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CHEMICAL CONVERSION OF HUMULENE TO CYCLOHUMULANOIDS ALONG THE BIOSYNTHETIC PATHWAY. STERPURENE, A HYDROCARBON FROM SILVER-LEAF DISEASE FUNGUS

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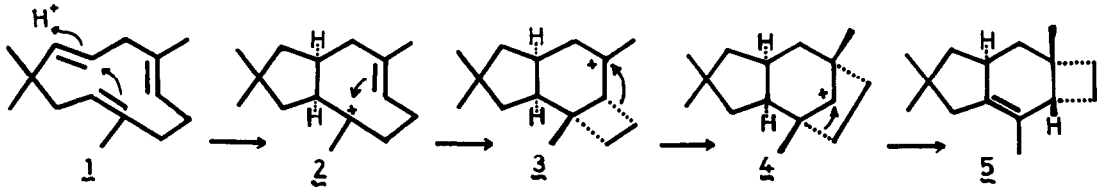
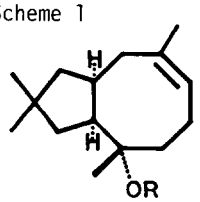
Summary: Sterpurene, a cyclohumulanoid obtained from silver-leaf disease fungus, was chemically derived from humulene via a route analogous to biosynthesis.

Sterpurene (5)[1] is a precursory hydrocarbon of oxygenated metabolites[2] of the silver leaf disease fungus, Streum purpureum. Chemistry of the products from this fungus has intensively studied by Ayer and his coworkers. Biosynthetic studies[3] indicated that the sterpurene was derived from humulene via protoilludyl cation (3) (Scheme 1). We wish to report here a chemical conversion of humulene to sterpurene along the biosynthetic pathway.[4]

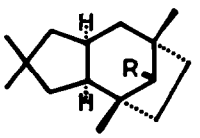
Humulene was converted to a cyclooctenol 6[5] through treatment with $Hg(NO_3)_2$[6] followed by Li-$EtNH_2$. Reaction path forming a bridged compound 9 on treatment of 6 with HCO_2H was shown[5] to be through protoilludyl cation (3), employing a deuterated material. The cyclooctenol 6 was converted to a methoxy ether 7[7] (2 eq MeI, 2 eq NaH, THF, refl. 30 min; 96%), which was treated with 2 eq of BBr_3 in CH_2Cl_2 at -78 °C for 30 min to give a bridged bromide 11[7] (21%) and an ether 12[8] (21%). The reaction leading to the bromide was interpreted analogously to the previously described formolysis (6→9)[5], that is, the generated cation 2 furnished first the protoilludyl cation 3 and then rearranged to 4 to give concertedly the β-bromide 11.[9] Treatment of 11 with 2 eq of AgOAc in AcOH at 90° for 7 h afforded racemic sterpurene (5)[7] in 61% yield accompanied by a small amount (10%) of a bridged acetate 10.[7,10] The synthetic sterpurene was spectrally identical with natural product. Since the sterpurene (5) was quantitatively converted to the formate 9 whose stereostructure was known on standing in HCO_2H at rt for 3 h, the acetate 10 could be formed from 5.



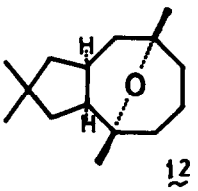
Scheme 1



6 R = H
7 R = CH_3



8 R = OH
9 R = OCHO
10 R = OAc
11 R = Br



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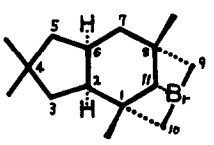
Acknowledgment. We are grateful to Prof. W. A. Ayer (Univ. of Alberta) for his kindly showing us the manuscript describing isolation of sterpurene prior to publication.

