

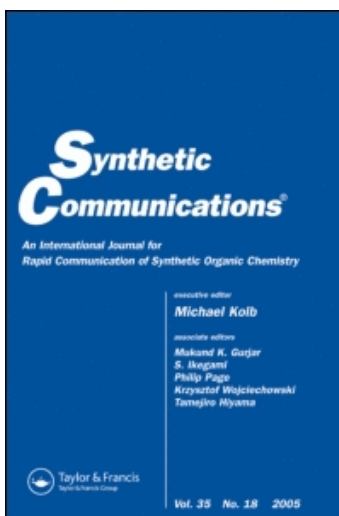
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Longifolene as a Chiron: Extraction of the Bicyclic Core of the Spongian-Type Diterpenoids

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LONGIFOLENE AS A CHIRON: EXTRACTION OF THE BICYCLIC
CORE OF THE SPONGIAN-TYPE DITERPENOIDS

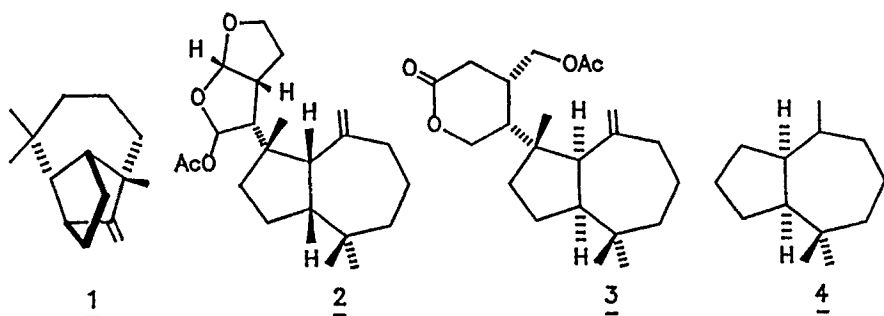
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Abstract: A short degradation of (+)-longifolene 1 to hydroazulene (+)-9 is described. Restructuring of 1 to a novel tricyclic framework (-)-10 is also reported.

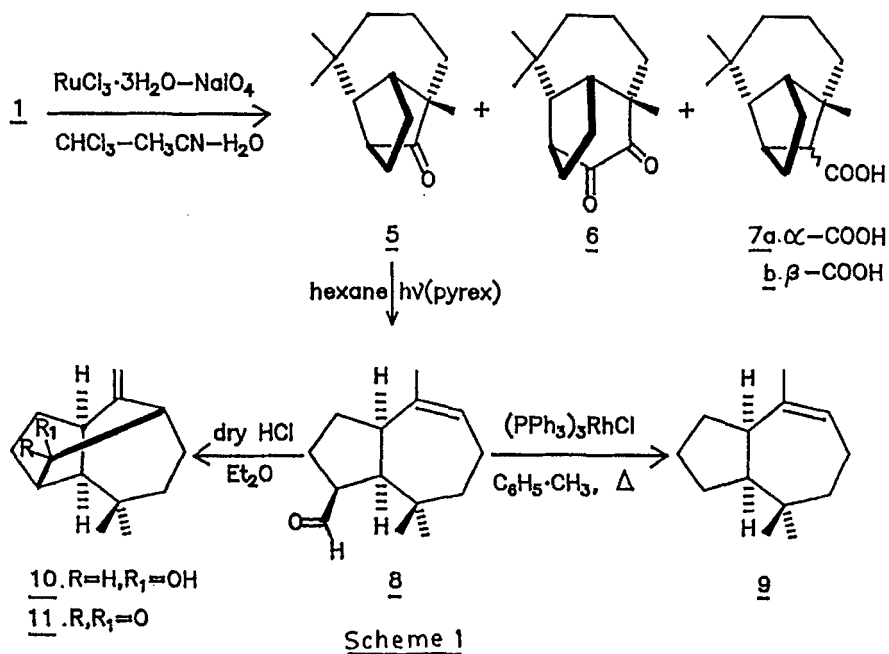
(+)-Longifolene 1 is an abundantly, commercially available (more than 100 ton quantity) sesquiterpene hydrocarbon, whose interlaced tricyclic framework is eminently suited for access to diverse polycyclic frameworks through degradation and/or restructuring protocols.¹ Indeed, 1 has been gainfully utilised in several syntheses of naturally occurring sesquiterpenes by Dev,² Nayak,³ us⁴ and others.⁵ Our interest in the molecular architecture of 1 was rekindled by the recent reports of fairly wide occurrence of spongian derived diterpenoids, e.g., 2 and 3 in Nature from marine

sources.⁶ These novel diterpenoids are characterised by the presence of a cis-fused bicyclic hydroazulenic core 4 and an oxygenated side-chain. Herein, we describe a short, three step sequence from 1, which delivers a hydroazulenic precursor based on 4, in chiral form and with requisite cis-ring junction stereochemistry.⁷



