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AN UNUSUAL REDUCTION OF A CROSS CONJUGATED DIENONE. STEREOSELECTIVE SYNTHESIS OF (-)-DICTYOLENE[1]

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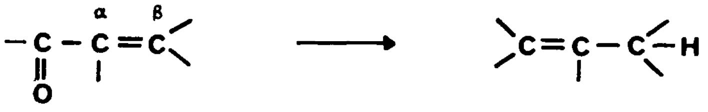
Among the known procedures for effecting the reduction of an enone **I** to the corresponding transposed olefin **II**, the recently described tosylhydrazine-catecholborane-sodium acetate method is potentially one of the most useful due to the mild reaction conditions and the certitude concerning the eventual position of the double bond.[2] In a previous communication[3] we demonstrated the feasibility of effecting this transformation (**I**→**II**) with predictable stereoselectivity at the β carbon of the original enone system thus adding greater synthetic utility to this already valuable reaction sequence. We now report an unusual reduction of 6-*epi*-α-santonin using this method, and its application to the synthesis of (-)-dictyolene (**8**), a novel diterpene alcohol from the antibiotic extracts of the marine alga *Dictyota acutiloba*.[4]

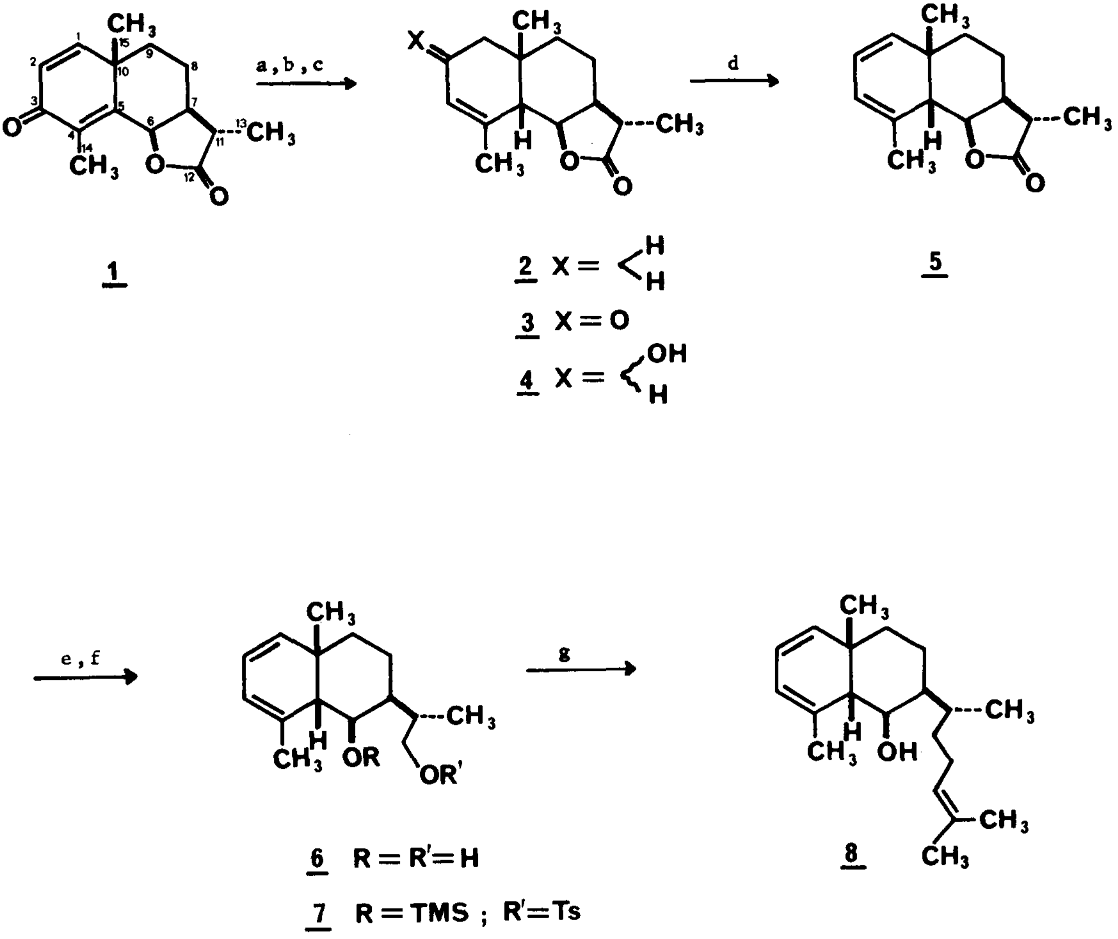


I

II

Sequential treatment of 6-*epi*-α-santonin (**1**)[5] with excess tosylhydrazine, catecholborane, and sodium acetate trihydrate stereoselectively produced a single olefin **2** (>50%, mp 98-99°C),[6] and not the expected mixture of dienes. It had been anticipated,[3] however, that the hydrogen introduced at C-5 would have the β-configuration based on the likelihood that the reduction at C-3 in the intermediate tosylhydrazone(s) would occur from the less hindered α-face. This stereochemical assignment was supported by the analogous transformation of α-santonin to the known[7] 5,6,11β(H)-eudesm-3-enolide and was subsequently confirmed by the successful synthesis of dictyolene.

Construction of the required cyclohexadiene system in **8** was completed by first subjecting olefin **2** to Collins allylic oxidation,[8] which smoothly afforded enone lactone **3**, mp 218-220°C, in 71% yield. Although base treatment of the tosylhydrazone[9] derived from **3** did produce the desired diene **5**, a simpler and higher yielding procedure consisted of 1,2-reduction of enone **3** using NaBH$_4$-CeCl$_3$ in methanol[10] followed by dehydration in hot HMPA[11] to give the



