

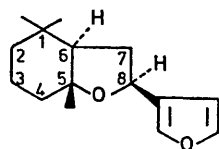
Total Synthesis of Ancistrofuran, a Defensive Compound from the Termite *Ancistrotermes cavithorax*

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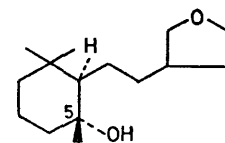
Summary The principal component of the defensive secretion from the major soldiers of the termite *Ancistrotermes cavithorax* has been shown to be ancistrofuran (1); this structural assignment has now been confirmed by detailed spectroscopic considerations and by total synthesis.

We propose here structure (1) for the major component of the defensive secretion of the major soldiers on the basis of spectroscopic evidence and total synthesis.† The assignment of relative configuration was based upon a detailed n.m.r. analysis of the corresponding hydrogenolysis product (2); no information on absolute stereochemistry is currently available.

THE termite *Ancistrotermes cavithorax* is a prevalent species in West Africa which builds extensive subterranean nests. Field studies have shown that the defensive secretion of *A. cavithorax* soldiers is repellent to common ant predators.¹ This repellency is thought to be an important factor in the lower predation observed for this termite in comparison with other common species such as *Macrotermes bellicosus*.



(1)



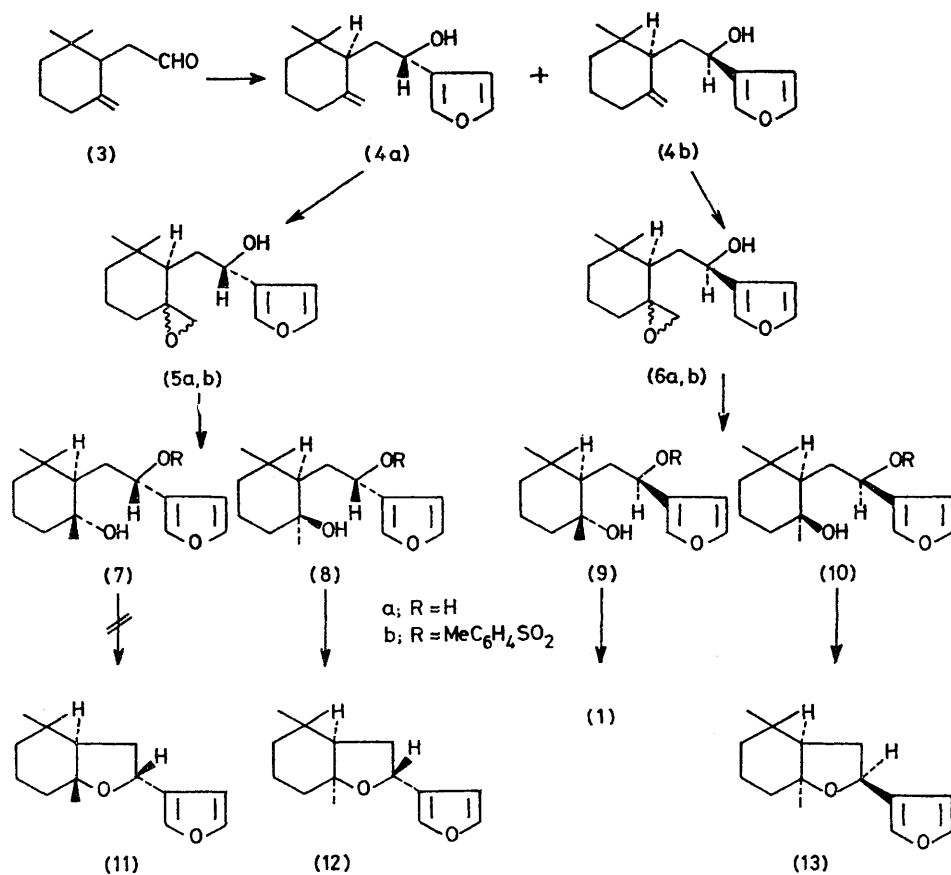
(2)

† Evidence in support of the structure of ancistrofuran (1) has also been obtained from the preparation of phenyl-substituted analogues. These were formed by $\text{Hg}(\text{OAc})_2$ -catalysed reaction of derivatives with a hydroxy function at C-5 and a C-7, C-8 olefinic bond.

