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SYNTHESES OF FURANOTERPENES: PERILLENE, DENDROLASIN, NEOTORREYOL, AND TORREYAL

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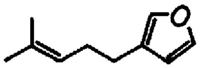
We have recently reported the oxygenation of acyclic conjugated dienes with singlet oxygen to afford 1,4-endoperoxides,[1] which are then easily dehydrated to furans in excellent yield.[2] From both the synthetic and the biogenetic points of view, it is of interest to convert naturally-occurring 1,3-diene to the corresponding furan by these two-step reactions. We now wish to describe an application of our synthetic scheme to a stereospecific total synthesis of relatively simple furanoterpenes, i. e., perillene (1) and dendrolasin (2), which have been found in a species of ant, *Lasius* (*Dendrolasius*) *fulginosus* *Latr*.,[3] and neotorreyol (3) and torreyal (4), which have been isolated, together with 2, from the wood oil of *Torreya* *nucifera* Sieb. and Zucc.[4]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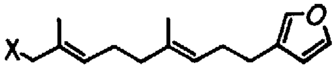
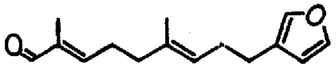


2: X = H
3: X = OH



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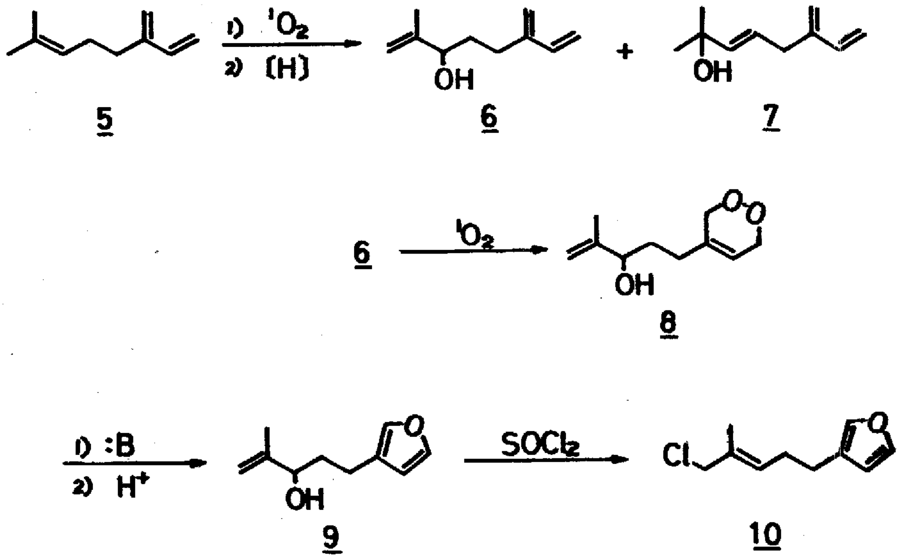
β-Myrcene (5) was chosen as the starting material because of its easy availability and its economy. The principle of the synthesis was based on the use of the "ene" reaction and the 1,4-cycloaddition reaction of singlet oxygen, and the SNi' chlorination of the allylic alcohol produced. Initially, 5 was oxygenated with singlet oxygen to give a mixture of hydroperoxides;[1,5] the mixture was then reduced with thiourea in 10% aqueous methanol at 0 - 10° for

