

Journal of The Chemical Society, Chemical Communications

NUMBER 1/1978

4 JANUARY

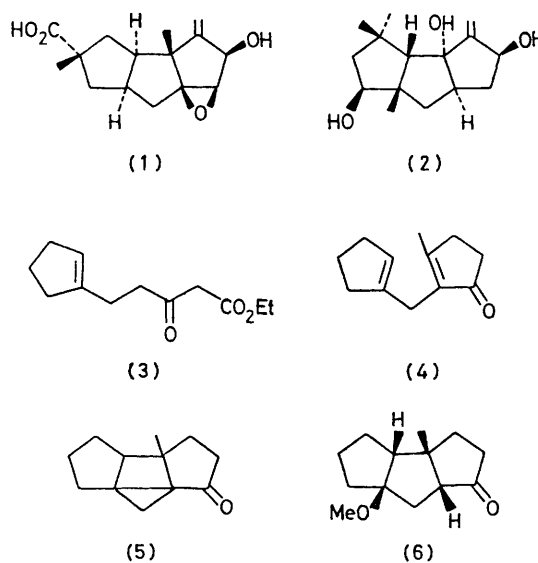
Photocyclisations of Dicyclopent-1-enyl Methanes to Tricyclo[6.3.0.0^{2,6}]undecanes: a Synthesis of the Hirsutane Carbon Skeleton

By JOSEPH S. H. KUEH, MICHAEL MELLOR, and GERALD PATTENDEN*
(Department of Chemistry, The University, Nottingham NG7 2RD)

Summary Irradiation of the dicyclopent-1-enyl-methane (4) in methanol leads to [2+2] cycloaddition, followed by *in situ* addition of methanol to the presumed intermediate bicyclo[2.1.0]pentane (5) producing the *cis,syn,cis*-tricyclo[6.3.0.0^{2,6}]undecane (6) in high yield; the general method is applied in a synthesis of the hirsutane carbon skeleton found in hirsutic acid (1) and related natural sesquiterpenes.

THE antibiotic hirsutic acid (1) from *Stereum hirsutum*,¹ belongs to a group of sesquiterpenoids showing structures based on the linear fusion of cyclopentane rings; other representative members are 'coriolin' from *Coriolus concors*,² and the 'capnellane' triol (2) which is found in the soft coral *Capnella imbricata*.³ Methods for the synthesis of the basic tricyclic ring system present in these molecules are limited.^{4,5} We have found that the photochemical intramolecular [2+2] cycloaddition of dicyclopent-1-enyl-methanes, followed by *in situ* addition of methanol to the strained cyclopropane ring in the presumed intermediate bicyclo[2.1.0]pentanes (*viz.* 5),⁶ offers an easy synthesis of this ring system. Here we report the method and its application in a synthesis of the hirsutane carbon skeleton found in hirsutic acid (1), coriolin, and related natural products.

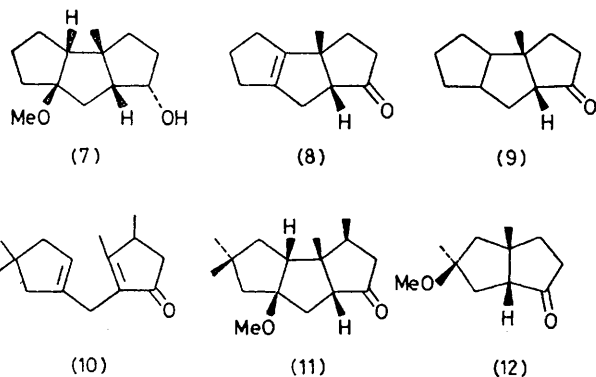
Alkylation of the dianion derived from ethyl acetoacetate with cyclopent-1-enylmethyl bromide first led (86%) to the substituted β -keto ester (3), which by reaction with bromoacetone in the presence of sodium hydride, followed by aldol cyclisation gave the dicyclopent-1-enyl-methane (4).⁷ Irradiation of (4) in methanol, through a Pyrex filter using a medium-pressure 100 W mercury lamp, resulted in the



formation of the tricyclo[6.3.0.0^{2,6}]undecanone (6), ν_{\max} (CHCl₃) 1720 cm⁻¹, τ 6.77 (OMe), 7.34—7.92 (m, \cdot CH₂CO \cdot CH \cdot CH₂), 7.92—8.76 (m, 9H), and 8.77 (Me); semicarbazone m.p. 189—191 °C, in >90% isolated yield. An analysis of the ¹H n.m.r. spectra using the shift reagent Eu(hfod)₃ suggested that the tricycle had the *cis,syn,cis*-stereochemistry shown, and this was confirmed by an X-ray analysis of the 3,5-dinitrobenzoate derivative† of the corresponding *endo*-carbinol (7) prepared from (6) by reduction with lithium aluminium hydride.

† We thank Dr. M. J. Begley, University of Nottingham, for the X-ray data, which will be published separately.

