

Sesquiterpenoids. Part XLVII.† Structure, Configuration, Conformation, and Thermal Rearrangement of Furanodienone, Isofuranodienone, Curzerenone, Epicurzerenone, and Pyrocurzerenone, Sesquiterpenoids of *Curcuma zedoaria* ‡

By Hiroshi Hikino,* Chohachi Konno, Kunio Agatsuma, and Tsunematsu Takemoto, Pharmaceutica Institute, Tohoku University, Aoba-yama, Sendai, 980 Japan

Isao Horibe, Kazuo Tori, Masako Ueyama (*nee* Ohtsuru), and Ken'ichi Takeda, Shionogi Research Laboratory, Shionogi & Co. Ltd., Fukushima-ku, Osaka, 553 Japan

Five new furo-sesquiterpenoids, furanodienone [(1*E*,4*E*)-8,12-epoxygermacra-1(10),4,7,11-tetraen-6-one] (1), isofuranodienone [(1*E*,4*Z*)-8,12-epoxygermacra-1(10),4,7,11-tetraen-6-one] (2), curzerenone [6,7-dihydro-5β-isopropenyl-3,6β-dimethyl-6-vinylbenzofuran-4(5*H*)-one] (3), epicurzerenone [6,7-dihydro-5α-isopropenyl-3,6β-dimethyl-6-vinylbenzofuran-4(5*H*)-one] (4), and pyrocurzerenone [6,7-dihydro-1,5,8-trimethylnaphtho-[2,1-*b*]furan] (15) have been isolated from the rhizomes of *Curcuma zedoaria* Roscoe, and their structures have been elucidated on the basis of chemical and spectroscopic evidence. The conformation of the ten-membered ring in (1) and (2) has been determined by use of the intramolecular internuclear Overhauser effect. Thermal rearrangements of these sesquiterpenoids are described.

WE have for some time been examining the constituents of the crude drug zedoary, the rhizomes of *Curcuma zedoaria* Roscoe (Zingiberaceae), and have hitherto reported the isolation and identification of several new sesquiterpenoids.⁴ We now describe the isolation of five novel sesquiterpenoids containing a furan ring which have been designated as furanodienone, isofuranodienone, curzerenone, epicurzerenone, and pyrocurzerenone, and discuss the determination of their structures and conformations, and their thermal rearrangements.¹⁻³ One of the rearrangements represents the first example of an elemene-germacrane-cadinane transformation.^{2,§}

Furanodienone and Isofuranodienone.—Furanodienone and isofuranodienone have the same molecular formula (C₁₅H₁₈O₂). The u.v. and i.r. spectra of furanodienone (λ_{max} 241 and 269 nm; ν_{max} 1645 cm⁻¹) and of isofuranodienone (λ_{max} 223 and 248 nm; ν_{max} 1667 cm⁻¹) indicated αβ-unsaturated carbonyl groups. The presence of another oxygen atom in each molecule in a furan ring was suggested by positive colour tests in vanillin-hydrochloric acid, Ehrlich, and Liebermann-Burchard reactions. In the n.m.r. spectrum of each substance in [2H]chloroform, vinyl proton (δ 7.08 for furanodienone; 7.00 for isofuranodienone; data below in this order), vinyl methyl (δ 2.13; 1.91), and methylene (δ 3.69; 3.13 and 3.49) signals are weakly coupled to each other and are interpreted as arising from a furan ring having α-H, β-Me, and α'-methylene substituents. The u.v. maxima for the electron transfer absorption found at somewhat longer wavelengths (λ_{max} 269; 248 nm) are indicative of conjugation of the carbonyl groups with the furan rings at their β'-positions. Furthermore, in each spectrum, two vinyl proton (δ 5.16 and 5.80; 5.20

and 6.10) and two vinyl methyl (δ 1.30 and 1.99; 1.55 and 1.89) signals also appear; the observation of long-range couplings between the respective vinyl proton and methyl signals indicates the presence of two trisubstituted olefinic linkages carrying a methyl group. One of the vinyl protons (δ 5.16; 5.20) was further coupled to a methylene and also to the α'-methylene of the furan; this leads to the extension of the environment of the furan unit in each molecule. The other vinyl proton signal appears at somewhat lower field (δ 5.80; 6.10) as a singlet, broadened by long-range coupling with the vinyl methyl group, which demonstrates that the carbon bearing this vinyl proton is adjacent to the carbonyl group. The presence of these functional groups and the molecular formula require that both substances have monocarbocyclic skeletons. Since only one carbon and two hydrogen atoms, which must constitute a methylene group, remain to be assigned, connection of the partial structures deduced above by this methylene group leads to the conclusion that both compounds are 8,12-epoxygermacra-1(10),4,7,11-tetraen-6-ones, and consequently are geometric isomers with respect to either or both the trisubstituted double bonds. In agreement with this conclusion, the mass spectra of the two substances are very similar, showing base peaks at *m/e* 122 due to a retro-Diels-Alder type fragmentation.

