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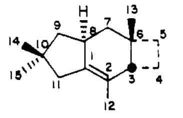
A Stereoselective Electroreductive Cyclization Pathway to the Isolactarane-type Sesquiterpene 1-Sterpurene

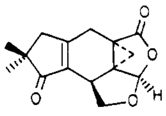
Summary: The isolactarane-type sesquiterpene 1-sterpurene (**1**) was prepared by capitalizing upon a facile electroreductive cyclization that served to convert bisenoate **3** to the trans diester **4a**.

Sir: In 1981, Ayer and co-workers reported the isolation and characterization of several metabolites produced by the fungus *Stereum purpureum*, the causative agent of the so-called silver leaf disease of a variety of trees and scrubs.[1] 1-Sterpurene (**1**) was isolated from the neutral metabolites and was tentatively assigned the interesting isolactarane-type skeleton shown; it is believed to be the biogenetic precursor of the more highly oxygenated members of the series including, for example, sterepolide (**2**).[2] The only reported synthesis of **1** is that of Murata, Ohtsuka, Shirahama, and Matsumoto, who described the conversion of humulene to **1** under conditions that are believed to be analogous to those involved in its biosynthesis.[3] We now report a total synthesis of 1-sterpurene (**1**) that makes use of a number of interesting and useful aspects associated with electroreductive cyclization reactions.[4]



1

STERPURENE



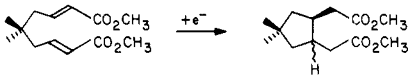
2

STEREPOLIDE

One analysis of the problem is illustrated in Scheme I. Key features include the use of an intramolecular electrochemically induced cyclization to convert **3** to **4a**, an acyloin condensation to form the six-membered ring, and a photo [2 + 2] cycloaddition between enone **6a** and ethylene to construct the cyclobutane ring system.

Invariably, cyclization of the bisenoate **3** led to a mixture of trans and cis cyclopentane diesters **4a** and **4b**. In accord with our previous report involving the electroreductive cyclization of an enoate onto an aldehyde or ketone, the trans product dominates over the cis.[4] As illustrated in Table I the trans/cis ratio varied from 2.6:1 to 11.6:1. A priori, the stereochemical outcome appears to be of no consequence to the sterpurene (**1**) problem since the pro-C_1 carbon in **4** is destined to become sp^2 hybridized. However, as will become apparent, the "natural" propensity toward trans stereoselectivity proved to be beneficial.[5]

Table I

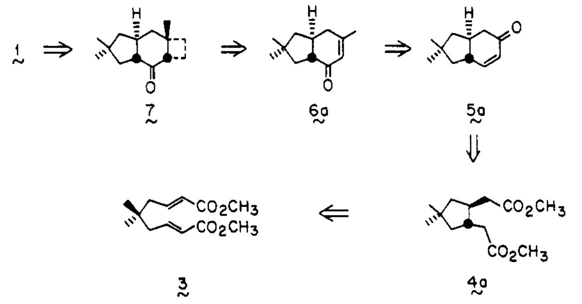


3 4a,b

electrode	proton source	trans/cis ratio	yield (%)
Hg	AcOH, H_2O[a]	2.6:1	82–87
Hg	$CH_2(CO_2Et)_2$[b]	7.5:1	66[c]
glassy carbon	$CH_2(CO_2Et)_2$[b]	7.1:1	73[c]
Cu	$CH_2(CO_2Et)_2$[b]	11.6:1	58[c]

[a] 9:1 CH_3CN/H_2O, 0.9 M Et_4NOTs. [b] CH_3CN, 0.2 M Et_4NOTs. [c] Unoptimized yield.

Scheme I



A Ruhlmann-modified acyloin condensation (4.3 equiv of Na, 4.9 equiv of Me_3SiCl, toluene, reflux, 17 h) served to generate the requisite six-membered ring.[6] However, hydrolysis of the initially formed bis(silyl enol) ether proved problematic. Eventually, it was discovered that heating to 45 °C for 4 h in a mixture of 2:2:1 THF/AcOH/H_2O was most effective, affording the desired acyloin product in 58% yield overall from **4a**. Mesylation (1.5 equiv of MsCl, 1.5 equiv of Et_3N, CH_2Cl_2, –50 to 0 °C) followed by elimination (5 equiv of LiBr, 15 equiv of Li_2CO_3, DMF, reflux 2 h) provided enone **5** in 75% yield, thereby setting the stage for the addition of the pro-C_6 methyl group (1.1 equiv of MeLi, Et_2O, 0 °C to room temperature) and conversion of the resulting tertiary allylic alcohol to enone **6a** (2 equiv of PCC/Celite, CH_2Cl_2, room temperature; 71% from **5**).[7]

While photocycloaddition of ethylene to the trans-fused enone **6a** proceeded smoothly, the cis-fused isomer **6b** proved unreactive under the same conditions (450-W Hanovia, Pyrex, ethylene, –60 to –70 °C). This initially somehwat surprising result can be rationalized by using the Wiesner model for photocycloaddition.[8] Consider, for example, the excited state representations A* and B*, wherein the β-carbon is pyramidal and the methyl substituent is oriented pseudoequatorial. Clearly, the approach of any agent, including a comparatively small molecule of ethylene, should experience an energy raising interaction with the cis-oriented five-membered ring in B*.