Catalytic ruthenium oxidation of 1 led to the formation of longicamphenilone 5, longidione 6 and epimeric mixture of longifolic acids 7, from which the desired 5 could be conveniently obtained in 35-40% yield, Scheme 1.⁸ Irradiation of 5 with a 450 W Hg lamp through a pyrex filter resulted in the expected Norrish-type I cleavage to the bicyclic aldehyde 8 in ~ 40% yield.^{1a,9} Reductive decarbonylation in 8 using the Wilkinson catalyst furnished the bicyclic hydroazulenic hydrocarbon (+)-9 in 52% yield, Scheme 1.

The unsaturated aldehyde 8 showed marked propensity towards intramolecular ene reaction on exposure to



acids. The best condition that we could obtain was through exposure to dry HCl gas which furnished the tricyclic olefinic alcohol (-)-10 as a single stereoisomer. Further oxidation of 10 with tetra-*n*-propylammonium perruthenate¹⁰ gave the β, γ -unsaturated ketone. (-)-11. Both 10 and 11 embody a restructured longifolene skeleton in which a bridged bicyclo(3.2.1)-octane moiety reminiscent of many terpenic natural products is present.

Experimental Section^{11,12}

Ruthenium catalysed oxidation of longifolene 1

To a stirred biphasic solution of sodium metaperiodate (20 g, 93 mmol), water (60 ml), acetonitrile

(40 ml), carbon tetrachloride (40 ml) and longifolene (4 g, 19.6 mmol) was added $\text{RuCl}_3 \cdot 3\text{H}_2\text{O}$ (120 mg, 0.46 mmol). The reaction mixture was vigorously stirred for 8h at room temperature, diluted with water and extracted with dichloromethane. The organic layer was washed, dried and evaporated to leave a viscous residue (3.8 g) which was chromatographed on a silica gel column using 4% EtOAc : hexane as the eluent to furnish unreacted longifolene 1 (264 mg, 6.6%) followed by longicamphenilone 5 (1.45 g, 36%); m.p. 49-50 °C, (lit.⁸ m.p. 50-51 °C). Further elution with 8% EtOAc : hexane yielded longidione 6 (252 mg, 5.5%); m.p. 92-93 °C (lit.⁸ m.p.93-94 °C). Finally, the column was washed with EtOAc to furnish longifolic acids 7a,b (772 mg, 16.7%) as a 33 : 67 ratio as determined from the ¹H NMR integration of the well separated ester methyl signals.

2,6,6-Trimethylbicyclo[5.3.0]dec-2-ene-8-carboxaldehyde 8:

A solution of 5 in cyclohexane (500 mg, in 130 ml, 0.018 mmol), degased with N_2 was irradiated for 1h in a quartz immersion well (pyrex filter) with a 450 W Hanovia mercury vapour lamp. Solvent was evaporated under reduced pressure and the residue on careful chromatography on a silica gel column using 3% EtOAc : hexane as eluent furnished the aldehyde 8

(130 mg, 43%) based on the recovered starting material. $[\alpha]_D + 75.46$ (C, 1.39, CHCl_3); IR (neat): 2920 (br), 2725, 1710, 1440 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3): 6.9.77 (2H, d, $J=6\text{Hz}$, CHO), 5.58 (1H, br s, olefinic), 2.97-2.62 (2H, m), 2.20-1.12 (9H, m), 1.22 (3H, br s), 1.12 (3H, s), 1.08 (3H, s); ^{13}C NMR (25.0 MHz, CDCl_3): 6205.59, 138.65, 128.21, 59.88, 52.94, 42.35, 36.33, 35.82, 30.94, 30.41, 29.47, 25.35, 24.59, 24.23. Anal. Calcd. for $\text{C}_{14}\text{H}_{22}\text{O}$: C, 81.5; H, 10.76. Found: C, 81.34; H, 10.57.