The geometries of the double bonds in the *cis-trans*-isomers were determined by measuring intramolecular internuclear Overhauser effects (n.O.e.).⁵ To avoid ambiguities and to separate overlapping signals, the n.O.e.s were measured in two solvents, CDCl₃ and C₆D₆. Saturation of the 10-Me and the 4-Me signals in the spectrum of furanodienone in C₆D₆ exerted no

† Part XLVI, H. Hikino, Y. Hikino, R. Nakamura, M. Ono, and T. Takemoto, *Yakugaku Zasshi*, 1972, **92**, 498.

‡ Parts of the material contained herein have been published in preliminary form: see refs. 1—3.

§ A similar transformation has since been found in the thermal rearrangement of the shyobunones; M. Iguchi, A. Nishiyama, S. Yamamura, and Y. Hirata, *Tetrahedron Letters*, 1969, 4295.

¹ H. Hikino, K. Agatsuma, and T. Takemoto, *Tetrahedron Letters*, 1968, 2855.

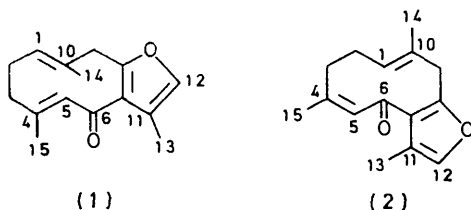
² H. Hikino, K. Agatsuma, C. Konno, and T. Takemoto, *Tetrahedron Letters*, 1968, 4417.

³ H. Hikino, C. Konno, T. Takemoto, K. Tori, M. Ohtsuru, and I. Horibe, *Chem. Comm.*, 1969, 662.

⁴ Cf. H. Hikino, C. Konno, and T. Takemoto, *Chem. and Pharm. Bull. (Japan)*, 1972, **20**, 987.

⁵ J. H. Noggle and R. E. Schirmer, 'The Nuclear Overhauser Effect,' Academic Press, New York and London, 1971.

effect on the 5-H and the 1-H signals, respectively, suggesting that both the trisubstituted double bonds are *trans*.⁶ Although apparent increases in the areas of the 1-H and 5-H signals (7 and 22%, respectively) were observed on irradiation at the position of the 4-Me signal (δ ca. 2) in CDCl_3 , they must be due to overlap of signals arising from other protons close to 1- and 5-H. On the other hand, in the spectrum of isofuranodienone, no interaction between the 1-H and 10-Me signals was observed, suggesting that the 1,10-double bond is *trans*,⁶ while saturation of the 4-Me signal gave rise to a considerable enhancement in the area of the 5-H signal (33% and 30%^b),* demonstrating that the 4,5-double bond is *cis*. These facts enable us to deduce the structures of furanodienone and isofuranodienone as (1) and (2) respectively.



The conformations of the ten-membered rings in these two terpenoids were then studied, first by a more extensive determination of n.o.e. values. In (1), an increase in the integrated intensity of the 1-H signal (6%^a and 10%^b) was caused by saturating the 5-H signal, and *vice versa* (6%^a and 7%^b), indicating that the ten-membered ring adopts a conformation in which 1- and 5-H are in close proximity, and consequently that 4-Me and 10-Me are *syn*. The observations of n.o.e. interactions between the 1- and 9 α -H signals (7%^b), and between the 9 β -H and 10-Me signals (4%^a and 4%^b) reveal that the two pairs of hydrogens are very close together. In the spectrum of (1), the 1-H signal appears as a doublet of doublets due to vicinal spin couplings to the 2-methylene protons, the spacings (7.5 and 7.5 Hz), when judged from the Karplus relationship, indicating that the dihedral angles between 1- and 2-H are ca. 30 and 150°. The aromatic solvent induced shifts of the signals on passing from CDCl_3 to C_6D_6 solutions, $\Delta\delta$, were also instructive.⁷ Thus, the $\Delta\delta$ value of +0.11 p.p.m. for the 11-Me signal in furanodienone implies that 11-Me is situated in front of the 6-carbonyl group.⁸ The upfield shift ($\Delta\delta$ -0.10 and -0.23 p.p.m.) of the 4-Me and 10-Me signals show that both methyl groups lie behind but near the reference plane.⁸ The $\Delta\delta$ values for the other protons are negative and demonstrate that the protons are located behind the carbonyl group. These data clearly define the preferred conformation of (1) as depicted in the Figure (A).

