Tetrahedron Letters,Vol.28,No.42,pp 5017-5020,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

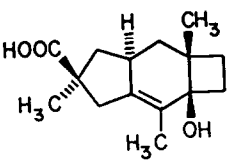
TOTAL SYNTHESIS OF (±)-STERPURIC ACID

Leo A. Paquette,* Ho-Shen Lin, and Michael J. Coghlan

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

Abstract: The unusual sesquiterpenoid fungal metabolite sterpuric acid (1) has been assembled in 11 steps and 11% overall yield from the readily available vinyl sulfone 2.

The fungus *Stereum purpureum* (class Basidiomycetes) is recognized to be responsible for the destruction of plum, apple, and other fruit trees, as well as mountain ash, cotoneaster, and aspen.[1] Trees infected by this fungus develop foliage with a dull leaden or metallic luster, thus the colloquial term "silver leaf disease". When grown under laboratory conditions in malt extract-dextrose-peptone liquid culture, *S. purpureum* furnishes a broth, extracts of which contain sterpuric acid (1),[2] a new sesquiterpenoid of unusual type, as a major constituent.[3] Ayer and coworkers have unequivocally established

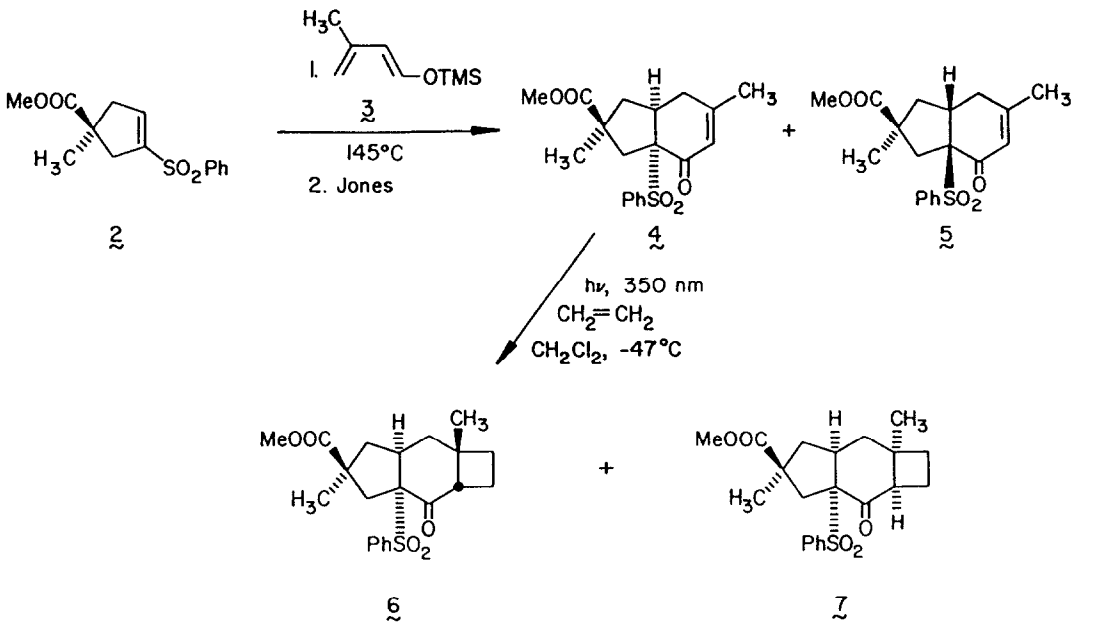


1

the structure of 1 by single crystal X-ray analysis. Biosynthetic studies suggest that 1 is elaborated in vivo from acetate units via humulene and the protoilludyl cation.[4]

