

## A Total Synthesis of ( $\pm$ )-Modhephene

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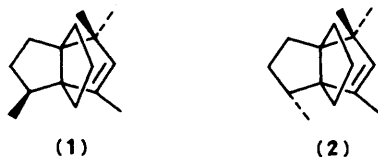
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A new approach to the [3.3.3] propellane system *via* a key photochemical oxa-di- $\pi$ -methane rearrangement has culminated in a synthesis of the sesquiterpene hydrocarbon ( $\pm$ )-modhephene (**1**).

The novel sesquiterpene hydrocarbon modhephene (**1**), bearing the unique carbocyclic [3.3.3] propellane framework, has attracted world-wide synthetic interest and many new and imaginative strategies have been developed towards its synthesis.<sup>1</sup> In this communication, we describe a conceptually new approach to (**1**) and epimodhephene (**2**) in which the pivotal steps are the photochemical oxa-di- $\pi$ -methane rearrangement of the tricyclic system (**3**) to the strained tetracycle (**4**) and regioselective reductive cleavage to (**5**) bearing the [3.3.3] propellane skeleton, Scheme 1. We emphasize that the (**3**)  $\rightarrow$  (**5**) sequence, although developed in our quest for (**1**), constitutes a new general approach to the [3.3.3] propellanes.<sup>2</sup>

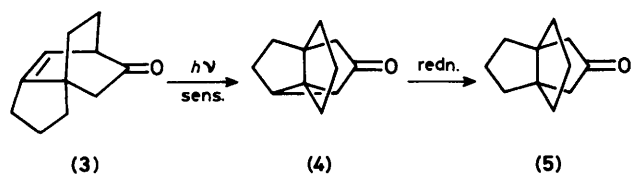
Reaction of the readily available<sup>3</sup> bicyclic enone (**6**) with MeMgI and work-up in aqueous protic media furnished a mixture of highly labile conjugated dienes (**7**) in 86% yield. The crude (**7**) was immediately treated with the ketene

equivalent  $\alpha$ -chloroacrylonitrile to furnish the Diels-Alder adducts (**8**) and (**9**) (43%). Hydrolysis of (**8**) and (**9**) with ethanolic sodium sulphide furnished the tricyclic ketones (**10**)<sup>†</sup> and (**11**)<sup>†</sup> (58%, 4:1), readily separable on chromatography, which were fully characterised on the basis of their <sup>1</sup>H and <sup>13</sup>C n.m.r. data (Scheme 2).

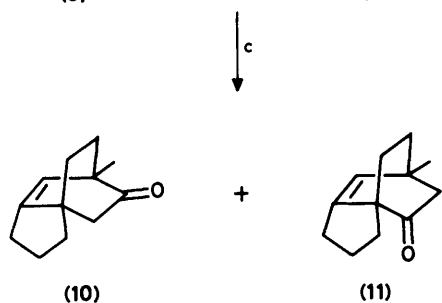
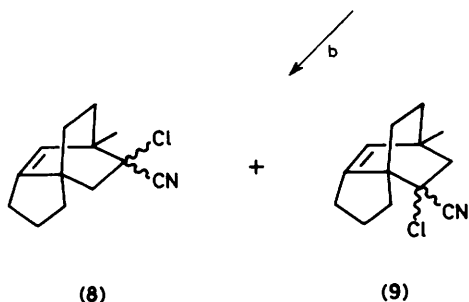
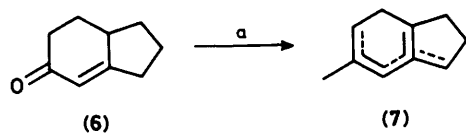


Scheme 1

<sup>†</sup> Compound (**10**):  $\nu_{\max}$  (neat) 3025 and 1720  $\text{cm}^{-1}$ ; <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ ; 100 MHz)  $\delta$  5.44 (1H, unresolved t) 2.42–1.40 (12H, m), and 1.2 (3H, s); <sup>13</sup>C n.m.r. ( $\text{CDCl}_3$ ; 25.0 MHz)  $\delta$  214.4 (s), 156.2 (s), 120.6 (d), 49.6 (s), 46.9 (s), 45.9 (t), 35.8 (t), 31.9 (t), 31.7 (t), 30.2 (t), 26.1 (t), and 17.8 (q); (**11**):  $\nu_{\max}$  (neat) 3025 and 1720  $\text{cm}^{-1}$ ; <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ ; 100 MHz)  $\delta$  5.80 (1H, t,  $J \sim 1$  Hz), 2.5–1.4 (12H, m), and 1.25 (3H, s); <sup>13</sup>C n.m.r. ( $\text{CDCl}_3$ ; 25.0 MHz)  $\delta$  211.9, 147.7, 129.2, 59.8, 48.0, 38.2, 35.1, 29.8, 29.6, 28.6, 26.1, and 24.1; (**12**):  $\nu_{\max}$  (neat) 3020 and 1720  $\text{cm}^{-1}$ ; <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ ; 100 MHz)  $\delta$  2.4–1.3 (13H, m) and 1.2 (3H, s); <sup>13</sup>C n.m.r. ( $\text{CDCl}_3$ ; 25.0 MHz)  $\delta$  215.4 (s), 62.3 (s), 57.5 (s), 53.4 (t), 50.5 (d), 43.5 (t), 42.9 (s), 38.2 (t), 34.6 (t), 28.6 (t), 24.8 (t), and 19.9 (q); (**13**):  $\nu_{\max}$  (neat) 3020 and 1720  $\text{cm}^{-1}$ ; <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ ; 100 MHz)  $\delta$  2.1–1.3 (11H, m), 1.2 (3H, s), 1.0 (3H, s), and 0.84 (3H, s); <sup>13</sup>C n.m.r. ( $\text{CDCl}_3$ ; 25.0 MHz)  $\delta$  219.4 (s), 64.0 (s), 58.5 (s), 52.3 (s), 45.5 (d), 41.4 (s), 40.0 (t), 33.8 (t), 30.7 (t), 29.0 (t), 25.9 (t), 25.1 (q), 19.7 (q), and 17.9 (q); (**14**):  $\nu_{\max}$  (neat) 1740  $\text{cm}^{-1}$ ; <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ ; 100 MHz)  $\delta$  3.04–2.61 (two sets of AB quartets, each 2H) and 1.1–0.95 (m, Me); (**15**):  $\nu_{\max}$  (neat) 1740  $\text{cm}^{-1}$ ; <sup>1</sup>H n.m.r. ( $\text{CDCl}_3$ ; 100 MHz)  $\delta$  1.61–1.30 (two sets of m, each 1H) and 1.1–0.95 (m, Me).