On the other hand, in the ^1H n.m.r. spectrum of (2),

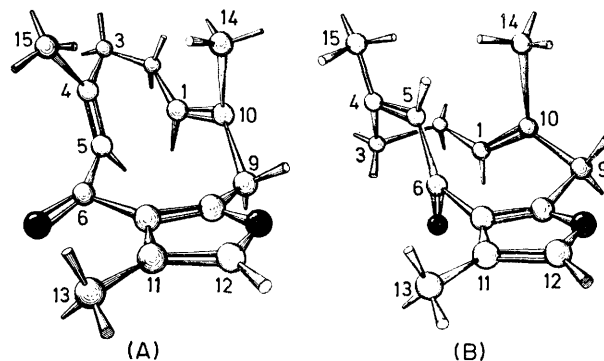
* *a* in CDCl_3 , *b* in C_6D_6 .

† Since these substances were incorrectly characterized in a previous paper, the terms curzerenone and epicurzerenone are now assigned to the *trans*- and *cis*-elementary derivatives, respectively.

n.o.e. interactions were observed between the 5-H and 10-Me signals (14%^a and 16%^b), between the 1- and 9 α -H signals (9%^a and 9%^b), and between the 9 β -H and 10-Me signals (12%^a and 10%^b), indicating the close proximity of these pairs of protons. The spectrum of (2) exhibits the 1-H signal as a doublet of doublets, whose splittings (8.8 and 7.0 Hz) show the dihedral angles between 1- and 2 α -H and between 1- and 2 β -H to be ca. 30 and ca. 150°, respectively. The solvent-induced shifts for all the signals in this case are all upfield, indicating that all the protons observed lie behind the carbonyl group.⁸ The above data indicate that the conformation of (2) is as illustrated in the Figure (B).

The u.v. maxima and the i.r. absorption band for the conjugated carbonyl group in (1) show longer wavelength shifts relative to those in (2). These findings may be explained by the difference of the distorted features of the cross conjugated systems [see Figure (A) and (B)].

Curzerenone and Epicurzerenone.—Curzerenone and epicurzerenone,[†] both $\text{C}_{15}\text{H}_{18}\text{O}_2$, have similar spectral properties thus suggesting that they are structurally very similar. The u.v. and i.r. spectra of both substances show absorptions indicative of β -furoyl systems (λ_{max} 272 nm and ν_{max} 1675 cm^{-1} ; λ_{max} 270 nm and ν_{max} 1675 cm^{-1} , respectively). The ^1H n.m.r. spectra



The molecular conformations of furanodienone (1) (A) and isofuranodienone (2) (B)

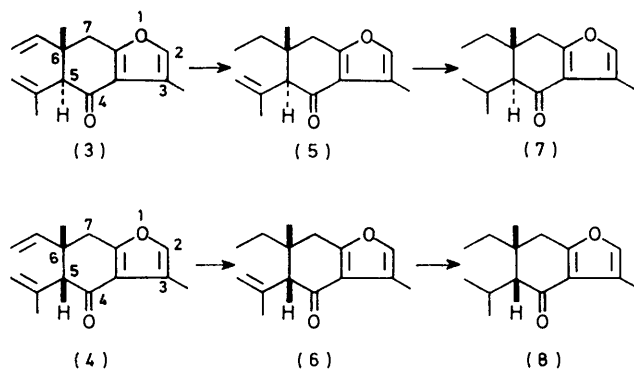
with the aid of double resonance experiments demonstrate the following structural elements; an α -H (δ 7.08 for curzerenone; 7.10 for epicurzerenone; data in this order below) and a β -Me (δ 2.17; 2.20) on a furan ring, a methylene group (δ 2.73, 2.97; 2.72, 3.03) flanked by quaternary carbons and weakly coupled to the α -H of the furan, a tertiary methyl group (δ 1.19; 1.24), a vinyl proton (δ 4.95, 4.95, 5.81; 5.05, 5.08, 6.00) on a quaternary carbon atom, an isopropenyl group (δ 1.82, 4.75, 4.99; 1.75, 4.73, 4.94), and an isolated methine

⁶ K. Takeda, K. Tori, I. Horibe, H. Minato, N. Hayashi, S. Hayashi, and T. Matsuura, *J. Chem. Soc. (C)*, 1970, 985, and references therein.

⁷ P. Laszlo, *Progr. N.M.R. Spectroscopy*, 1967, **3**, 231.

