HETEROCYCLES, Vol. 10, 1978

FACILE SYNTHESES OF PERILLENE AND DENDROLASIN

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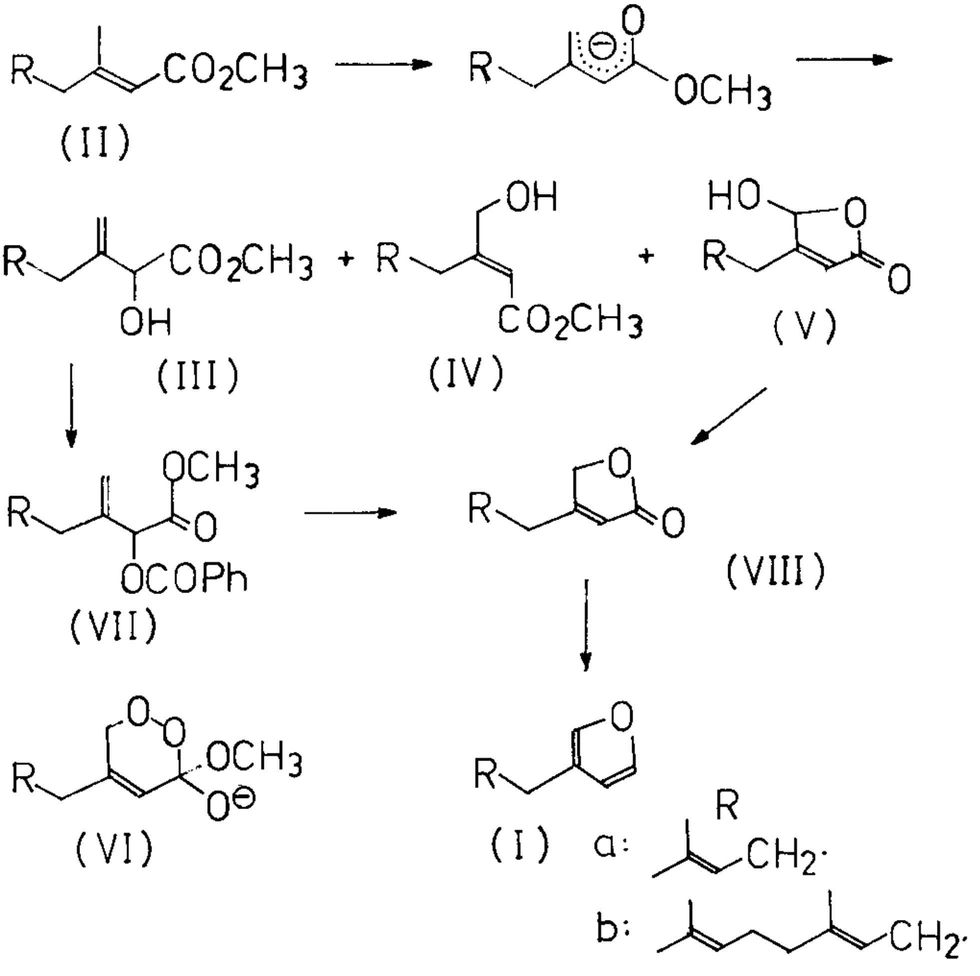
A synthesis of perillene (Ia) was accomplished using the regioselective oxidation of the dienolate anion generated from methyl geraniate (IIa). Dendrolasin (Ib) was also synthesized from methyl farnesoate (IIb).

The syntheses of relatively simple 3-substituted furano terpens, perillene (Ia) and dendrolasin (Ib) which is hypothetically an alarm and defence substance in some species of ants have been achieved through various methods.[1] There has been, however, no synthetic approach to these natural products by regioselective oxidation of geraniol and farnesol derivatives.

