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EXTRACTS OF *CEDRELA ODORATA* L.—IV[1]
THE STRUCTURE OF ODORATIN, AN UNDECANORTRITERPENE

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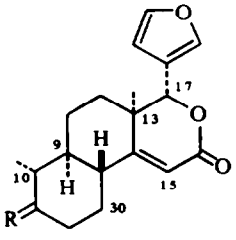
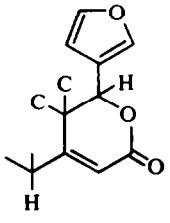
Abstract—An extract of *Cedrela odorata* L. has given a bicarbocyclic undecanortriterpene, odoratin (**1**), which is biogenetically related to the bicyclononanolide group of limonoids.

THE LIMONOIDS (TETRANORTRITERPENES), phytochemically characteristic of the Meliaceae and Rutaceae, show a high degree of structural variation which can easily be rationalized by simple biogenetic arguments.[2] The genus *Cedrela* has been extensively investigated and the chemical variability of *C. odorata*, the West Indian cedar, has been reported.[1] We describe in this paper the isolation of a new compound, odoratin,[3] as the only limonoid occurring in a specimen of *C. odorata* obtained from St. Elizabeth, Jamaica and the arguments for the assignment of the structure (**1**) to this compound. The triterpenes odoratone and odoratol[4] were also obtained from this extraction.



1 R = O
1 R = --OCH_2CH_2O--



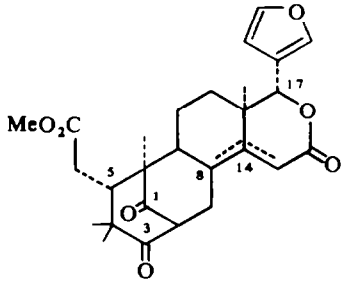
A

The molecular formula $C_{19}H_{22}O_4$ for odoratin, indicated by analysis, was confirmed by mass spectrometry (M^+ 314, 2%). NMR data[5] however showed that despite this molecular formula there were some points of structural similarity with other limonoids. There were the characteristic bands associated with a β-substituted furan [ν_{max} 1500, 877 cm^{-1}; δ 7·48 (m), two α-furan H; 6·45 (m), one β-furan H]. In addition, the low field region of the NMR spectrum of odoratin had a singlet at δ 5·11 (1H) and a doublet (J = 2·2 Hz) at δ 5·89 (1H). These data could be reasonably interpreted in terms of the part structure A. The singlet is ascribed to the proton allylic to the furan and situated on carbon bearing oxygen while the doublet is assigned to the olefinic

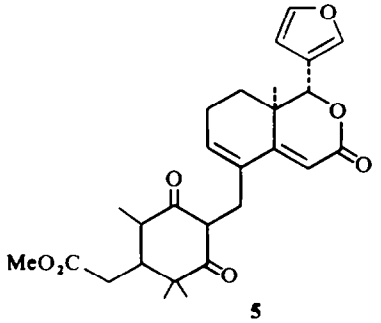
hydrogen. The magnitude of the coupling constant indicates that the proton allylic to this hydrogen is nearly at right angles to the plane of the double bond.[6] This partial structure receives support from the IR spectrum which has a broad band in the carbonyl region at 1710 cm^{-1} and from UV data [λ_{max} 213 nm (ε 17, 100)].

A further structural feature of odoratin, revealed by the NMR spectrum, was the presence of two Me groups—one tertiary (δ 1·10) and the other secondary (δ 1·04, J = 7 Hz). Odoratin has no OH groups (IR) and the presence of the fourth oxygen as a ketone was confirmed by the preparation of an ethylene ketal (**2**), $C_{21}H_{26}O_5$, m.p. 233–235°, which will be referred to later. There was no evidence for further unsaturation in odoratin and the delineation of the nature of the oxygen atoms required that the molecule was bicarbocyclic.

