The Synthesis of Torreyal, Neotorreyol, and Dendrolasin

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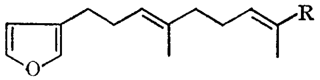
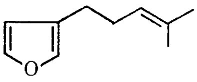
THE title compounds (I)—(III) have been isolated from the oil from *Torreya nucifera* Sieb. & Zucc.,[1] and dendrolasin (III) has also been found in a species of ant, *Lasius* (*Dendrolasius*) *fulginosus* Latr.[2] and sweet potato fusel oil.[3] A synthesis of these sesquiterpenes is described here, as well as a synthesis of perillene (IV), isolated some time ago from *Perilla citriodora* Makino,[4] and later from the same species of ant as dendrolasin,[5] but which appears never to have been synthesized.



(I) R=CH_2·OH
(II) R=CHO
(III) R=Me



(IV)

The principle of the synthesis was based on the use of a double Claisen–Cope type reaction that we have already described for the synthesis of sinensal.[6,7] A preliminary experiment (details of which will be published elsewhere) using furfuryl alcohol (V) and 1-ethoxy-2-methylbuta-1,3-diene (VI)[8] indicated that smooth conversion in the presence of mercuric acetate into the aldehyde (VII) could be effected, but when 3-hydroxymethylfuran (VIII) was subjected to the reaction under the same conditions (100° for 18 hr.), only the corresponding diene-ether (IX) was isolated.† Pyrolysis of (IX) at 350°, either in the evaporation chamber of a gas chromatograph or through a

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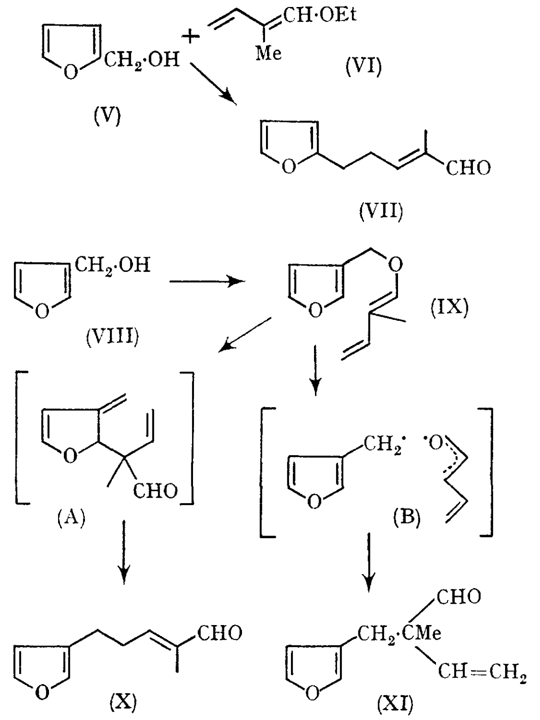
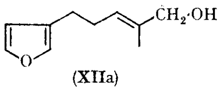
† All new compounds gave the expected microanalytical results, and all were fully characterized by i.r., n.m.r., and mass spectra.

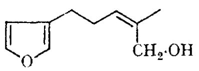
column of glass helices, led to the desired aldehyde (X) as the main product.



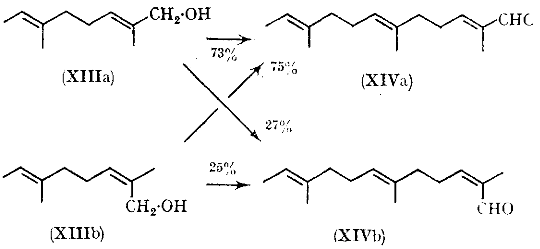
The reaction led to a by-product, identified as (XI) by its n.m.r. spectrum,‡ δ 1·13 p.p.m. (s, 3H, CH$_3$), 2·69 (2H, furan-CH$_2$–C $\leqslant$), 6·1 (1H, furan β-H), 7·1—7·4 (2H, furan α-H), 9·33 (CHO), 4·9—5·3 (2H, =CH$_2$), 5·83 (q, –CH=), and mass spectrum (main fragment at *m/e* 81, C$_5$H$_5$O$^+$). The desired aldehyde (X) was a mixture of *cis*- and *trans*-isomers, since there were two aldehyde proton signals in the n.m.r. spectrum, one at δ 9·28 p.p.m. corresponding to the *trans*-aldehyde, and one at 9·97 p.p.m., corresponding to the *cis*-aldehyde,§ and reduction of this mixture with lithium aluminium hydride let to a mixture of the corresponding *cis*- and *trans*-alcohols (XIIa) and (XIIb). These were readily separated by gas chromatography; they had identical mass spectra, but one had the n.m.r. signal for the carbinol protons at 3·80 p.p.m., and the methyl group at 1·57 p.p.m., the other at 3·92 p.p.m., with the methyl group at 1·78 p.p.m. Comparison of these results with the n.m.r. spectra of *cis*- and *trans*-crotyl alcohol led to the assignment of the compound with the carbinol hydrogens at higher field to the *trans*-configuration (XIIa). It was not, in fact, necessary to separate these alcohols for subsequent stages of the synthesis, since we could show on the models (XIIIa) and (XIIIb) that the unsaturated aldehyde mixture resulting from the next stage of the reaction was independent of the configuration at C-2 of the starting materials, giving from either (XIIIa) or (XIIIb), the unsaturated aldehydes (XIVa) and (XIVb), always in proportions 3 : 1 under our conditions, with the C-6 double bond always *trans*.** Reduction of the toluene-*p*-sulphonates¶ of the alcohol mixture (XIIa) and (XIIb) with lithium aluminium hydride in ether gave perillene (IV) isolated by gas chromatography, and identified by spectral characteristics.[5]