We now wish to report four steps syntheses of perillene (Ia) and dendrolasin (Ib) from methyl geraniate (IIa) and methyl farnesoate (IIb) involving a facile synthetic method of 3-substituted Δ^2-butenolides. The solution of the lithium dienolate prepared from methyl geraniate (IIa) by the treatment with one equivalent of lithium diisopropylamide — hexamethyl phosphoric triamide complex at -78° C in tetrahydrofuran[2] was added to an oxygenated solution of tetrahydrofuran containing two equivalents of triethyl phosphite at -78° C.[3] Oxygen was bubbled continuously for 15 minutes, and then aqueous ammonium chloride solution was added. After the usual work-up procedure the oxidation products (IIIa), (IVa) and (Va) were isolated from the reaction mixture by chromatography on silica gel in 66.0%, 11.4% and 8.9% yield respectively. (IIIa): ir(film) 3420, 1735, 1645 and 920 cm^{-1}; nmr(CCl_4) 1.62 and 1.69 (each 3H, s), 2.1 (5H, m), 3.26 (1H, OH), 3.76 (3H, s), 4.50 (1H, s), 4.96 (1H, s), 5.08 (1H, m) and 5.10 ppm (1H, s); ms molec. ion m/e 198.1259 (Calc. for $C_{11}H_{18}O_3$, m/e 198.1256). (IVa): ir(film) 3360, 1715 and 1650 cm^{-1}; nmr(CCl_4) 1.61 and 1.68 (each 3H, s), 2.1 - 2.5 (4H, m), 2.94 (1H, OH), 3.68 (3H, s), 4.12 (2H, d, J = 1.5 Hz), 5.13 (1H, m) and 5.89 ppm (1H, m); ms molec. ion m/e 198.1255 (Calc. for $C_{11}H_{18}O_3$, m/e 198.1256). (Va): ir(film) 3360, 1745 and 1645 cm^{-1}; nmr(CCl_4) 1.64 and 1.72 (each 3H, s), 2.4 (4H, m), 5.12 (1H, m), 5.76 (1H, s) and 5.96 ppm (1H, s); ms molec. ion m/e 182.0935 (Calc. for $C_{10}H_{14}O_3$, m/e 182.0943). The formation of (Va) which is one of the oxidation products in γ-position may be postulated occuring through the intermediate (VIa). The successful lactonization of (IIIa) was achieved by heating with anhydrous lithium iodide as follows. After the benzoylation of (IIIa) with benzoyl chloride in pyridine (92% yield), the benzoate (VIIa) was reacted with anhydrous lithium iodide in dimethyl formamide[4] at the reflux temperature for five hours to give the desired lactone (VIIIa) (53% yield): ir(film) 1780, 1745, 1640 and 900 cm^{-1}; nmr (CCl_4) 1.64 and 1.72 (each 3H, s), 2.4 (4H, m), 4.65 (2H, d, J = 1.5 Hz), 5.09 (1H, m) and 5.72 ppm (1H, m); ms molec. ion m/e

166.0986 (Calc. for $C_{10}H_{14}O_2$, m/e 166.0994). Finally, butenolide (VIIIa) was treated with diisobutylaluminium hydride in tetrahydrofuran at -25° C[5] to give perillene (Ia).



In the same manner as the case of methyl geraniate (IIa) the oxidation of methyl farnesoate[6] (IIb) gave (IIIb) (66% yield): ir (film) 3440, 1735, 1645 and 920 cm^{-1}; nmr(CCl_4) 1.60 and 1.68

(each 3H, s), 2.1 (8H, m), 2.92 (1H, d, J=4 Hz, OH), 3.78 (3H, s), 4.48 (1H, d, J=4 Hz), 4.98 (1H, s), 5.08 (2H, m) and 5.12 ppm (1H, s); ms molec. ion m/e 266.1899 (Calc. for $C_{16}H_{26}O_3$, m/e 266.1882), (IVb) (10% yield): ir(film) 3360, 1715 and 1650 cm^{-1}; nmr(CCl_4) 1.59 (6H, s), 1.66 (3H, s), 1.9-2.5 (8H, m), 2.95 (1H, OH), 3.65 (3H, s), 4.08 (2H, d, J=1.5 Hz), 5.06 (2H, m) and 5.85 ppm (1H, m); ms molec. ion m/e 266.1865 (Calc. for $C_{16}H_{26}O_3$, m/e 266.1882) and (Vb) (3% yield): ir(film) 3340, 1745 and 1645 cm^{-1}; nmr(CCl_4) 1.58, 1.61 and 1.66 (each 3H, s), 1.8-2.5 (8H, m), 5.04 (2H, m), 5.73 (1H, s) and 5.94 ppm (1H, s); ms molec. ion m/e 250.1538 (Calc. for $C_{15}H_{22}O_3$, m/e 250.1569). The lactol (Vb) was reduced with sodium borohydride and then acidified to give butenolide (VIIIb). After the benzoylation of (IIIb) the benzoate (VIIb) was heated with anhydrous lithium iodide in dimethyl formamide to give butenolide (VIIIb) (53% yield): ir(film) 1780, 1745, 1640 and 900 cm^{-1}; nmr(CCl_4) 1.62, 1.65 and 1.69 (each 3H, s), 1.9-2.5 (8H, m), 4.63 (2H, d, J=1.5 Hz), 5.05 (2H, m) and 5.73 ppm (1H, m); ms molec. ion m/e 234.1614 (Calc. for $C_{15}H_{22}O_2$, m/e 234.1612). Dendrolasin (Ib) was derived from (VIIIb) by the treatment with diisobutylaluminium hydride. The spectral data of these synthesized perillene (Ia) and dendrolasin (Ib) were identical with those of the natural ones.

The simple synthetic procedure of 3-substituted Δ^2-butenolides described here should prove useful in the natural products syntheses. Further extentions of our method are continued.

ACKNOWLEDGEMENT We thank Dr. T. Sakai and Dr. Y. Naya (the Institute of Food Chemistry) for giving us the spectral data of natural perillene and dendrolasin.

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Received, 28th September, 1978