At the time this problem was under investigation the bicyclononanolide group of limonoids was recognised through a series of elegant experiments which included X-ray analysis of a heavy atom derivative.[7,8] The easy base-catalysed cleavage of



3 $\Delta^{8(14)}$
4 Δ^{14}, 8β—H



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suitable examples *e.g.* mexicanolide (**3**) and carapin (**4**) to the diene lactone **5** through cleavage of the C_9—C_{10} bond had been demonstrated.[9,10] Clearly, an alternative mode of decomposition of carapin (**4**), involving a reverse Michael reaction (cleavage of the C_5—C_{10} bond) and a β-dicarbonyl cleavage (of the C_2—C_3 bond) would lead directly to **1** as a biogenetically acceptable structure for odoratin. This type of fragmentation has not yet been observed *in vitro*, but β-dicarbonyl and retroaldol cleavages of the C_2—C_3 bond have been reported in derivatives of swietenine.[7] Evidence in support of this structure has been obtained in the following way.

The carbonyl absorption at 1710 cm^{-1} indicated that the ketone was in a six membered, or larger, ring. An attempt at dehydrogenation with DDQ in boiling benzene led to recovery of starting material. However, SeO_2 in AcOH led to a mixture of products from which a phenol $C_{19}H_{18}O_5$, m.p. 265–268°, could be obtained by prep. TLC. The incorporation of an extra oxygen atom suggested initial oxidation to an α-diketone followed by aromatization to a catechol derivative. The IR spectrum had carbonyl absorption at 1660 cm^{-1} and this together with the UV data [λ_{max} 219, 244 and 352 nm (ε 14,000, 8700 and 13000)] showed that the ene-lactone of odoratin was now conjugated with the aromatic ring as a cinnamic acid ester. A large shift of the UV maxima on addition of base [λ_{max} 265 and 413 nm (ε 6500 and 18,200)]

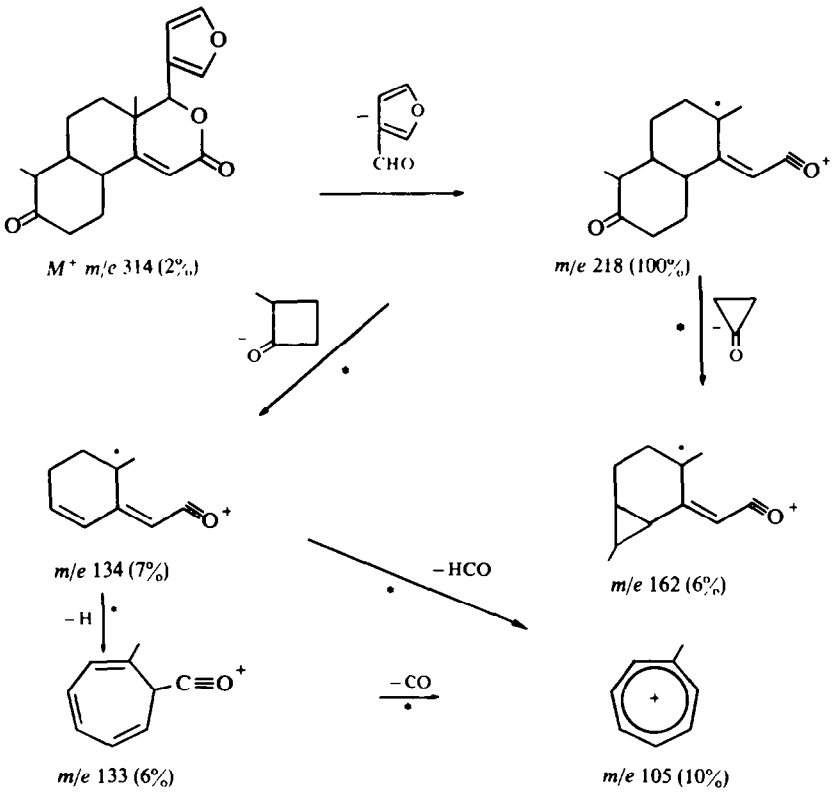
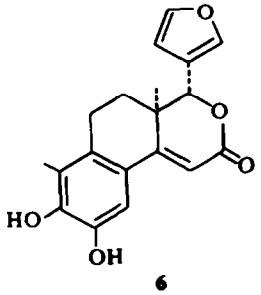


FIG 1.