2,6,6-Trimethylbicyclo[5.3.0]dec-2-ene 9

The aldehyde 8 (70 mg, 0.34 mmol) and tris(triphenylphosphine)rhodium (I) chloride catalyst (14 mg, 0.34 mmol) in dry benzene (15 ml), was heated in a sealed-tube under N_2 at 120-130 $^\circ\text{C}$ for 10h. The reaction mixture was diluted with hexane and filtered through a florisil pad. The residual oil was purified on a 15% AgNO_3 - silica gel column. Elution with hexane furnished 9 as a volatile liquid (31.5 mg, 52%). $[\alpha]_D + 19.34$ (C, 0.81, CHCl_3); IR (neat): 2890(br), 1440, 1355 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3): 6 5.36 (1H, t, $J=7\text{Hz}$, olefinic), 2.72-2.24 (1H, m), 2.21-2.01 (1H, m), 1.96-1.10 (10H, m), 1.72 (3H, br s), 1.03 (3H, s), 0.92 (3H, s); ^{13}C NMR (25.0 MHz, CDCl_3): 6 138.53, 123.65, 52.65, 46.12, 36.17, 35.00, 33.23, 30.00, 27.35, 26.53, 25.53, 24.06. Satisfactory analysis could not be obtained due to the labile nature of this hydrocarbon.

8,8-Dimethyl-11-methylene-tricyclo[4.4.1.0^{3,7}]undecan-2-ol 10

Dry HCl gas was bubbled into a solution of enaldehyde 8 (100 mg, 0.48 mmol) in dry diethyl ether (25 ml) until saturation at 0 °C. The mixture was left aside at 0 °C for 18h. The reaction mixture was neutralized with saturated NaHCO₃ solution under cooling and the organic layer was washed and dried. Evaporation of the solvent furnished the crude alcohol which was purified on a silica gel column using 10% EtOAc : hexane as the eluent. Recrystallisation from hexane yielded 10 (56 mg, 56%), m.p. 98-99 °C; [α]_D - 61.57° (C, 1.15, CHCl₃); IR (neat): 3356, 2905, 1445 cm⁻¹; ¹H NMR (100 MHz, CDCl₃): δ 4.78 (2H, d, J=7Hz), 4.08 (1H, d, J=8Hz), 2.70 (1H, br s, CHOH), 2.08-1.22 (11H, m), 1.00 (3H, s), 0.96 (3H, s); ¹³C NMR (25.0 MHz, CDCl₃): δ 154.76, 110.47, 73.88, 54.99, 47.89, 41.41, 38.82, 35.82, 35.53, 34.47, 34.06, 32.88, 28.23, 21.05. Anal. Calcd. for C₁₄H₂₂O: C, 81.50; H, 10.76. Found: C, 81.35; H, 10.76.

8,8-Dimethyl-11-methylene-tricyclo[4.4.1.0^{3,7}]undecan-2-one 11

To a mixture of alcohol 10 (50 mg, 0.243 mmol) in 10 ml of dry dichloromethane containing finely ground 4°A molecular sieves (20 mg) and 4-methylmorpholine N-oxide (35 mg, 3 mmol) was added tetra-n-propylammo-

nium-perruthenate (TPAP, 3 mg) and the reaction stirred further for 4h. The reaction mixture was filtered through a florisil pad and the filtrate was processed in the usual manner. The residue was purified on a short length silica gel column using 10% EtOAc : hexane as the eluent to furnish the ketone 11 (44 mg, 89%). $[\alpha]_D^{25} - 80.8^\circ$ (C, 1.23, CHCl_3); IR (neat): 3065, 2945, 2860, 1720, 1640, 1460, 890 cm^{-1} ; ^1H NMR (100 MHz, CDCl_3): δ 4.84 (2H, d, $J=14\text{Hz}$), 3.08-2.86 (2H, m), 2.72-2.54 (1H, m), 2.10-1.20 (9H, m), 1.06 (3H, s), 0.93 (3H, s); ^{13}C NMR (25.0 MHz, CDCl_3): δ 216.60, 150.53, 110.94, 53.88, 53.18, 49.88, 41.94, 35.23, 34.59, 33.94, 31.82, 30.94, 28.76, 26.76. Anal. Calcd. for $\text{C}_{14}\text{H}_{20}\text{O}$: C, 82.30; H, 9.87. Found: C, 82.43; H, 9.77.

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