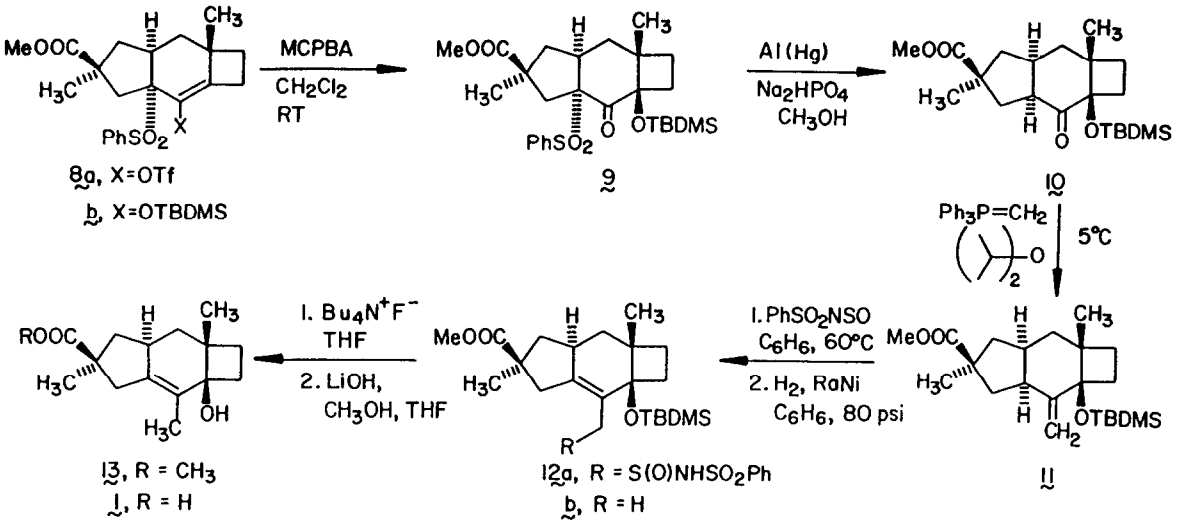
Despite the novel structural features of this family of fungal metabolites,[5] only two reports have appeared outlining efforts directed toward the synthesis of the fundamental sterpurene skeleton.[6] In this communication, we wish to record the first total synthesis of the more highly oxygenated 1. The route holds the prospect of being potentially adaptable to other members of this class.[2,3]

The readily available[7] vinyl sulfone 2 was selected as starting material since it



possesses those structural elements present in ring A of **1** and is appropriately activated for involvement as a dienophile in [4+2] cycloaddition.[8] Heating **2** with 2.7 equiv of **3**[9] at 145 °C in the presence of a small amount of 2,6-di-*tert*-butyl-4-methylphenol for 5 days and direct Jones oxidation provided **4** and **5** (66%)[10] in a ratio of 2.1:1. Dichloromethane solutions of major enone **4** were next subjected to irradiation with 350 nm light in the presence of ethylene at -47 °C. Because the [2+2] cycloadducts were also sensitive to the incoming radiation, maximum efficiency was realized when **4** was approximately half-consumed. Under these circumstances, **6** and **7** could be obtained after chromatographic separation in yields of 71 and 23%, respectively.[10] That ethylene had been captured preferentially from the direction cis to the phenyl sulfonyl substituent was established by single crystal X-ray analysis.[12]

In preparation for introduction of a vinylic methyl group, **6** was transformed into the enol triflate **8a** [$NaN(SiMe_3)_2$, THF, -75 °C; Tf_2NPh, -75 °C → rt; 82%]. However, **8a** proved singularly unreactive toward substitutive alkylation,[13] presumably as a direct consequence of the prevailing steric congestion. Consequently, silyl enol ether **8b** was prepared [$KN(SiMe_3)_2$, THF -70 °C; TBDMSCl, -70 → 5 °C; 95%] and treated *at room temperature*[14] with MCPBA in CH_2Cl_2 solution. These conditions led to the formation of keto sulfone **9** as the



major product (66%).[15]

With **9** in hand, it was an easy matter to accomplish chemospecific reductive cleavage of the α-sulfonyl substituent (93% of **10**). Since no tendency was exhibited for concurrent loss of the α-silyloxy substituent, introduction of the angular tertiary hydroxyl group in this manner proved to be most expedient. Furthermore, the requisite neighboring alkyl group could now be installed by standard Wittig olefination (78% of **11**). However, this intermediate proved exceptionally recalcitrant to double bond isomerization in the presence of such transition metal salts as $RhCl_3 \cdot 3H_2O$. This unreactivity was efficiently circumvented by first engaging **11** in an ene reaction with N-sulfinylbenzenesulfonamide[16] and implementing reductive desulfurization of **12a** with W-2 Raney nickel *in benzene solution*[17] (81% for the two steps). The remarkable success achieved with this relatively obscure two-step sequence prompts our strong recommendation for consideration of its utilization in other related contexts.

