Iridoids: The Revised Structure of Specionin

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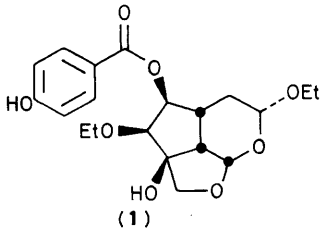
The revised structure of specionin has been proved by total synthesis; the key step involves a Norrish I type fragmentation of a norbornanone precursor.

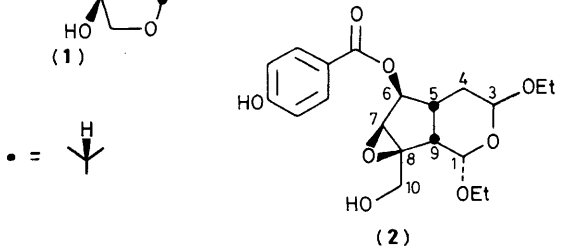
The iridoid specionin has been isolated from the leaves of *Catalpa speciosa* Warder and has been assigned the structure (**1**) on the basis of spectral data.[1] It is an effective antifeedant against the Eastern spruce budworm which infests North American fir and spruce forests.

Recently we have synthesized substance (**1**) and observed that it was not identical with the natural material.[2] Comparison of the spectral data of the synthetic and natural substances led us to propose structure (**2**) for specionin. For both substances the relative configurations of H-1,-5,-6,-7, and -9 are identical as has been confirmed by nuclear Overhauser effect measurements.[1,2]† The proposed structure (**2**) was mainly based on the ^{13}C n.m.r. data.[2,3]

In this communication we describe the synthesis of (±)-(**2**) which confirms this structure for specionin.‡ The starting material is the known compound (**3**);[4] *m*-chloroperbenzoic acid (*m*CPBA) induced cyclization to (**4a**) (95%) followed by selective protection of the primary hydroxy function afforded (**4b**) (81%). Successive Swern oxidation[5] (77%) and reductive cleavage of the ether bond, to the carbonyl function, led to (**5a**) (94%). After oxidation of the hydroxy function to the aldehyde (**5b**) (96%), Norrish I type fragmentation of the norbornanone framework and direct acid treatment of the crude intermediates (**6a**) and (**6b**) (no dialdehyde could be detected) afforded with concomitant silyl ether cleavage a mixture of the four diastereoisomers (at C-1 and C-3) (**6c**) in 64% overall yield (ratio 1 : 4 : 1 : 4 for respectively C-1 and C-3 OEt; αβ, ββ, βα, and αα). The stage was now set for the functionalization of the five-membered ring. Although the isomers can be separated we decided, as a first approach, to use the mixture in the subsequent steps. Epoxidation of (**6c**), from the least hindered *exo* face (94%) followed by oxidation of the alcohol to the aldehyde and 1,8-diazabicyclo[5.4.0]-



(**1**)

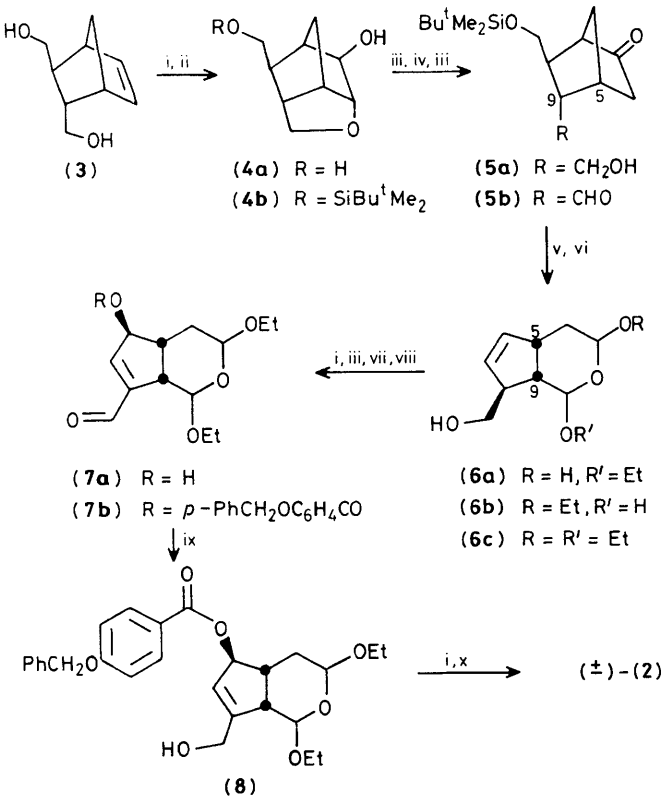


(**2**)

• = H

† The relative configuration of 3-H has only been proved for (**1**); the configuration at C-3 in the natural material is uncertain (see ref. 1).

‡ Satisfactory spectroscopic (^1H n.m.r., i.r, and mass) data were obtained for all isolated pure compounds. For the mixtures (**6**) to (**8**) only details of the ^1H n.m.r. spectra were of diagnostic value. All yields are isolated yields.



Scheme 1. *Reagents:* i, *m*CPBA, CH_2Cl_2, room temp.; ii, Bu^{t}Me$_2$SiCl, DBU, CH_2Cl_2, room temp.; iii, $(COCl)_2$, dimethyl sulphoxide, Et_3N, CH_2Cl_2, −60 °C; iv, Al–Hg, EtOH, tetrahydrofuran, room temp.; v, irradiation at 254 nm, EtOH; vi, $MeC_6H_4SO_2OH$, EtOH, room temp.; vii, DBU, CH_2Cl_2, room temp.; viii, *p*-$PhCH_2OC_6H_4COCl$, Et_3N, CH_2Cl_2, room temp.; ix, $NaBH_4$, EtOH, 0 °C; x, Pd–C, H_2, EtOH.

undec-7-ene (DBU) mediated epoxide opening (β-elimination) gave (**7a**) (52%). Formation of the 6-(*p*-benzyloxy)benzoate (**7b**) and reduction of the aldehyde function led to (**8**) (45% unoptimised yield). Because of problems in separating the products from the reagent (h.p.l.c.) only part of the mixture (with a different ratio) was carried through the final steps. Finally, epoxide formation and deprotection of the phenolic function (*ca.* 60% unoptimised yield) gave a mixture of the four (C-1, C-3) diastereoisomers. H.p.l.c. separation (reversed phase column RSiL-C18-HL-D, eluent MeOH–H_2O) allowed isolation of a sample of synthetic (±)-(**2**) which was identical (^{1}H n.m.r. spectroscopy, h.p.l.c. and g.c. retention times on co-injection) with an authentic sample of specionin.

As the starting material (**3**) is available in enantiomerically pure form[6,7] the route described would permit the asymmetric synthesis of (**2**).

We thank Professor Nakanishi for his kind gift of a sample of authentic specionin. We are also grateful to the NFWO and the 'Ministerie voor Wetenschapsbeleid' for their financial support.

Received, 17th July 1985; Com. 1042

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