⁸ J. D. Connolly and R. McCrindle, *J. Chem. Soc. (C)*, 1966, 1613.

group (δ 3.01; 2.95) for each substance, all the hydrogens being accommodated. Partial hydrogenation of both substances over Raney nickel in methanol resulted in saturation of the vinyl groups to give the dihydro-derivatives (5) and (6) which were further hydrogenated with platinum in methanol to furnish the tetrahydro-derivatives (7) and (8). The mass spectra of curzerenone and epicurzerenone exhibited base peaks at m/e 122 which are attributed to fragments generated by a



retro-Diels–Alder type cleavage. These data lead us to conclude that both substances possess the same overall structure, 6,7-dihydro-5-isopropenyl-3,6-dimethyl-6-vinylbenzofuran-4(5*H*)-one, and consequently are epimers with respect to C-5 or C-6. In confirmation, alkaline treatment of curzerenone and epicurzerenone in both cases gave the same equilibrium mixture of the two compounds.

Since curzerenone and epicurzerenone show no optical activity, both are racemic. Therefore, the remaining problem was to determine the relative configurations at C-5 and C-6. To this end, n.O.e. measurements for curzerenone and epicurzerenone, and benzene-induced solvent shifts for (7) and (8) were examined.¹ However, all signals in the spectra of curzerenone and epicurzerenone in [²H]chloroform became broader as the temperature was lowered to -40° , thus showing that these compounds are rapidly inverted at room temperature on the n.m.r. time scale, and that the above two methods are not of use in these structural determinations.

We next attempted to establish the configurations by a chemical transformation, the first being the Cope rearrangement of (1) and (2). Orbital symmetry rules⁹ require that on pyrolysis a germacra-*trans*-1(10),*trans*-4-diene such as (1) gives a *trans*-elemene-1,3-diene, while a germacra-*trans*-1(10),*cis*-4-diene such as (2) affords a *cis*-elemene-1,3-diene. Further, (1) and (2) have conformations which will furnish a *trans*- and a *cis*-elemene-1,3-diene unless these are changed before the reaction. Pyrolysis of (1) at 200° resulted in Cope

rearrangement to yield curzerenone and that of (2) under the same conditions formed epicurzerenone. This is the first instance where a *cis*-elemene type product is generated by Cope rearrangement of an 8,12-epoxygermacra-1(10),4-diene derivative. However, since it has recently been reported that *trans*,*cis*-germacra-1(10),4-diene congeners which contain a furan ring may undergo abnormal Cope rearrangement,¹⁰ the present results cannot be regarded as providing confirmation for the stereochemistry of curzerenone and epicurzerenone.

Further efforts to correlate curzerenone, assumed to be a *trans*-elemene, with a known isofuranogermacrene (curzerene) (9)¹¹ succeeded in determining the stereochemistry of curzerenone and epicurzerenone. Reduction of curzerenone with lithium aluminium hydride in ether gave two products (10) and (11). Their i.r. spectra revealed the disappearance of the carbonyl groups and the formation of hydroxy-groups (ν_{\max} 3525; 3550 cm^{-1}). The ¹H n.m.r. spectrum of the main product (10) shows most of the signals found in the spectrum of curzerenone, and a newly formed (C-4) CHOH signal (δ 4.69), which constitutes an AB quartet (J 5.8 Hz) with the 5-H signal. The spectrum of the minor product (11) shows close correspondence to that of (10), a newly formed (C-4) CHOH signal and 5-H also constituting an AB quartet (J 7.5 Hz). The stereochemistry of these alcohols will be discussed later. When (10) was oxidized with chromium trioxide–pyridine complex, the original curzerenone was quantitatively regenerated, which confirmed that epimerization at C-5 had not taken place during the hydride reduction. Acetylation of (10) with acetic anhydride in pyridine led to an acetate (12) (ν_{\max} 1730 and 1220 cm^{-1} ; δ 1.96 and 4.78). Treatment of (12) with lithium–ammonia brought about elimination of the acetoxy-group to furnish, though in rather poor yield, a derivative identified as the natural isofuranogermacrene (9) by comparisons of t.l.c. and g.l.c., and of the i.r. and ¹H n.m.r. spectra. However, the compound epimeric with (9) is unknown, and it is possible that the properties of this hypothetical compound are indistinguishable from those of (9) within the criteria chosen. Therefore, in order to corroborate the identity, the deacetoxy-derivative was further hydrogenated over platinum in methanol to afford a tetrahydro-derivative which was identical with tetrahydroisofuranogermacrene (13) by g.l.c.–mass spectral examination. This chemical correlation of curzerenone with (9) has thus verified the configuration of curzerenone as a *trans*-elemene (3), and consequently, that of its epimer, epicurzerenone, as being a *cis*-elemene derivative (4).