* Metastable peak observed.

locates one of the phenolic groups *para* to the conjugated ester.[11] This result is entirely consistent with structure **1** for odoratin and allows the formulation of the catechol as **6**.

Further evidence for the environment of the ketone in odoratin was secured by spin decoupling which showed that the hydrogen which is coupled to the secondary Me group resonated at δ 2·3. This is in agreement with its location α to the ketone. Moreover, irradiation of the secondary Me resulted in the collapse of the multiplet at 2·3 to a clean doublet (J = 11 Hz). This indicates that there is one other adjacent proton and that the arrangement is *trans*-diaxial.



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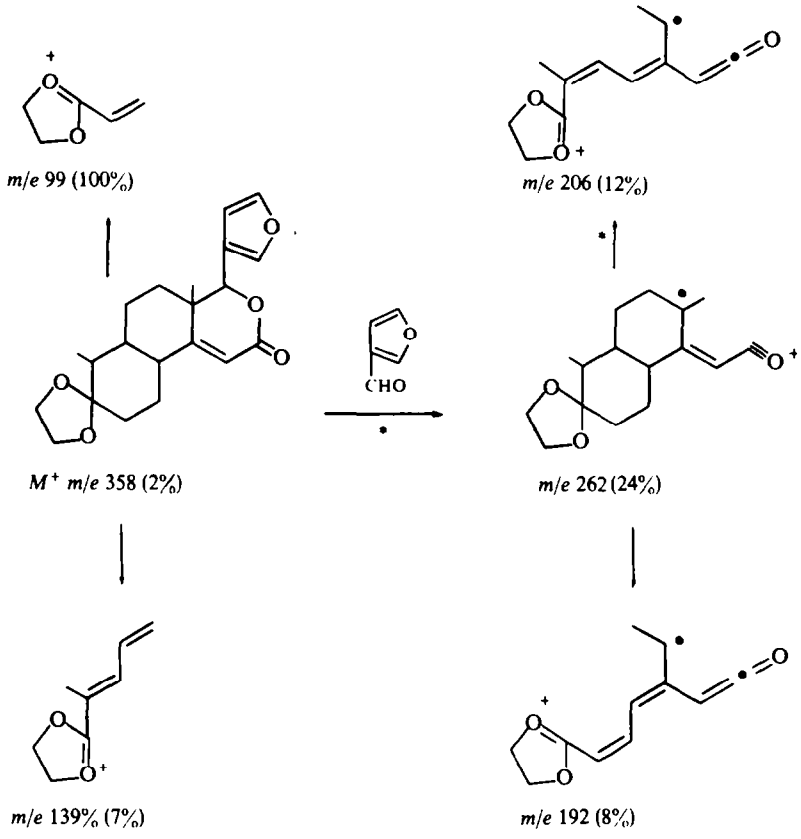


FIG 2.

* Metastable peak observed.

The chemical shift of the olefinic proton in odoratin (**1**) is similar to that in carapin (**4**) (δ 5·78)[10] suggesting the same substitution at C_{30}. It excludes the possibility of a C_{30} ketone which would result in a large downfield shift of H_{15}.[5]

The structure of odoratin as **1** is fully supported by its mass spectral fragmentation pattern and that of its derived ethylene ketal. Figs. 1 and 2 detail the essential features. The fragments observed for the ethylene ketal (Fig. 2) confirm the structure **1** by defining the relative positions of the atoms not apparent in the part structure **A**. Similarly the structure **6** of the SeO_2 oxidation product is strongly supported by its fragmentation pattern (Fig. 3) which consists of fragments derived from cleavage in the lactone ring.