As a result of the unreactive nature of **6b**, it proved useless as an intermediate en route to 1-sterpurene (**1**).

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

(2) Murata, Y.; Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1981**, *22*, 4313.

(3) Trost, B. M.; Chung, J. Y. L. *J. Am. Chem. Soc.* **1985**, *107*, 4586.

(4) Fox, D. P.; Little, R. D.; Baizer, M. M. *J. Org. Chem.* **1985**, *50*, 2202.

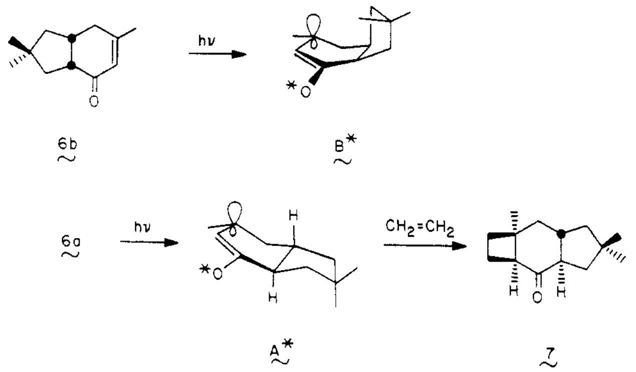
(5) See supplementary material paragraph.

(6) Ruhlmann, K. *Synthesis* **1971**, 236.

(7) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682.

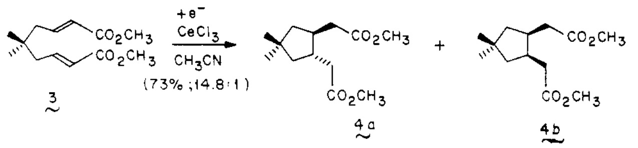
(8) Wiesner, K. *Tetrahedron* **1975**, *31*, 1655. Marini-Bettolo, G.; Sahoo, S. P.; Poulton, G. A.; Tsai, T. Y. R.; Wiesner, K. *Tetrahedron* **1980**, *36*, 719.

0022-3263/86/1951-4497$01.50/0



Consequently, it became clear that it would be worthwhile to attempt to find conditions that would increase the amount of the trans-diester **4a** produced in the electroreductive cyclization or isomerize the cis-fused enones **5b** and **6b** to the trans isomers **5a** and **6a**. Perhaps with little surprise, all attempts to accomplish the latter objective met with failure. However, a partial solution to the problem was achieved by *conducting the electroreductive cyclization in the presence of cerium(III) chloride.* In this way (Hg, −2.3 V vs. SCE, 0.2 M n-Bu_4NBr, 2.0 equiv of $CH_2(CO_2Et)_2$, 1.3 equiv of a suspension of $CeCl_3$ in CH_3CN, 0.033 M concentration of substrate, room temperature), the trans/cis ratio of isomers **4a** and **4b** increased to 14.8:1 (73%). Of equal interest was the observation that, upon the addition of cerium chloride, the current density increased nearly fivefold. Presumably, a complex between cerium chloride and the substrate is formed at some stage along the reaction coordinate and is related to the increase in the trans stereoselectivity. We intend to investigate these observations in considerably greater detail.

Finally, the synthesis was completed by treatment of ketone **7** with methyllithium (1.1 equiv, Et_2O, 0 °C) followed by dehydration (2.3 equiv of $SOCl_2$, pyridine, 0 °C, 60% from **7**)[9] to afford a volatile hydrocarbon whose ^1H and ^{13}C NMR as well as IR spectra nicely matched those derived from authentic 1-sterpurene (**1**).



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Supplementary Material Available: Details concerning mode of preparation of materials as well as spectral data (IR, NMS, MS, analysis) and details concerning stereochemical assignments (11 pages). Ordering information is given on any current masthead page.

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(9) Due to the highly volatile nature of 1-sterpurene (**1**), isolation proved difficult. As a result, the isolated yield of **1** corresponded to 42% for the two steps (addition of C_2 methyl group followed by dehydration). The 60% yield given in the text refers to that obtained by capillary column GC analysis with the aid of an internal standard.

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