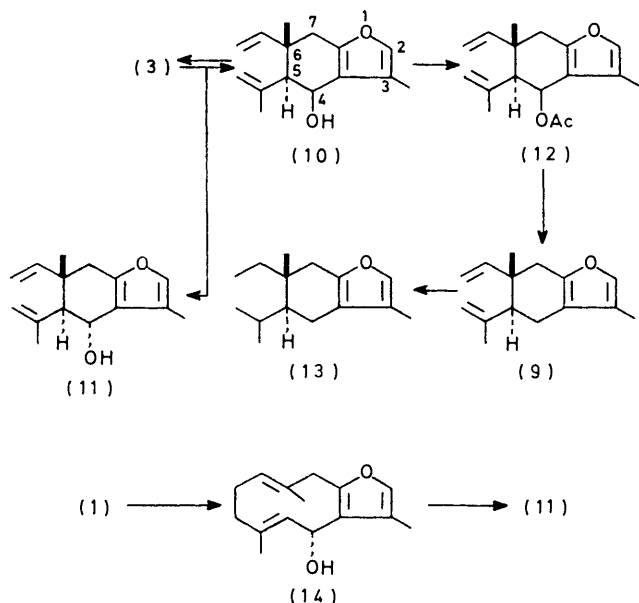
The stereochemistry of the alcohols obtained by the above hydride reduction of (3) was deduced as follows. Reduction of (1) with lithium aluminium hydride in ether gave an alcohol (14). Although this alcohol must

⁹ R. Hoffmann and R. B. Woodward, *J. Amer. Chem. Soc.*, **1965**, **87**, 4389.

¹⁰ K. Takeda, I. Horibe, and H. Minato, *J. Chem. Soc. (C)*, **1970**, 2704.

¹¹ H. Hikino, K. Agatsuma, C. Konno, and T. Takemoto, *Chem. and Pharm. Bull. (Japan)*, **1970**, **18**, 752; H. Ishii, T. Tozoy, M. Nakamura, and K. Takeda, *Tetrahedron*, **1968**, **24**, 625.

be racemic, its molecule must adopt the most stable conformation in which the 4-hydroxy-group is equatorial. Since it is known that the stereochemistry of products formed by the Cope rearrangement of germacra-1(10),4-dienes is defined by the conformation of the starting



dienes, the pyrolysis product of (14) is consequently represented by structure (11). The elemadienol (11) obtained in this way was identical with the minor product produced by the previous reduction of (3) which leads to the structure (10) for the major product.*

Pyrocurzerenone.—In pyrocurzerenone, $C_{15}H_{16}O$, the absence of hydroxy or carbonyl absorption in the i.r. spectrum suggests that the oxygen atom is ethereal. This conclusion was reinforced by positive colour reactions for the furan ring, and further by inspection of the 1H n.m.r. spectrum where signals of an AX_3 type (δ 7.10 and 2.31) are attributed to α -H and β -Me protons on a furan ring. The presence of a proton (δ 6.91) and a vicinal methyl group (δ 2.25) on a benzene ring weakly coupled to each other, a proton (δ 6.69) and a methyl group (δ 1.92) on an olefinic linkage (J 1.4 Hz), and four allylic protons (δ 2.05–2.75) were further indicated by the spectrum (see Experimental section). On this basis, pyrocurzerenone should possess a bicarbocyclic ring fused to a furan ring. An n.o.e. (ca. 10%) was observed between the signals due to the β -Me on the furan ring and the vinyl proton on the olefinic linkage, thus demonstrating that both are close together. The u.v. spectrum (λ_{max} 233, 239, 249, 283, and 293 nm) suggests the presence of a benzofuran system further conjugated with an olefinic bond.¹²

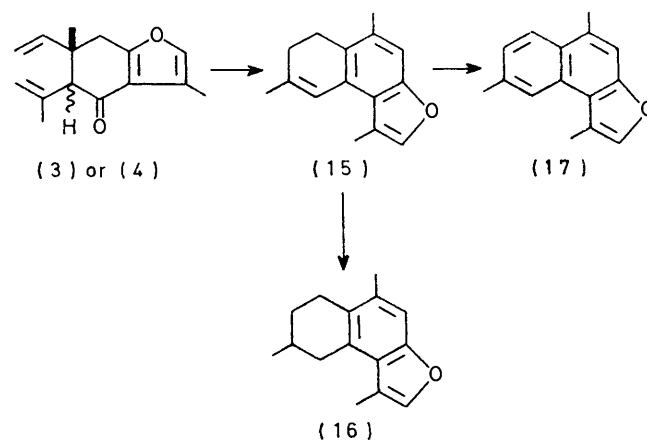
* A concurrent chemical investigation of the structure of curzerenone has been reported: S. Fukushima, M. Kuroyanagi, Y. Akahori, Y. Saiki, and A. Ueno, *Yakugaku Zasshi*, 1968, **88**, 792; 1970, **90**, 863.