Treatment of the tricyclic ketone (6) with boron tri-bromide (-10°C , CH_2Cl_2), followed by ethanolic silver nitrate, effected sequential demethoxylation of the methyl ether, and bromination-dehydrobromination, leading (95%) to the alkene (8), ν_{max} 1720 cm^{-1} , τ 7.3—8.7 (m, 13H) and 8.76 (Me), which was hydrogenated ($\text{PtO}_2\text{-MeOH}$) to the parent tricyclic undecanone (9), ν_{max} 1725 cm^{-1} , τ 7.2—9.3 (m, 15H) and 8.79 (Me).



In a similar manner, irradiation of the dicyclopent-1-enyl-methane (10), ν_{max} 1695 and 1645 cm^{-1} , τ 4.87 (:CH), 7.08 (:C-CH₂C:), 7.1—7.5 (m, 3H), 7.7—8.2 (m, 4H), 7.98 (:CMe), 8.8 (d, J 7 Hz, CHMe), and 8.95 (CMe₂), in methanol, led (ca. 60%) to (11), τ 6.82 (OMe), 7.16—9.1 (m, 11H), 8.88 (CMe), 8.90 (CMe), 8.94 (CMe), and 9.02 (d, J 7 Hz, CHMe), containing the hirsutane carbon skeleton. Analysis of the ¹H n.m.r. spectra of (11) using the shift reagent Eu(hfd)₃ suggested that, like (6), the molecule assumes the *cis,syn,cis*-conformation, with the extra methyl group (at C-8) *exo*.^{8†}

The same general photoprocess was also applied in a synthesis of the bicyclo[3.3.0]octanone (12), ν_{max} 1734 cm^{-1} , τ 6.86 (OMe), 7.4—8.5 (m, 9H), 8.70 (Me), and 8.78 (Me), from 3-methyl-2-(2-methylprop-2-enyl)cyclopent-2-enone, but so far efforts to apply the approach to other polycyclic systems based on the fusion of six-membered with five-membered carbocycles have been unsuccessful.

We thank the S.R.C. for a fellowship (to M.M.).

(Received, 10th October 1977; Com. 1060.)

† Hirsutic acid and capnellane both have *cis,anti,cis* stereochemistry.

¹ F. W. Comer, F. McCapra, I. H. Qureshi, and A. I. Scott, *Tetrahedron*, 1967, **23**, 4761.

² S. Takahashi, H. Naganawa, H. Iinuma, T. Takita, K. Maeda, and H. Umezawa, *Tetrahedron Letters*, 1971, 1955.

³ Y. M. Sheikh, G. Singy, M. Kaisin, H. Eggert, C. Djerassi, B. Tursch, D. Dalozze, and J. C. Braekman, *Tetrahedron*, 1976, **32**, 1171.

⁴ For approaches to the hirsutane skeleton see: F. Sakan, H. Hashimoto, and A. Ichihara, *Tetrahedron Letters*, 1971, 3703; P. T. Lansbury, N. Y. Wang, and J. E. Rhodes, *ibid.*, 1972, 2053; S. Nozoe, J. Furukawa, U. Sankawa, and S. Shibata, *ibid.*, 1976, 195; Y. Ohfune, H. Shirahama, and T. Matsumoto, *ibid.*, 1976, 2795.

⁵ For recent approaches to cyclopentane annelation see: S. A. Monti, F. G. Cowherd, and T. McAninch, *J. Org. Chem.*, 1975, **40**, 858; J. P. Marino and L. J. Browne, *ibid.*, 1976, **41**, 3629; M. E. Jung and J. P. Hudspeth, *J. Amer. Chem. Soc.*, 1977, **99**, 5509; B. M. Trost and D. E. Keeley, *ibid.*, 1976, **98**, 248; J. P. Marino and W. B. Mesberger, *ibid.*, 1974, **96**, 4050; P. L. Fuchs, *ibid.*, 1974, **96**, 1607; A. B. Smith, *J.C.S. Chem. Comm.*, 1975, 274; S. Danishefsky and J. Dynak, *ibid.*, 1975, 7; E. Piers, C. F. Lau, and I. Nagakura, *Tetrahedron Letters*, 1976, 3233; E. Wada, T. Nakai, and M. Okawara, *Chem. Letters*, 1976, 1025; G. A. McAlpine, R. A. Raphael, A. Shaw, A. W. Taylor, and H.-J. Wild, *J.C.S. Perkin I*, 1976, 410.

⁶ Cf. M. J. Jorgenson, *J. Amer. Chem. Soc.*, 1966, **88**, 3463; H. Kristinsson and G. S. Hammond, *ibid.*, 1967, **89**, 5970.

⁷ M. J. Bullivant and G. Pattenden, *J.C.S. Perkin I*, 1976, 249.

⁸ For a recent synthesis of the *cis,syn,cis*-tricycloundecane system see: P. E. Eaton, C. Giordano, G. Schloemer, and U. Vogel, *J. Org. Chem.*, 1976, **41**, 2238.