The absolute configuration of the ene-lactone system of odoratin (**1**) is based on circular dichroism studies. This chromophore is associated with a positive Cotton effect at 264 nm, $\Delta\varepsilon = +7{\cdot}0$. Assuming that the lactone ring is in the more stable conformation with the furan residue quasi-equatorial, this result completely defines the stereochemistry at C_{13} and C_{17} by application of the modified octant rule to such systems.[12] The values obtained are also closely similar in position, sign and magnitude with those of carapin (**4**) ($\Delta\varepsilon_{265\,nm} = +6{\cdot}8$).[13] This absolute configuration was

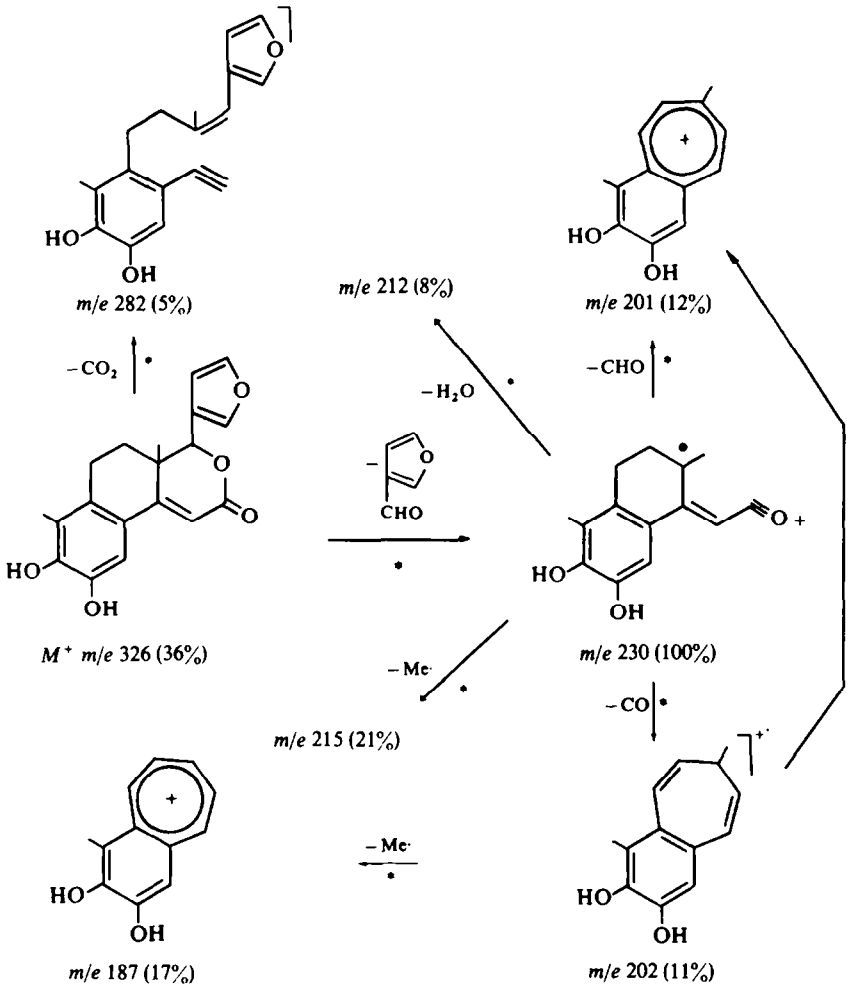
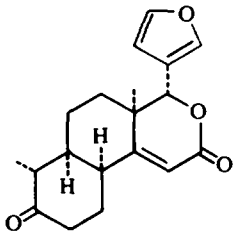


FIG 3.

* Metastable peak observed.

also assigned by Dreyer[14] on the basis of comparison with the Cotton effect of deoxylimonin ($\Delta\varepsilon_{267\ nm} = +5{\cdot}84$) and supports the biogenetic relationship of odoratin with the limonoids. The $n \rightarrow \pi^*$ transition of the carbonyl group is responsible for a negative Cotton effect ($\Delta\varepsilon = -1{\cdot}21$) at 302 nm.

Evidence has already been adduced that the relationship between H_{10} and H_9 is *trans*-diaxial and given the sign of the Cotton effect of the ketone and the interpretation of the size of the allylic coupling alluded to earlier, there are two alternative stereochemical formulations **1** and **7** possible for odoratin. The argument used by Taylor[15] for the assignment of the configuration at C_8 in carapin (**4**), which is based only on the magnitude of the coupling of H-15, is not applicable to odoratin (**1**). In carapin (**4**) the stereochemical possibilities are limited by the presence of the three carbon bridge ($C_{3,-4,-5}$). For odoratin we favour structure **1** for the following reason.



