53. Synthesis of the (+)-Enantiomer of Taonianone, a Furanoid Diterpene from Brown Algae

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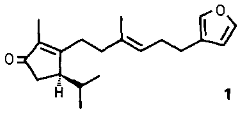
Dedicated to Prof. *W. P. Neumann* on the occasion of his 60th birthday

(15.I.87)

The constitution and absolute configuration of the furanoditerpene taonianone (**1**) has been established by synthesis starting from (–)-carveol (**2**).

Introduction. – The furanoid diterpene (+)-taonianone has been first isolated in 1981 by *Murphy et al.* [1] from brown algae *Taonia australasica*. Subsequent structure elucidation by the same authors led to formula **1** for this natural compound, which – according to *Faulkner* [2] – 'seems completely out of place chemotaxonomically. There are no other algal metabolites with this type of structure, which is very different from the diterpene phenols previously isolated from *Taonia atomaria*'. No indication for the absolute configuration at the chiral centre in **1** was mentioned by *Murphy et al.*



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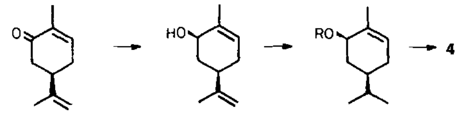
In a recent paper by *Yoshikoshi* and coworkers [3], the first synthesis for this unique natural compound has been reported. In the meantime [4] [5], we had already finished the successful execution of a strategy similar to the latter and wish to report our findings here.

Results and Discussion. – To produce the left-hand part of the target molecule, we reduced (–)-(*R*)-carvone (*Aldrich*, 95% e.e.) at low temperature [6] yielding (–)-*cis*-carveol (**2**) exclusively (*Scheme 1*). Selective hydrogenation of the side-chain double bond succeeded on reaction of *Adams* catalyst in the presence of Et_3N. The resulting (–)-dihydrocarveol (**3a**) was then protected as its acetate **3b**, thereby avoiding intermediate formation of a cyclic enol ether during the following ozonolysis step.

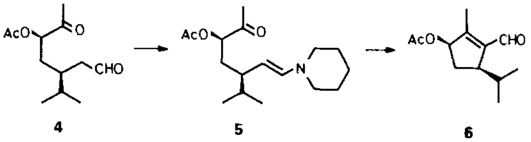
Scheme 1



(–)-(*R*)-Carvone **2** (–)-*cis*-Carveol **3a** R = H
3b R = Ac

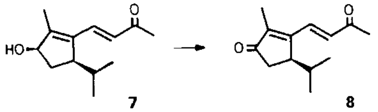
At −78°, **3b** was treated with O_3. Reductive workup with dimethylsulfide produced oxo-aldehyde **4** in near-to-quantitative yield. Up to here, all substances displayed a negative rotation, whereas the open-chain compound **4** is characterized by $[\alpha]_D^{20} = +10.4°$. Compound **4**, upon reaction with piperidine, chemoselectively formed the enamine **5**, which, without prior isolation, was directly subjected to aldol-ring-closure using excess AcOH while kept at below room temperature *(Scheme 2)*.

Scheme 2



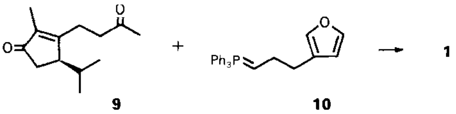
The air-sensitive aldehyde (+)-**6** was formed in 73% overall yield, and, on reaction with alkaline acetone as a solvent, aldol condensation took place. The resulting crystalline ketone (−)-**7** (m.p. 101–106°; 76% yield) caused considerable problems during hydrogenation, since no specificity could be achieved under various conditions. However, if the OH group was oxidized first by pyridinium dichromate in 88% yield to (−)-**8** *(Scheme 3)*, neutral *Ra*-Ni in MeOH selectively furnished saturation at the disubstituted double bond (92% yield). Compound (+)-**9**, of the established (*R*)-configuration crystallized at 0°. The overall yield from (*R*)-carvone to (+)-**9** amounts to 40%. The unpolar diketone **8** exhibited a surprisingly high optical rotation of $[\alpha]_D^{20} = -219.5°$.

Scheme 3



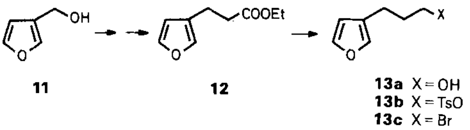
Having the optically active diketone **9** in our hands, we directly undertook coupling with the appropriate *Wittig* reagent **10** *(Scheme 4)*. After several failures, we found that treatment of the phosphonium salt with BuLi in xylene led to the formation of a purple solution of **10**, which, upon addition of **9** at ambient temperature, furnished a 31% yield of a single isomer of **1** (vinyl proton at 5.16 ppm). The configuration in the side-chain is undoubtedly established to be *trans* (CH_3 *quadruplet* in the ^{13}C-NMR at 15.99 ppm), whereas the *cis*-isomer is expected to resonate at 22.9 ppm [7]. Moreover, the ^{13}C-NMR spectrum was completely identical with the values reported by *Murphy et al.* [1] for natural (+)-taonianone. Our synthetic material displayed $[\alpha]_D^{20} = +10.6°$, and from its relation to (−)-(*R*)-carvone, the (*R*)-configuration for the natural product can be established.

Scheme 4



Preparation of the ylide **10** was achieved in a conventional way, starting from known [8] 3-furylmethanol **11**. The extremely labile mesylate resulting from **11** was treated with malonic ester, and the product decarboxylated by NaCl in DMSO to form the furylpropionate **12**. Reduction of **12** with $LiAlH_4$ led to a homologous alcohol **13a** in 30% overall yield (from diethyl furan-3,4-dicarboxylate). The latter was transformed into the corresponding bromide **13c** *via* its tosylate **13b**. The results of this investigation proved, that the structure elucidation by spectroscopy [1] has been correct, indeed, and regarding the unknown absolute configuration, our results confirm the findings by *Yoshikoshi* and coworkers [3].

Scheme 5



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