# 265. Biogenetic-Type Total Synthesis of (±)-2-Deoxystemodinone

Preliminary Communication

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*Summary*

A biogenetic-type total synthesis of (±)-2-deoxystemodinone (**1**), by solvolytic rearrangement of the 1-methylbicyclo[2.2.2] oct-2-yl methanesulfonate **4**, is described.

We have previously shown [1] that the *Wiesner* napelline strategy [2], based on the solvolytic rearrangement of a bicyclo[2.2.2]-5-octen-2-yl methanesulfonate [3] (*a* in the *Scheme*), is very advantageous for the synthesis of the stemodin- and aphidicolin-type diterpenes. In our 'first-generation approach' [4] to these compounds, we decided, as other groups [5–9], to proceed *via* a suitable 17-norstemodan-13-one and the known 17-noraphidicolin-16-one and generate the C(13) (stemodin-type) or C(16) (aphidicolin-type) chiral centers later.

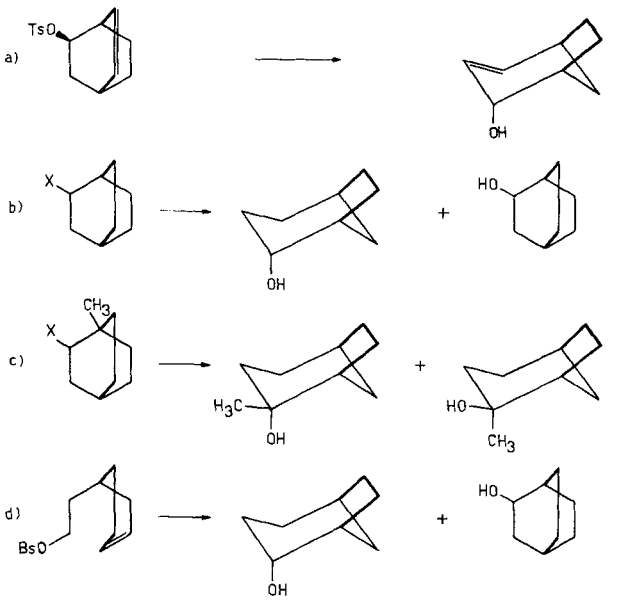
On successfull conclusion of this work, it appeared to us that these centers could be stereoselectively created, simultaneously with the construction of the skeleton, by a related rearrangement. In a 'second-generation approach' we have, therefore, explored this possibility which resembles the postulated biogenetic route [10].

In support of this plan, we should quote that the *exo*-bicyclo[3.2.1]octan-2-ol is the only rearranged solvolysis product of bicyclo[2.2.2]octan sulfonates (*b* in the *Scheme*) [11].

Since the OH–C(13) group in the stemodin-type compounds is also *exo*-configurated to the ethylene bridge, we have conjectured that, by solvolysis of a suitable substituted 1-methylbicyclo[2.2.2]oct-2-yl methanesulfonate, the C(13) chiral center might emerge from the rearrangement in the correct configuration.

Experiments reported [12] on a simpler system (*c* in the *Scheme*) were casting some doubts on the correctness of our hypothesis, which on the other hand was supported by biogenetic considerations.

*Scheme*

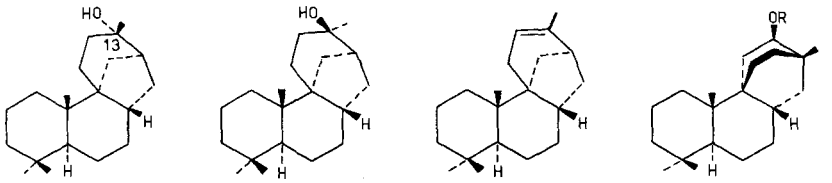



X = leaving group

In fact, we had observed that in all diterpenoids having a bicyclo[3.2.1]octane moiety, originated by a [2.2.2]→[3.2.1] rearrangement [10] [13] [14] and an oxygen function at the former bridgehead C-atom, this last group, whose stereochemistry has never been related to the rearrangement before, is always *exo* to the two C-bridge of the [3.2.1]-system[1]).

From all compounds which would have enabled us to verify our hypothesis, **1** was the simplest and more suitable target, not only from a synthetic point of view, but also because we had already in our hands all the possible products of rearrangement (**2** and **3**) [1a] [1b].

We have, therefore, decided to synthesize again compound **1** by solvolysis of the methanesulfonate **4**. Thus, the totally synthetic alcohol **5** [15], which we prepared as




**1** **2** **3** **4** R = Ms
**5** R = H

[1]) Besides the compounds mentioned above, other examples (more can be found in the literature) are represented by the diterpene stemarin and by the aconite alkaloids.

described for related compounds [1b], was dissolved in $CH_2Cl_2$ and treated with methanesulfonyl chloride in the presence of $Et_3N$ at 0° until TLC ($SiO_2$) monitoring (30% $Et_2O$ in hexane) indicated the disappearance of the starting material; the methanesulfonate **4** was in fact unstable and hydrolyzed on TLC to the rearranged products.

Though we suspected that solvolysis might have occurred already during workup, the crude mixture was dissolved in acetone/$H_2O$ 2:1 and stirred at room temperature in the presence of $CaCO_3$ to give in a 95% yield (±)-**1**, (±)-**2** and (±)-**3** in a 7.0:1.0:8.7 ratio[2]).

We feel that this result not only constitutes a more stereoselective[3]) and direct total synthesis of (±)-**1**, but also seems to indicate that the *exo*-configuration of the OH–C(13) group is related to the rearrangement of the bicyclo[2.2.2]octan carbonium ion intermediate [16][4]).

We hope that further elaboration of this strategy, at present in progress, may lead to fully stereospecific syntheses of **1** and related compounds.

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[2]) For the conversion of **2** and **3** into **1** s. [1a] and [15].
[3]) As compared to our previous results [1b].
[4]) In view of our results, it seems to us that such an intermediate, which according to [17] (*d* in the *Scheme*) could have been postulated in the biogenesis of cedrol [18] should be on the contrary ruled out since in this compound the OH–C(6) is *endo*-configurated to the ethylene bridge.