(XIIa)



(XIIb)



Treatment of the alcohol mixture (XIIa) and (XIIb) with the diene-ether (VI) and mercuric acetate yielded an aldehyde fraction that appeared to be pure on preparative gas chromatography, but

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‡ N.m.r. spectra were measured on a Varian A60 spectrometer in carbon tetrachloride solution against tetramethylsilane as internal standard.

§ *cii*-2-Methyl-2-enals are uncommon in the literature. E. Bertele and P. Schudel (*Helv. Chim. Acta*, 1967, **50**, 2445) report in a footnote a personal communication from U. Schwieter that such aldehydes have an n.m.r. signal at 10·02 p.p.m. We have recently isolated some aldehydes of this nature, and also find a signal in this region. A table of n.m.r. values for various unsaturated carbonyl compounds is given by G. Büchi and H. Wüest, *Helv. Chim. Acta*, 1967, **50**, 2440.

** The theoretical justification for the C-6-*trans* configuration will be discussed in a forthcoming publication; it depends on the supposition that a pseudo-equatorial conformation for the larger group in the intermediate will be preferred. See ref. 6, and A. Viola, E. J. Iorio, K. K. Chen, G. M. Glover, U. Nayak, and P. J. Kocienski, *J. Amer. Chem. Soc.*, 1967, **89**, 3462.

¶ Toluene-*p*-sulphonates were made using anhydrous potassium hydroxide in dry ether, as described by E. Wenkert and B. L. Mylari, quoted in a footnote in L. K. Montgomery and J. W. Matt, *J. Amer. Chem. Soc.*, 1967, **89**, 6556. The use of pyridine generally gives tars.

which was actually a 4 : 1 mixture of natural torreyal (II), with a *trans*-double bond adjacent to the aldehyde group, and the isomer with a *cis*-double bond next to the aldehyde group. Apart from the small n.m.r. signal at 9·98 p.p.m. arising from this isomer, the n.m.r. spectrum was practically identical with that given by natural torreyal,[1] and the respective mass and i.r. spectra were indistinguishable. After several recrystallizations, the semicarbazone had m.p. 131—132° and gave no m.p. depression with natural torreyal semicarbazone, for which Hirose *et al.* found m.p. 132—133.[†] The alcohol, neotorreyol (I) (3,5-dinitrobenzoate, m.p. 95°) was made by lithium aluminium hydride reduction of the aldehyde (II), and again apart from small signals at 4·00 and 1·78 p.p.m. arising from the presence of the *cis*-isomer, was identical with natural neotorreyol. Lithium aluminium hydride reduction of the toluene-*p*-sulphonate of neotorreyol[¶] led to dendrolasin (III), the n.m.r., i.r., and mass spectra of which were identical with those of the natural material. Direct comparisons with natural torreyal, neotorreyol, and dendrolasin were possible, thanks to very generous samples provided by Dr. Y. Hirose, to whom we are most grateful.

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[1] T. Sakai, K. Nishimura, and Y. Hirose, *Bull. Chem. Soc. Japan*, 1965, **38**, 381.
[2] A. Quilico, F. Piozzi, and M. Pavan, *Tetrahedron*, 1957, **1**, 177.
[3] Y. Hirose, M. Abu, and Y. Sekiya, *J. Chem. Soc. Japan*, 1961, **82**, 725.
[4] H. Suzuki, *J. Pharm. Soc. Japan*, 1936, **56**, 841.
[5] A. Baggini and M. Pavan, *Tetrahedron Letters*, 1967, 3893.
[6] A. F. Thomas, *Chem. Comm.*, 1967, 947.
[7] A. F. Thomas, *Chimia* (*Switz.*), 1967, **21**, 594.
[8] B. M. Mikhailov and L. S. Povarov, *Zhur. obshchei Khim.*, 1959, **29**, 2079.