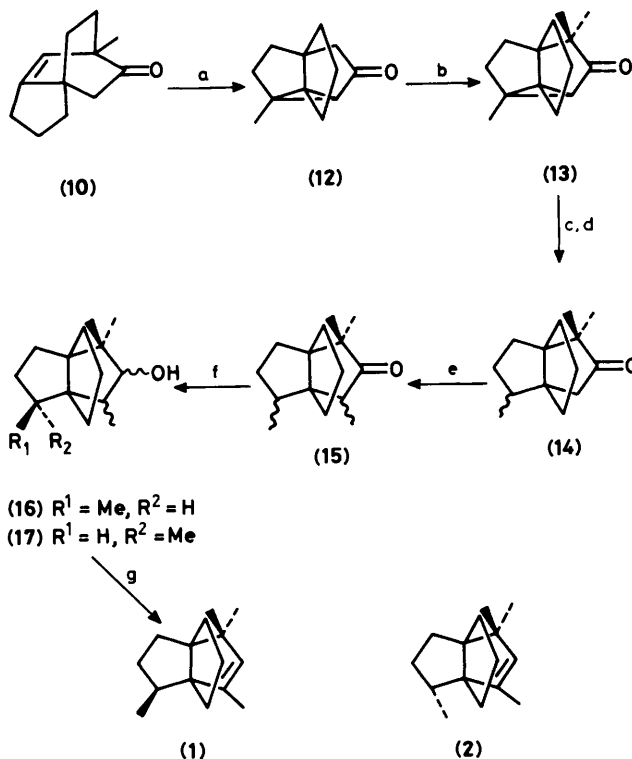


Scheme 1



**Scheme 2.** a, MeMgI-Et<sub>2</sub>O, H<sub>3</sub>O<sup>+</sup>; b, CH<sub>2</sub>=C(Cl)CN, toluene, 80 °C, 14 h; c, Na<sub>2</sub>S·9H<sub>2</sub>O-EtOH, reflux, 10 h.

The major, required β,γ-unsaturated ketone (10) was irradiated in acetone with a 450 W Hanovia medium-pressure lamp in a quartz vessel to furnish the strained cyclopropyl ketone (12) in 50% yield. The presence of three quaternary C resonances at 62.3 (s), 57.5 (s), and 42.9 (s) and the absence of olefinic C resonances were fully consistent with the tetracyclic structure (12)<sup>†</sup> derived from (10) through oxa-di-π-methane rearrangement.<sup>4</sup> The stage was now set for the introduction of the *gem*-dimethyl group at the desired position and this was achieved through exhaustive methylation with KOBu<sup>t</sup>-MeI to furnish (13)<sup>†</sup> (55%). Reductive C-C bond cleavage in (13) was effected through metal-ammonia reduction and (14) was obtained as a mixture (~1:1) of methyl epimers after pyridinium chlorochromate (PCC) oxidation. The separation of the methyl epimers of (14) at this stage proved capricious and was deferred till the penultimate step. Selective methylation of (14) with lithium hexamethyldisilazide-MeI proceeded smoothly to give (15) (60%) and further reduction with LiAlH<sub>4</sub> furnished an epimeric mixture of alcohols (16) and (17) (70%), which were fortunately amenable to chromatographic separation. However, dehydration of (16) and (17) presented considerable problems but could be ultimately effected with POCl<sub>3</sub>-pyridine containing traces of 1,8-



**Scheme 3.** a, *hν*-acetone, 45 min; b, Bu<sup>t</sup>OK-MeI, THF; c, Li-liq. NH<sub>3</sub>, NH<sub>4</sub>Cl; d, PCC-molecular sieves 4 Å; e, (Me<sub>3</sub>Si)<sub>2</sub>NH-Bu<sup>n</sup>Li-MeI, THF, 0 °C; f, LiAlH<sub>4</sub>-Et<sub>2</sub>O, 30 min; g, POCl<sub>3</sub>-pyridine-DBU, 4 h.

diazabicyclo[5.4.0]undec-7-ene (DBU) to furnish (1) and (2) in 36 and 24% yield, respectively, which were found to be spectroscopically identical with the authentic spectra provided by Professor Paquette (Scheme 3).

We thank Professor L. A. Paquette for the authentic spectra for comparison. The help of Mr. S. Satyanarayana and Mr. K. Srinivas Rao in recording the <sup>1</sup>H and <sup>13</sup>C n.m.r. spectra is greatly appreciated. This research was supported by C.S.I.R. and U.G.C. through a special assistance programme in Organic Chemistry.

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