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A SYNTHESIS OF THE TRICYCLO[6.3.0.0^{2,6}]UNDECANE SYSTEM.[1]

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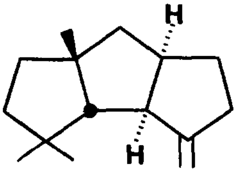
ABSTRACT: A short and efficient synthetic route to the tricyclo[6.3.0.0^{2,6}]undecane ring system is described; the key steps are photochemical annelation of an enolized β-diketone to produce a 1,5-diketone (the de Mayo reaction) followed by intramolecular reductive coupling using a low valence titanium species (McMurry's reagent).

In recent years a number of sesquiterpenes have been isolated which possess a carbon skeleton made up of three linearly fused five-membered rings. Compounds which incorporate this tricyclo[6.3.0.0^{2,6}]undecane system include the capnellanes[2] (which are oxidized forms of capnellene, **1**) and hirsutene, **2**, and its oxidized analogues hirsutic acid, complicatic acid and the coriolins.[3] Widespread interest in these compounds has developed because of their antibiotic and antitumor acitivity and this has lead to the development of a number of synthetic routes to the tricyclo[6.3.0.0^{2,6}]undecane ring system.[4] We present here a route to this ring system which has the advantage of brevity, ready availability of starting materials, and high yields. The route is outlined in the scheme and involves photoaddition of a cyclopentene to an enolized cyclohexane-1,3-dione (the de Mayo reaction[5]) followed by intramolecular reductive coupling of the diketone photoproduct with a low valence titanium species (McMurry's reagent[6]).



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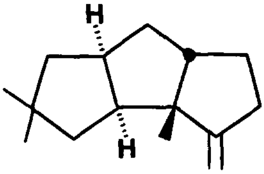

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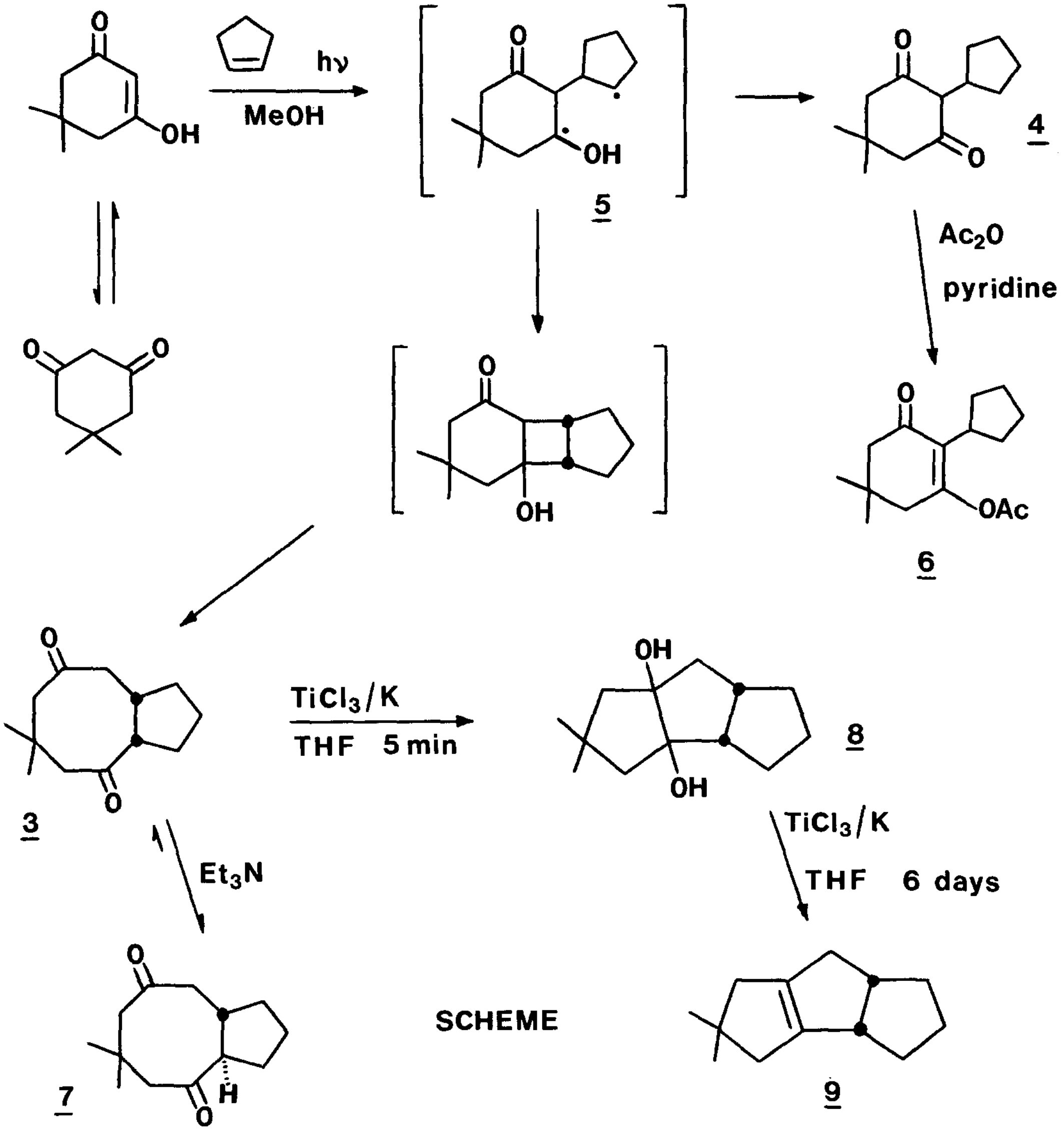
Irradiation[7] of a 1% solution of 5,5-dimethylcyclohexane-1,3-dione (dimedone) in methanol in the presence of excess cyclopentene using U.V. light of wavelength 254 nm resulted in complete conversion of the diketone to a mixture of two products, the cyclooctanedione **3** (90%) and the cyclohexane dione **4** (10%). Following removal of solvent, the dione **4** was separated from **3** by extraction into aqueous base and because of its apparent instability was characterized[8] as its enol acetate. Dione **4** presumably arises from intramolecular disproportionation of the presumed[5] biradical intermediate **5**.

