

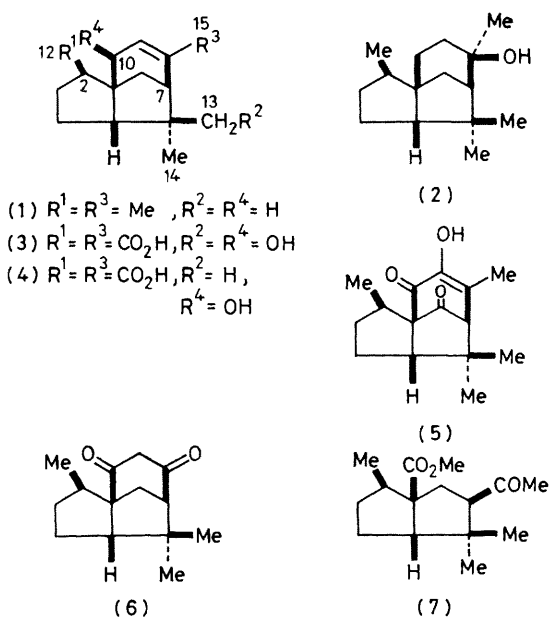
Cedrenoid Sesquiterpenes. Synthesis of the (\pm) Stork-Clarke β -Diketone

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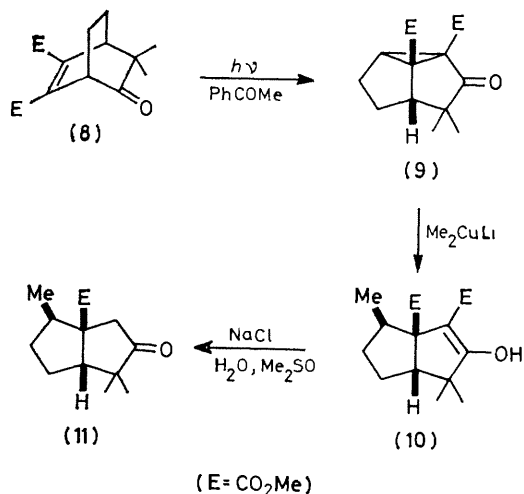
Summary (\pm)-2 β ,6,6-Trimethyltricyclo[5.3.1.0^{1,5}]undecane-8,10-dione (**6**) has been synthesized from dimethyl 6,6-dimethyl-5-oxobicyclo[2.2.2]oct-2-ene-2,3-dicarboxylate (**8**).

THE cedrenoid sesquiterpenes are characterized by the tricyclo[5.3.1.0^{1,5}]undecane skeleton, as in cedrene (**1**) and cedrol (**2**).¹ They differ in their states of oxidation at a variety of ring and substituent carbon atoms, as exemplified by shellolic acid (**3**),² laccishelloic acid (**4**),³ and α -pipitzol (**5**).⁴



(**6**) that is also potentially adaptable to the introduction of substitution at C-12 and C-13, as in (**3**).

Hydrogenation of the Diels-Alder adduct⁷ of 6,6-dimethylcyclohexa-2,4-dienone and dimethyl acetylenedicarboxylate gave (**8**).^{8†} This on irradiation in acetophenone as solvent and photosensitizer gave the oxa-di- π -methane product⁹ (**9**) (76%), m.p. 82–83 °C. Treatment of (**9**) with lithium dimethylcuprate¹⁰ gave (**10**), m.p. 76.5–78.5 °C‡ It was expected that this homoconjugate addition product would have the desired β -configuration of the carbon bearing the entering methyl group as depicted in (**10**),¹⁰ but this was only unambiguously established on completion of the synthesis of (**6**). Demethoxycarbonylation of (**10**) with NaCl in hot, wet Me₂SO¹¹ gave (**11**) (74%) as a mobile oil.



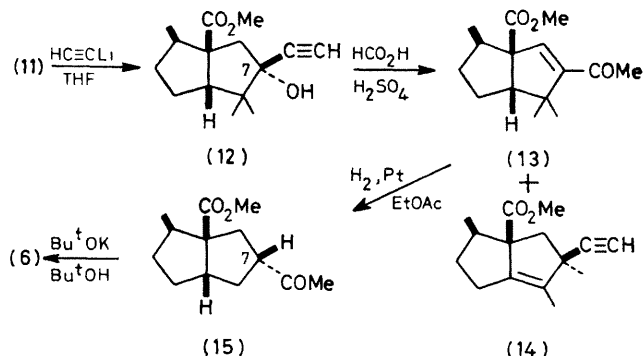
Stork and Clarke⁵ were the first to achieve the synthesis of a cedrenoid sesquiterpene and their synthesis of (**2**) was followed by several other total syntheses of (**1**) and (**2**).⁶ The only more highly oxygenated cedrenoids that have been synthesized are α -pipitzol (**5**) and its stereoisomer, β -pipitzol.⁴ We have undertaken a novel approach to the synthesis of (**2**) that is designed to be applicable to the eventual synthesis of many of the more highly oxygenated cedrenoids, a feature that is not shared by most of the previous syntheses of (**1**) and (**2**). We chose as our initial goal the β -diketone (**6**), a key intermediate in the synthesis of Stork and Clarke,⁵ which they obtained by base catalysed cyclization of the keto ester (**7**). This intermediate has the potentiality of providing a route to cedrenoids bearing oxygen at C-10 and C-15. We report now a synthesis of