The synthesis of sterpuric acid was completed by sequential exposure of **12b** to tetra-*n*-butylammonium fluoride and saponification (90% overall). The synthetic sample of **1** was spectroscopically identical to the natural product.[18] Thus, sterpuric acid has been stereoselectively assembled in 11 steps from the vinyl sulfone **2** in 11% overall yield.

Acknowledgment. We thank the National Institutes of Health (Grant GM 30827) for financial support and Bruce P. Gunn for some preliminary feasibility studies.

References and Notes

(1) (a) Westcott, C, "Plant Disease Handbook, Third Edition", van Nostrand Reinhold, Toronto, 1971, pp 354-355. (b) Hepting, G. H. "Diseases of Forest and Shade Trees of the United States", U.S. Dept. of Agriculture Forest Service, Agriculture Handbook No. 386, Washington, 1971, pp 61, 84, 90, 236, 400.

(2) Ayer, W. A.; Saeedi-Ghomi, M. H.; Van Engen, D.; Tagle, B.; Clardy, J. *Tetrahedron* **1981**, *37*, *Supplement No. 1*, 379.

(3) Ayer, W. A.; Saeedi-Ghomi, M. H. *Can. J. Chem.* **1981**, *59*, 2536.

(4) Ayer, W. A.; Nakashima, T. T.; Saeedi-Ghomi, M. H. *Can. J. Chem.* **1984**, *62*, 531.

(5) Ayer, W. A.; Browne, L. M. *Tetrahedron* **1981**, *37*, 2199.

(6) (a) Murata, Y.; Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1981**, 4313. (b) Moens, L.; Baizer, M. M.; Little, R. D. *J. Org. Chem.* **1986**, *51*, 4497.

(7) Prepared by sequential methylation and selenosulfonation [Bock, T. G.; Collins, S. *J. Org. Chem.* **1981**, *46*, 3249; Gancarz, R.; Kice, J. L. *Ibid.* **1981**, *46*, 4899] of methyl 3-cyclopentenylcarboxylate [Deprés, J.-P.; Greene, A. E. *J. Org. Chem.* **1984**, *49*, 928].

(8) (a) Paquette, L. A.; Crouse, G. D. *J. Org. Chem.* **1983**, *48*, 141. (b) Kinney, W. A; Crouse, G. D.; Paquette, L. A. *Ibid.* **1983**, *48*, 4986.

(9) Rosner, A.; Tolkiehn, K.; Krohn, K. *J. Chem. Res. (M)*, **1978**, 3831.

(10) This yield takes into account the amount of **2** or **4** recovered from the initial Diels-Alder step or photolysis reaction.

(11) The structure assigned each compound is in full accord with its IR, 300-MHz ^{1}H NMR, ^{13}C NMR, and mass spectra. In addition, elemental analyses were obtained in numerous instances.

(12) Courtesy of Dr. J. C. Gallucci (Ohio State University).

(13) See, for example: (a) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1980**, 4313. (b) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4630. (c) Hayashi, T.; Katsuro, Y.; Kumada, M. *Tetrahedron Lett.* **1980**, 3915.

(14) Compare Paquette, L. A.; Lin, H.-S.; Gallucci, J. C. *Tetrahedron Lett.* **1987**, 1363.

(15) Two minor rearranged products are generated concurrently. Their structures will be discussed in the full paper.

(16) (a) Deleris, G.; Kowalski, J.; Dunoguès, J.; Calas, R. *Tetrahedron Lett.* **1977**, 4211. (b) Deleris, G.; Dunoguès, J.; Calas, R. *Ibid.* **1979**, 4835. (c) Deleris, G.; Dunoguès, J.; Gadras, A. *Ibid.* **1984**, 2135.

(17) Use of the previously recommended[16] ethanol solvent furnished no **13b**.

(18) We thank Professor W. A. Ayer for graciously providing us with copies of the IR and ^{1}H NMR spectra.

(Received in USA 22 July 1987)