The cyclooctanedione **3** was isolated as a white crystalline solid which was pure enough for use directly in subsequent reactions. Samples for characterization were obtained by recrystallization from pentane and had m.p. 114-115°C. The structure follows from ^{1}H-n.m.r., ^{13}C-n.m.r, I.R. and mass spectra,[8] and by analogy with the results of analogous photoadditions between dimedone and cyclohexene, and between cyclopentene and cyclohexane-1,3-dione.[5,9]



SCHEME

The cis stereochemistry of the cyclooctane-cyclopentane ring fusion of **3** was confirmed by epimerization (triethylamine or p-toluenesulfonic acid in refluxing benzene) to the more stable[9] trans fused system **7** (m.p. 62.5-63°C).[8]

McMurry has demonstrated that treatment of titanium trichloride with a variety of reducing agents yields low valence titanium species which will couple ketones to give olefins.[6] This reaction has been applied to acyclic dicarbonyl compounds to give cycloalkenes,[10] but, as far as we are aware, has not been reported for cycloalkanediones. Treatment of anhydrous titanium trichloride in refluxing dry T.H.F. with potassium metal under dry nitrogen gave a black mixture which smoothly and rapidly (less than 5 minutes) converted the diketone **3** to a substance identified as the diol **8** as the only product.[11] Assuming that a cis diol is produced, two possible structures exist for **8** depending upon the relative stereochemistry of the two ring fusions. Samples of **8** prepared by this route appear to be mainly a single isomer (95:5) whose stereochemistry is not readily deduced from the available data.[8] Extended exposure of **8** to the reaction conditions (6 days at reflux) resulted in the clean conversion of **8** to the olefin **9** as the only product. Compound **9** was isolated following an aqueous work-up as a colourless oil and a sample purified by preparative gas chromatography possessed the expected ^{1}H-n.m.r., ^{13}C-n.m.r., I.R. and mass spectral characteristics.[8]

The transformations described provide a new and simple entry into the tricyclo-[6.3.0.0^{2,6}]undecane system which should be capable of adaptation to allow the preparation of members of the capnellane and hirsutane family of natural products and their analogues.