† In a previous paper, this substance was inappropriately named furanocadinene.²

‡ The synthesis of pyrocurzerenone has recently been reported: V. Viswanatha and G. S. Krishna Rao, *J.C.S. Perkin I*, 1974, 450.

Hydrogenation of pyrocurzerenone over platinum in methanol gave a dihydro-derivative (16), whose 1H n.m.r. spectrum showed the disappearance of the trisubstituted double bond and the formation of a secondary methyl group and three aliphatic protons. The u.v. spectrum of dihydropyrocurzerenone (16) (λ_{max} 216, 248, 254, 262, 281, and 291 nm) shows it to have a benzofuran chromophore.¹²

Compounds (3) and (4) were subjected to pyrolysis in the hope of obtaining Cope rearrangement products (1) and (2), but heating at 250–270° for 6 h afforded a product which was neither the expected (1) nor (2) but was identified as pyrocurzerenone. When the curzerenones or, as found later, pyrocurzerenone were heated as high as 350°, two main products were formed in a ratio of 1:3. The major product, now named furanocadalene,† has a molecular formula $C_{15}H_{14}O$ which demonstrates the occurrence of dehydrogenation during the pyrolysis of pyrocurzerenone. The 1H n.m.r. spectrum of furanocadalene shows signals originating from an α -H (δ 7.29) and a β -Me (δ 2.31) on a furan

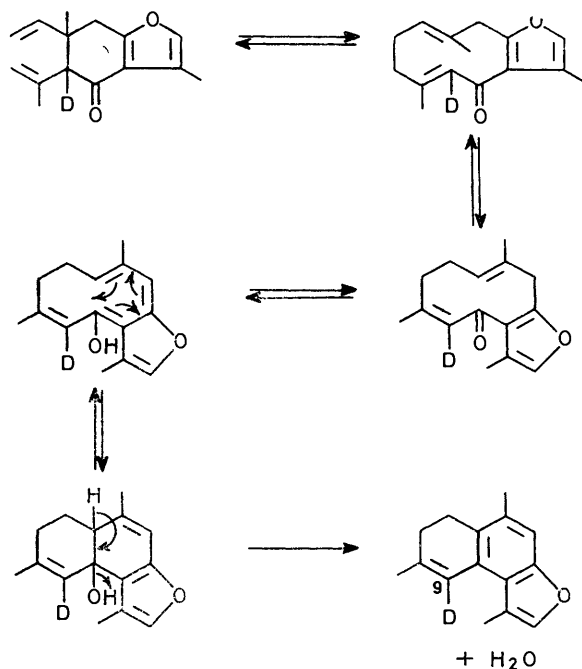


ring, two sets of isolated protons (δ 7.27 and 7.98) and vicinal methyls (δ 2.51 and 2.64) on benzene rings, and two vicinal protons (δ 7.16 and 7.80) on a benzene ring; one of the isolated aromatic protons (δ 7.98) is *m*- and *p*-coupled with the above vicinal aromatic protons. Two n.o.e. interactions were found between the signals due to the β -Me (δ 2.53) on the furan and the isolated aromatic proton (δ 7.98) (ca. 20%), and between the signals due to the aromatic methyl group (δ 2.64) and the aromatic proton (δ 7.80) (ca. 20%) which is *p*-coupled with the isolated aromatic proton (δ 7.98). The u.v. spectrum of furanocadalene (λ_{max} 223, 248, 301, 313, and 327 nm) suggests that it has a naphthofuran chromophore.¹²

The above evidence leads us to conclude that the structure of furanocadalene is (17), so that pyrocurzerenone is (15). To our knowledge pyrocurzerenone is the first sesquiterpenoid of the cadinane type to contain a furan ring.‡

¹² Cf. J. Romo and P. Joseph-Nathan, *Tetrahedron*, 1964, **20**, 2331.