References and Notes. 1) W. A. Ayer, M. H. Saeedi-Ghomi, Can. J. Chem., in press. See also ref. 2. 2) a) W. A. Ayer, M. H. Saeedi-Ghomi, D. Van Engen, B. Tagle, J. Clardy, Tetrahedron, 37, 279 (1981); b) W. A. Ayer, M. H. Saeedi-Ghomi, Tetrahedron Lett., 22, 2071 (1981). 3) W. A. Ayer, L. M. Browne, Tetrahedron Reports, in press and ref. 2b. 4) For biomimetic conversion of humulene to other cyclohumulanoids, see H. Shirahama, K. Hayano, Y. Kanemoto, S. Misumi, T. Ohtsuka, N. Hashiba, A. Furusaki, S. Murata, R. Noyori, T. Matsumoto, Tetrahedron Lett., 21, 4835 (1980) and references cited therein. 5) S. Misumi, T. Ohtsuka, Y. Ohfune, K. Sugita, H. Shirahama, T. Matsumoto, Tetrahedron Lett., 31 (1979). 6) S. Misumi, T. Ohtsuka, H. Hashimoto, Y. Ohfune, H. Shirahama, T. Matsumoto, Tetrahedron Lett., 35 (1979). 7) Spectral data of all of the products in this paper are consistent with the structures depicted in the figure. 5: IR (cm^{-1}) 1458, 1445, 1372; ^1H NMR (200 MHz, $CDCl_3$) δ 0.67 (1H, dd, J=11.5, 13.5), 0.93 (1H, m), 1.06 (3H, s), 1.08 (3H, s), 1.20 (3H, s), 1.51 (3H, s), 1.66 (1H, dd, J=7.5, 12), 2.10 (2H, s), 2.37 (1H, dd, J=10, 12), 2.64 (1H, m); ^{13}C NMR (25 MHz, $CDCl_3$) δ 17.8q, 24.8t, 27.9t, 29.3q, 29.6q, 30.3q, 37.0s, 37.7d, 38.0s, 39.4t, 44.5t, 44.7d, 48.6t, 127.7s, 136.9s. 7: ^1H NMR (60 MHz, CCl_4) δ 0.99 (3H, s), 1.07 (3H, s), 1.11 (3H, s), 1.70 (3H, s), 3.04 (3H, s), 5.33 (1H, t, J=7.5). 10: IR 1750, 1238; ^1H NMR (60 MHz, CCl_4) δ 0.84 (3H, s), 0.94 (3H, s), 1.08 (3H, s), 2.01 (3H, s), 4.52 (1H, s). 11: ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (3H, s), 0.98 (3H, s), 1.04 (3H, s), 1.10 (3H, s), 1.74 (1H, d, J=12), 1.90 (1H, m), 2.34 (1H, t, J=13), 3.64 (1H, s). 8) S. Misumi, Y. Ohfune, A. Furusaki, H. Shirahama, T. Matsumoto, Tetrahedron Lett., 2865 (1976). 9) The epimeric bromide 13 was obtained by bromination of 8[10] (10 eq CBr_4 and PPh_3, PhH, reflux, 3 days; 54%) and 13 gave 14 on debromination [1) 2 eq AgOAc, AcOH, rt, overnight; 2) $LiAlH_4$, THF, 0°, 30 min; 60%] as a result of migration of the 7,8-bond which was antiparallel to the C(11)-Br bond. Configuration of 14 was determined by lanthanide induced shift and decoupling studies of the ^1H NMR spectrum.



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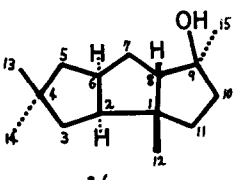

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13: ^1H NMR (200 MHz, $CDCl_3$) δ 0.96 (3H, s), 1.10 (3H, s), 1.12 (3H, s), 1.14 (3H, s), 4.31 (1H, s). 14: ^1H NMR (60 MHz, CCl_4) δ 0.90 (3H, s), 1.03 (3H, s), 1.18 (3H, s), 1.21 (3H, s); LIS ^1H NMR (200 MHz, $CDCl_3$, $Eu(fod)_3$ /14 = 0.133) δ 1.14 (3H, s, S=1.9, 13), 1.24 (3H, s, S=1.5, 14), 2.38 (3H, s, S=9.3, 12), 2.40 (1H, m, S=7.2, 7β), 2.82 (1H, m, S=9.7, 7α), 3.43 (3H, s, S=17.0, 15), 3.90 (1H, dd, J=7, 12, S=16.2, 10β), 4.59 (1H, t, J=7, S=22.0, 8β). 10) Y. Ohfune, H. Shirahama, T. Matsumoto, Tetrahedron Lett., 2869 (1976). 11) The acetate 10 was converted to 8 ($LiAlH_4$, ether, rt, 1 h) and identified.

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