, 97, 5280.

12. For a similar fragmentation involving silyloxy enol ethers see: L. F. Tietze and U. Reichert, Angew. Chem. Int. Ed. Eng., 1980, 19, 830.

13. For an alternative synthesis of pentalenene which produces the C-9-epimer concurrently see: L. A. Paquette and G. D. Annis, J. Am. Chem. Soc., 1983, 105, 7359.

14. (±)-Pentalenene has also been produced in low yield from the protoilludyl carbocation: Y. Ohfune, H. Shirahama, and T. Matsumoto, Tetrahedron Lett., 1976, 2869. For related studies of the synthesis of pentalenolactones and related compounds through biogenetic like cyclisation of humulene see: T. Ohtsuke, H. Shirahama, and T. Matsumoto, ibid, 1983, 24, 3851.

15. The hydrocarbon is probably identical with a compound reported earlier as a minor product derived via transannulation from humulene: S. Misumi, T. Ohtsuka, T. Ohfune, K. Sugita, H. Shirahama, and T. Matsumoto, Tetrahedron Lett., 1979, 20, 31.

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