Thermal Rearrangement of the Furanodienones.—As has been mentioned above, heating (1) and (2) at 200° resulted in Cope rearrangement to give (3) and (4), respectively. Heating both (3) and (4) at 240° caused



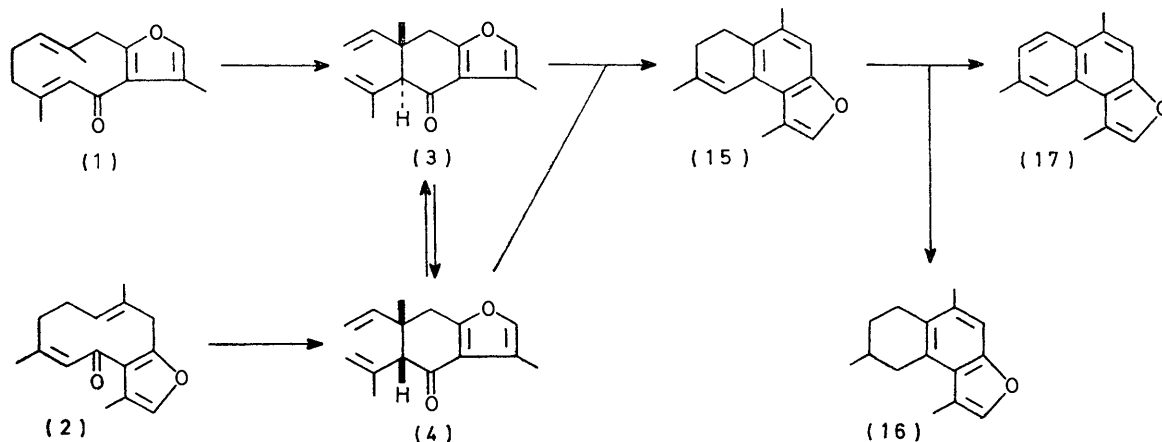
SCHEME 1

their slow interconversion. In order to clarify whether the interconversion takes place *via* germacra-1(10),4-diene intermediates by double Cope rearrangement or

However, since the rate of interconversion of the curzerenones is faster than that of the dihydrocurzerenones, it is possible that the former two interconvert partly by double Cope rearrangement.

As described above, heating of (3) and (4) at 270° led to thermal rearrangement to (15). For clarification of the mechanism of this reaction, 5-deuteriated curzerenones were subjected to pyrolysis at 350°. These reactions resulted in the formation of (15) and (17) which possessed deuterium at C-9, though only 30% of the deuterium originally present in the curzerenones remained in the products. This finding leads to the conclusion that the transformation of curzerenones to (15) proceeds through the mechanisms shown in Scheme 1. The decrease of the deuterium content of (15) and (17) as compared with the starting curzerenones may be rationalized if it is assumed that deuterium is lost at the OD group formed by enolization of the curzerenones (see above) by exchange with hydrogen from water generated by the transformation.

As also stated above, heating (3) and (4) at 350° gave (15) and (17) as minor and major products. From the last transformation, it is considered that pyrolysis of (3) and (4) first affords (15) which is then dehydrogenated to furnish (17). It seems likely that (17) would be formed from (15) by a transfer of hydrogen to another molecule of (15) or to the starting curzerenones. In confirmation, pyrolysis of (15) at 350° resulted in the formation of dihydropyrocurzerenone (16) together with (17), the former being identified with the substance obtained from (15) by hydrogenation over platinum in methanol. However, the yield of (16) in the pyrolysis was much less than that of (17). Compensating for



SCHEME 2

via enols by keto-enol tautomerization, the dihydrocurzerenones (5) and (6), in which the interconversion cannot occur through ten-membered monocarbocyclic intermediates were pyrolysed; the dihydrocurzerenones were still converted into each other. These observations indicate that the interconversion of (3) and (4) takes place at least partly by keto-enol tautomerization.

this discrepancy, hydrogen was detected in the reaction mixture, indicating that liberation of hydrogen from (15) also occurred during the pyrolysis.

In conclusion, it has been clarified that pyrolysis of (1) and (2) proceeds through (3) and (4) (and their interconversion), and (15), finally to (17) with the formation of (16) and hydrogen (Scheme 2).

EXPERIMENTAL

N.m.r. spectra were recorded at 100 MHz unless otherwise stated with tetramethylsilane as internal standard. Nuclear Overhauser effect experiments were carried out by measuring the integrated intensities of a signal with and without irradiation at the resonance frequency of another signal at a sweep rate of 0.4 Hz s^{-1} (at least four measurements were made); the carefully degassed solutions were ca. 5% (w/v) in CDCl_3 and C_6D_6 . Care was taken that the audio phase-sensitive detector of the spectrometer was not overloaded. The enhancement is expressed in %; accuracy $\pm 2\%$. N.m.r. spectral data, including the results of some double resonance experiments, for compounds marked with an asterisk, and n.m.r. and n.o.e. data for compounds marked with an obelus are given in Supplementary Publication No. SUP 21225 (16 pp., 1 microfiche).[†]

Isolation of Furanodienone, Isofuranodienone, Curzerenone, Epicurzerenone, and Pyrocurzerenone.—The crude drug zedoary, the dried rhizomes of *Curcuma zedoaria* Roscoe, was extracted with methanol. The light petroleum-soluble fraction was chromatographed over alumina, and the light petroleum eluate was rechromatographed over silica gel.