Solvent extracts (CH_2Cl_2) of the major soldiers were found to contain a terpenoid furanoether (*ca.* 3 $\mu\text{g}/\text{soldier}$) as the principal volatile component. High resolution mass spectrometry indicated a molecular formula $\text{C}_{15}\text{H}_{22}\text{O}_2$ (m/e 234.1616) and the n.m.r. spectrum suggested *inter alia* a 3-substituted furan unit [δ (CDCl_3) 0.89(3H,s), 1.02(3H,s), 1.14(3H,s), 2.10(2H,m), 4.84(1H,dd, J 7 and 8 Hz), 6.27(1H,m), and 7.29(2H,m)]. The compound gave a positive reaction with Br_2 in CCl_4 but was unaffected by *NO*-bis(trimethylsilyl)acetamide, NaBH_4 , and LiAlH_4 . Hydrogenolysis over 5% palladium-calcium carbonate gave quantitative conversion into an alcohol (2) [δ (CDCl_3) 0.80(3H,s), 0.92(3H,s), 1.16(3H,s), 1.9—2.3(2H,m), and 3.3—4.0(4H)]. Mass spectrometry indicated a molecular ion at m/e 240 and an ion at m/e 222 corresponding to the loss of water. This indicated the uptake of 3 equiv. of hydrogen by the furanoid.

alcohols (4a,b) as a separable mixture of diastereoisomers in a ratio of 60:40. Molecular models indicate that nucleophilic attack on γ -cyclohomocitral (3) would occur preferentially from the *re* face.⁵ At this stage, we therefore tentatively assigned the stereochemistry of the alcohols (4a) and (4b) as written, substantiated by later experiments (*vide infra*).

Epoxidation of these alcohols (4a,b) with *m*-chloroperbenzoic acid in CH_2Cl_2 gave mixtures of the diastereoisomeric epoxides (5a,b) and (6a,b) which were reduced with LiAlH_4 to the corresponding diols (7—10). Treatment of the diastereoisomeric mixture of diols (9) and (10) with 1 equiv. of toluene-*p*-sulphonyl chloride in pyridine gave ancistrofuran (1) and a single *cis*-fused ether (13). The synthetic material was identical to natural ancistrofuran as determined from mass spectral and 270 MHz n.m.r. data and comparative g.l.c. on 7 columns.



N.m.r. spectra of (2) recorded in CDCl_3 and $\text{C}_5\text{D}_5\text{N}$ showed negligible shifts in the signals of the *gem*-dimethyl group. It is known that a considerable downfield shift (*ca.* 0.3 p.p.m.) is seen in $\text{C}_5\text{D}_5\text{N}$ solvent relative to CDCl_3 for a methyl group bearing a 1,3-*syn*-axial relationship to a hydroxy function.² These results indicated, therefore, that the alcohol (2) possessed an equatorial hydroxy group.³

Assignment of structure has now been confirmed by synthesis of racemic (1). γ -Cyclohomocitral (3) was synthesised from 2,2-dimethylcyclohexanone.⁴ Addition of (3) to 3-furyl-lithium in tetrahydrofuran at -78°C gave the

Similar treatment of the diol mixture (7) and (8) gave a second *cis*-fused ether only. Since both (12) and (13) were diastereoisomerically pure, this indicated an $\text{S}_{\text{N}}2$ -type mechanism for displacement of the toluene-*p*-sulphonate leaving group. Assignment of the ring junction stereochemistry in bicyclic ethers of this type was effected using pyridine-induced n.m.r. shift data on the hydrogenolysis products in a similar manner to the assignment of (2).

It was interesting that only one diastereoisomer of the *trans*-fused compounds was formed from the initial mixture of (4a) and (4b). Studies of molecular models, however,

show that steric compression exists between the furan and the ring hydrogens at C-4 and C-6 in the conformation required for cyclization of the isomer (**7b**). This could account for the lack of cyclization from this isomer. The other diastereoisomer (**9b**) does not suffer this steric interaction and undergoes ready displacement of the toluene-*p*-sulphonate.

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¹ C. Longhurst, R. A. Johnson, and T. G. Wood, *Oecologia*, 1977, **32**, 101; C. Longhurst, Ph.D. Thesis, Southampton University, 1978.

² P. V. Demarco, E. Farkas, D. Doddrell, B. L. Mylari, and E. Wenkert, *J. Amer. Chem. Soc.*, 1968, **90**, 5480.

³ These observations are substantiated by studies of a number of phenyl-substituted analogues of (**2**). P. H. Briner, unpublished work.

⁴ P. Seifert and H. Schinz, *Helv. Chim. Acta*, 1951, **34**, 727; S. Julia, M. Julia, H. Linares, and J-C. Blondel, *Bull. Soc. chim. France*, 1962, 1952.

⁵ K. R. Hanson, *J. Amer. Chem. Soc.*, 1966, **88**, 2731.