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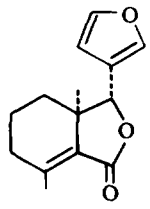

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Double irradiation located the proton to which H_{15} is coupled as a multiplet centred near δ 2·72. This multiplet, only a part of which could be observed, indicated that the proton has a large coupling (J = 12 Hz) to at least one neighbour. Models show that such a situation could only arise in **1**; in the alternative formulation (**7**) only small couplings should be observed.

The simarolides[16] and fraxinellone (**8**)[17] are believed to be biogenetically related to the limonoids. The constitution (**1**) of odoratin is of interest in that it represents an alternative for the extensive degradation of the limonoids.

EXPERIMENTAL

M.ps were determined on a Kofler hot stage apparatus and are uncorrected. UV data are for EtOH solns, IR spectra for Nujol mulls and CD data for a MeOH soln. NMR spectra were recorded in $CDCl_3$ at 60 MHz with TMS as internal reference. Mass spectra were obtained with an AEI MS-9 spectrometer. All evaporations were carried out at reduced pressure.

Isolation of Odoratin (**1**). Dried, finely ground heartwood of *Cedrela odorata* (500 g) was extracted by percolation with C_6H_6 (2 l). The oily residue obtained on evaporation was washed with light petroleum (b.p. 60–80°, 2 × 50 ml) and the residual gum (4·5 g) which had only one Ehrlich positive spot on TLC, was chromatographed on Al_2O_3. Elution with benzene–EtOAc (5:1) gave a fraction (466 mg) which crystallized from EtOAc to give *odoratin* (**1**) as prisms, m.p. 216–223°; $[\alpha]_D$ + 155° ($CHCl_3$, c 0·74); λ_{max} 213 nm (ε 17,100); ν_{max} 1710, 1500, 877 cm^{-1}; NMR: δ 7·48 (m, 2 α-furan H), 6·45 (m, β-furan H), 5·89 (d, J = 2·2 Hz, H-15), 5·11 (s, H-17), 1·10 (s, C-13 Me), 1·04 (d, J = 7·0 Hz, C-10 Me). (Found: C, 72·65; H, 7·2; O, 20·2%; M (mass spectrum) 314. $C_{19}H_{22}O_4$ requires C, 72·6; H, 7·05; O, 20·4%; M, 314].

Elution with C_6H_6–EtOAc (1:1) gave odoratone (355 mg) and elution with EtOAc gave odoratol (130 mg). The triterpenes were identified by comparison (m.p. and IR) with authentic samples.[4]

Odoratin ethylene ketal (**2**). A soln of odoratin (25 mg), ethane diol (110 mg) and a trace of TsOH in C_6H_6 (8 ml) was heated under reflux for 2 hr with TLC monitoring. The mixture was diluted with EtOAc, washed with aq. $NaHCO_3$, dried and evaporated. Crystallization of the residue from MeOH gave the *ketal* (**2**) as prisms, m.p. 233–235°. [Found: C, 70·1; H, 7·3% M (mass spectrum) 358. $C_{21}H_{26}O_5$ requires: C, 70·4; H, 7·3%; M, 358].

Selenium dioxide oxidation of odoratin. Odoratin (150 mg) and SeO_2 (150 mg) in t-BuOH (5 ml) and AcOH (0·5 ml) was heated under reflux for 5 hr. Solid material was removed by filtration and the solvent evaporated. The residue was dissolved in EtOAc and washed successively with aq. $NaHCO_3$ and H_2O. The product was separated by PLC to give the *catechol* (**6**), 26 mg, as pale yellow prisms from MeOH, m.p. 265–268° (dec); λ_{max} 219, 244 and 352 nm (ε 14,000, 8,700 and 13,000 respectively) shifting on addition of NaOH to 265 and 413 nm (ε 6,500 and 18,200); ν_{max} 3350, 3200, 1660, 1580, 1500 cm^{-1}. [Found: C, 69·6; H, 5·3%; M (mass spectrum) 326. $C_{19}H_{18}O_5$ requires: C, 69·9; H, 5·6%, M, 326].

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