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References and Notes

1. Contribution number 000 from the Photochemistry Unit, The University of Western Ontario.
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7. A Rayonet reactor equipped with low pressure mercury lamps was used. Solutions were irradiated in quartz tubes and the course of the reaction followed by gas chromatography.
8. Spectral data for 3: ν_{max} 1690 cm^{-1}; ^{1}H-n.m.r. (100 MHz, $CDCl_3$) 3.2-1.3 (m,20H), 1.23 (s,3H), 1.14 ppm (3H,s); ^{13}C-n.m.r. (200 MHz, $CDCl_3$) 210.94 (C=0), 210.85 (C=0), 58.78 (CH), 52.78 (CH_2), 52.48 (CH_2), 48.24 (CH_2), 38.41 (CH), 35.17 (C), 34.42 (CH_2), 32.68 (CH_3), 27.55 (CH_3), 23.29 (CH_2), 22.34 ppm (CH_2); m/e, calc. 208.1463, found 208.1463. Spectral data for 6: ν_{max} 1760, 1670 cm^{-1}; ^{13}C-n.m.r. (200 MHz, $CDCl_3$) 198.92 (sp^2) 167.84 (sp^2), 162.35 (sp^2), 138.36 (sp^2), 52.03 (CH_2), 43.02 (CH_2), 34.78 (CH), 32.48 (C), 30.57 (CH_2), 29.71 (CH_2), 27.99 (CH_3), 26.60 (CH_2), 21.01 (CH_3); m/e, calc. 205.1568, found 250.1569. Spectral data for 7: ν_{max} 1690 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$, 60 MHz), 2.9-1.5 (m, 20H), 1.05 (s, 6H); ^{13}C-n.m.r. (200 MHz, $CDCl_3$) 212.75 (C=0), 210.73 (C=0), 59.96 (CH), 52.08 (CH_2), 51.31 (CH_2), 50.77 (CH_2), 41.67 (CH), 35.74 (C), 34.75 (CH_2), 30.82 (CH_3), 29.59 (CH_2), 29.13 (CH_3), 23.11 (CH_2); m/e calc. 208.1463, found 208.1465. Spectral data for 8; ν_{max} 3400 cm^{-1}; ^{1}H-n.m.r. ($CDCl_3$, 100 MHz), 2.7 (2H, exch.), 2.5-1.2 (m, 14H), 1.17 (s,3H), 1.03 (3H,s); ^{13}C-n.m.r. ($CDCl_3$, 200 MHz), 89.80 (C-OH), 88.28 (C-OH), 55.00 (CH_2), 53.45 (CH), 53.21 (CH_2), 44.49 (CH_2), 39.70 (CH), 36.54 (C), 32.86 (CH_2), 32.05 (CH_3), 32.00 (CH_3), 26.59 (CH_2), 26.51 (CH_2); m/e, calc. 210.1620, found 210.1619. Spectra data for 9: ^{1}H-n.m.r. ($CDCl_3$, 100 MHz) 3.1-2.2 (m,3H), 2.1-1.2 (m,11H), 1.12 (s,3H), 1.08 (s, 3H); ^{13}C-n.m.r. ($CDCl_3$, 200 MHz), 145.82 (sp^2), 142.13 (sp^2), 47.12 (CH), 46.55 (CH), 45.29 (CH_2), 44.24 (C), 43.78 (CH_2), 38.03 (CH_2), 35.79 (CH_2), 30.82 (CH_3), 30.54 (CH_3), 30.12 (CH_2), 25.81 (CH_2); m/e, calc. 176.1565, found 176.1566.
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11. The reaction was carried out using the diketone, titanium trichloride and potassium in the molar ratio 1:4:15 at a concentration of ca .05M based upon diketone.

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