3 hr to afford a mixture of alcohols, 6 and 7 (6/7 = 2/3). The separation of the mixture into 6 and 7 was effected by chromatography on silica gel with dichloromethane: 6, 36% yield, bp 85°/11 mm, NMR (in $CDCl_3$) δ4.70 - 6.65 (m, 7H), 4.08 (t, J = 6.0 Hz, 1H, CHOH), 2.07 - 2.47 (m, 3H, allylic CH_2 and OH), and 1.73 (broad s, 3H) ppm. A solution of the alcohol 6 and Rose Bengal as a sensitizer in dichloromethane containing 5% methanol was again irradiated with a halogen lamp (Toshiba JD 100V 500W) under an oxygen atmosphere for 18 hr. After evaporation of the solvent, the reaction product was purified by chromatography on silica gel (dichloromethane) to afford the 1,4-endoperoxide 8 as a colorless liquid:[6] 70% yield, NMR (in $CDCl_3$) δ5.60 - 5.83 (m, 1H), 4.80 - 5.03 (m, 2H), 4.40 - 4.70 (m, 4H, OCH_2), 4.07 (t, J = 6.0 Hz, 1H, CHOH), 2.50 (s, 1H, OH), 1.43 - 2.35 (m, 4H), and 1.73 (broad s, 3H). Treatment of the peroxide 8 with an equivalent of lithium t-butoxide in tetrahydrofuran (THF) at 15 - 20° for 3 hr followed by dehydration with sulfuric acid and chromatographic purification of the product through neutral alumina furnished the furan 9 in 87% yield, NMR (in $CDCl_3$) δ7.27, 7.16 and 6.25 (three m, 3H, furan ring H), 4.72 - 5.03 (m, 2H), 4.07 (broad t, J = 6.0 Hz, 1H, CHOH), 2.50 (broad t, J = 8.0 Hz, 2H, furfuryl CH_2), 1.50 - 2.03 (m, 2H), and 1.73 (broad



s, 3H). Chlorination of the allylic alcohol 9 with thionyl chloride[7] in *n*-hexane under an argon atmosphere at 15 - 20° overnight gave only the *trans*-isomer of ω-chloroperillene (10): 90% yield, NMR (in CCl_4) δ7.24, 7.13 and 6.18 (three m, 3H), 5.49 (broad t, J = 6.0 Hz, 1H), 3.93 (s, 2H, CH_2Cl), 2.13 - 2.53 (m, 4H), 1.71 (broad s, 3H). The chloride 10 was used as the key-intermediate for the syntheses of all the furanoterpenes to be described here.

Treatment of the chloride 10 with lithium aluminum hydride in ether at 15 - 20° overnight afforded one of the simplest furanoterpene, i. e., perillene (1) in 92% yield, bp 80°/18 mm (lit.[8] bp 185 - 186°).

In order to construct a sesquiterpene structure, introduction of prenyl unit into the *trans*-ω-position of the perillene is required. Thus, the carbanion prepared from prenyl phenyl sulfide (11) and *n*-butyl lithium in the presence of 1,4-diazabicyclo[2.2.2]octane in THF was condensed with the chloride 10 at -30° for 1 hr. Usual work-up and purification of the product by column chromatography gave the sulfide 12, as a colorless liquid, in 84% yield: NMR (in CCl_4) δ7.02 - 7.34 (m, 7H), 6.11 (m, 1H, one of the furan ring H), 5.10 (broad t, J = 6.0 Hz, 1H), 4.87 (broad d, J = 10.0 Hz, 1H), 3.84 (d of d of d, J = 10.0, 9.0, and 6.0 Hz, 1H, CHS), 1.96 - 2.48 (m, 6H), 1.61, 1.55 and 1.30 (three broad s, 9H). According to the reported procedure,[9] the sulfide 11 was reduced with metallic lithium in ethylamine at -78° for 2 hr to afford dendrolasin (2) in 83% yield, bp 142°/11 mm (lit.[3] bp 148°/16 mm).

Similarly, the dianion prepared from *trans*-ω-hydroxyprenyl phenyl sulfide (13)[10] and 2 equivalent of *n*-butyl lithium in the presence of hexamethylphosphoric triamide was reacted with 10 in diglyme at -70° for 30 min to give the adduct 14 as a colorless requid in 83% yield. Subsequent reduction of the sulfide 14 with $Li\text{-}EtNH_2$ (-78°, 7 hr) afforded neotorreyol (3) in 73% yield.

11: X = H

13: X = OH

12: X = H

14: X = OH

Finally, the hydroxyfuran 3 was oxidized with manganese dioxide in n-hexane at the ambient temperature to give torreyal (4) quantitatively.

In conclusion, perillene (1), dendrolasin (2), neotorreyol (3), and torreyal (4) were obtained in 51, 38, 33, and 33% yields, respectively, based on the starting allylic alcohol 6. The spectral data of the synthesized products were identical with those of the published ones.[3,4,8,11] Further extension of our method to the synthesis of more complex furanoterpenes will be described in a forthcoming communication.

References and Notes

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