Treatment of (**11**) with lithium acetylide in tetrahydrofuran (THF) at -75 °C gave (**12**) (61%), m.p. 95–96 °C; the relative configuration at C-7 is assigned in the expectation that attack of the acetylide occurs at the β -face of (**11**). Compound (**12**) was subjected to Rupe rearrangement (hot HCO₂H–H₂SO₄)¹² to give (**13**) (30%) as a mobile oil. At low concentrations of H₂SO₄ this is accompanied by a second product (**14**); increase in the concentration of H₂SO₄ suppresses the formation of (**14**), but gives rise to increased polymerization. Hydrogenation of (**13**) over platinum in ethyl acetate gave (**15**) (80%) as a mobile oil, which is considered to be the C-7 epimer of (**7**), in the expectation that addition of hydrogen occurs at the β -face. Treatment of (**15**) with potassium *t*-butoxide in *t*-butyl alcohol [conditions that had been employed previously for the conver-

† Satisfactory elemental analytical and spectroscopic data were obtained for compounds (**8**)–(**20**), except (**16**), which was not purified.

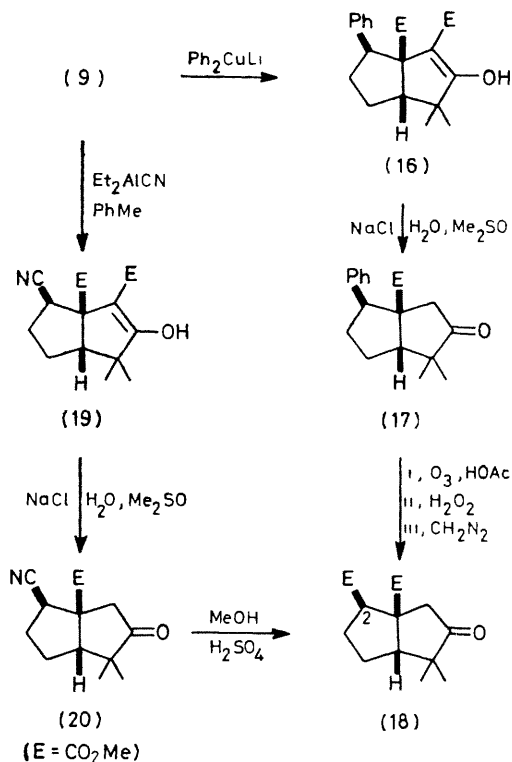
‡ Compound (**10**) was accompanied by two bicyclo[3.2.1]octane derivatives as minor products, formed by reductive cleavage of the cyclopropane ring; spectroscopic analysis shows that the yield of (**10**) was *ca.* 80%.

sion of (7) into (6)⁵] gave a product in 91% yield, shown to be (±)-(6) by direct spectroscopic comparison (i.r., mass, ¹H and ¹³C n.m.r.) with the optically active β-diketone (6)§



The viability of this synthetic approach to the introduction of a carboxylic acid function at C-2 has been demonstrated by treatment of (9) with lithium diphenylcuprate to give (16) as an oil, which was not purified but was subjected to demethoxycarbonylation as before to give (17), m.p. 125–127 °C, in 65% overall yield, which on ozonolysis in aqueous acetic acid followed by oxidative work-up¹³ and treatment with diazomethane gave (18), m.p. 63–65 °C, in 46% overall yield. Also, reaction of (9) with diethylaluminium cyanide in toluene¹⁴ gave (19) (56%) as a crystalline solid, m.p. 135–137 °C, which on demethoxycarbonylation as before gave (20) (69%) as a viscous oil. Treatment of (20) with methanolic sulphuric acid gave (18) in 41% yield.¶

We thank the Natural Sciences and Engineering Research Council of Canada for support of this work and Dr.



Martin Smith, Bruker Spectrospin (Canada) Ltd., for the ¹³C n.m.r. spectroscopic comparison of (+)-(6) and optically active (6).

(Received, 30th June 1980; Com. 706.)

§ We are greatly indebted to Professor Gilbert Stork for providing us with a generous sample of optically active (6), m.p. 202–204 °C. After recrystallization from dioxan (±)-(6) had m.p. 177.5–179 °C.

¶ That (18) has the β-configuration assigned at C-2 has been established by the independent synthesis of its α-epimer.

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