1

2 X = H, H

3 X = O

4 X = OH, H

5

6 R = R' = H

7 R = TMS ; R' = Ts

8

a) TsNHNH$_2$,EtOH, Δ, 3 h; catecholborane, CHCl$_3$, 0°→20°C, 2 h; NaOAc·3H$_2$O, Δ, 1 h. b) CrO$_3$·Pyr$_2$, CH$_2$Cl$_2$, rt, 9 h. c) NaBH$_4$, CeCl$_3$, MeOH, rt, 5 min. d) HMPA, 250°, 15 min. e) LiAlH$_4$, Et$_2$O, rt, 18 h. f) TsCl, 2 h, then TMSCl, 15 min, pyr., -40°C. g) C$_5$H$_9$MgCl, C$_5$H$_7$Cu, Et$_2$O, -25°C, 8 h; H$_3$O$^+$.

crystalline diene **5**, mp 100-101°C, in 56% yield. Verification that the stereochemistry at C-5, C-6, and C-11 remained unaffected was obtained by selective reduction (H_2-Pd/$CaCO_3$, EtOAc) of the 1,2 double bond in diene **5**, which regenerated olefin **2**.

In earlier work we developed a straightforward and practical procedure for effecting the "prenylation" of lactones of the type exemplified by **5**, which avoids possible epimerization at the α-carbon.[3] Application of this method to the present synthesis commenced with lithium aluminum hydride reduction of lactone **5** to give diol **6**, which on selective tosylation and silylation yielded the tosylate silyl ether **7**. This derivative was subjected to a coupling reaction with 3-methyl-2-butenylmagnesium chloride and pentynylcopper in ether, which was followed by brief exposure to acid to produce in30-40% overall yield from lactone **5** (-)-dictyolene (**8**), identified by spectral comparison with the natural product.[12,13]

The mechanism and generality of this novel transformation of cross conjugated dienones are currently under investigation.

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12. We have obtained $[\alpha]_D^{23}$ = -154° (c = 0.8, $CHCl_3$) for synthetic dictyolene (**8**) Although there is no optical rotation data available for natural dictyolene, it is reasonable to assume[4] that its absolute configuration is as depicted in structure **8**.

13. Compounds recently isolated from marine sources and which contain the C-6 hydroxy, C-7 eight carbon unit arrangement of dictyolene include : pachydictyol-A, pachydictyol-A epoxide, dictyol-A, dictyol-B, diloptiol, and dictyoxepin ; thus the simple entry described above into this structural type should find considerable synthetic application.

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