Elution with light petroleum and crystallization from the same solvent gave *pyrocurzerenone* (6,7-dihydro-1,5,8-trimethylnaphtho[2,1-b]furan) (15)* as needles, m.p. 76.5–77.5°, $[\alpha]_D \pm 0^\circ$ (c 10.0); m/e 212 (M^+); λ_{max} (EtOH) 233 (log ϵ 4.75), 239 (4.72), 249 (4.62), 283 (4.40), and 293 nm (4.40); ν_{max} (KBr) 1650, 1580, 1110, and 800 cm^{-1} (furan) (Found: C, 84.7; H, 7.45. $\text{C}_{15}\text{H}_{16}\text{O}$ requires C, 84.25; H, 7.6%).

Elution with light petroleum–benzene (1:1) and distillation under reduced pressure afforded *epicurzerenone* [6,7-dihydro-5 α -isopropenyl-3,6 β -dimethyl-6-vinylbenzofuran-4(5H)-one] (4)[†] as an oil, $[\alpha]_D \pm 0^\circ$ (c 10.0); m/e 230 (M^+) and 122 (100%); λ_{max} (EtOH) 220 (log ϵ 3.92) and 270 nm (3.44); ν_{max} (CCl_4) 1675 (enone), 3100, 1640, 994, 915, 892 (vinylidene, vinyl), 1566, and 1066 cm^{-1} (furan) (Found: C, 77.85; H, 8.1. $\text{C}_{15}\text{H}_{18}\text{O}_2$ requires C, 78.25; H, 7.9%).

Subsequent elution with the same solvent and distillation under diminished pressure furnished *curzerenone* [6,7-dihydro-5 β -isopropenyl-3,6 β -dimethyl-6-vinylbenzofuran-4(5H)-one] (3)[†] as an oil, $[\alpha]_D \pm 0^\circ$ (c 10.0); m/e 230 (M^+) and 122 (100%); λ_{max} (EtOH) 272 nm (log ϵ 3.44); ν_{max} (CCl_4) 1675 (enone), 3100, 1643, 990, 915, 898 (vinylidene, vinyl), 1565, and 1067 cm^{-1} (furan) (Found: C, 78.0; H, 8.0. $\text{C}_{15}\text{H}_{18}\text{O}_2$ requires C, 78.25; H, 7.9%).

Successive elution with the same solvent and crystallization from light petroleum yielded *isofuranodienone* [(1E,4Z)-8,12-epoxygermacra-1(10),4,7,11-tetraen-6-one] (2)[†] as needles, m.p. 70–71°, $[\alpha]_D \pm 0^\circ$ (c 10.0); m/e 230 (M^+) and 122 (100%); λ_{max} (EtOH) 223 (log ϵ 4.17) and 248 nm (3.95); ν_{max} (KBr) 1667 cm^{-1} (enone); positive vanillin–HCl, Ehrlich, and Liebermann–Burchard reactions.

Further elution with the same solvent and crystallization from light petroleum gave *furanodienone* [(1E,4E)-8,12-epoxygermacra-1(10),4,7,11-tetraen-6-one] (1)[†] as needles, m.p. 89.5–90.5°, $[\alpha]_D \pm 0^\circ$ (c 10.0); m/e 230 (M^+) and 122 (100%); λ_{max} (EtOH) 241 (log ϵ 2.98) and 269 nm (3.86); ν_{max} (KBr) 1645 cm^{-1} (enone); positive vanillin–HCl, Ehrlich, and Liebermann–Burchard reactions.

Partial Hydrogenation of Curzerenone over Raney Nickel in Methanol.—Curzerenone (123 mg) in methanol (5 ml) was hydrogenated in the presence of Raney Ni (130 mg).

The reaction was stopped after 1 mol of hydrogen had been absorbed. Evaporation of the filtrate yielded *dihydrocurzerenone* (5)* as an oil (115 mg); ν_{max} (CCl_4) 1678 (enone), 3090, 1642, 898 (vinylidene), 1565, and 1071 cm^{-1} (furan).

Hydrogenation of Epicurzerenone over Raney Nickel in Methanol.—Epicurzerenone (150 mg) in methanol (5 ml) was hydrogenated with Raney Ni (100 mg). The reaction was stopped after 1 mol of hydrogen had been consumed. Filtration and removal of the solvent furnished *dihydroepicurzerenone* (6)* as an oil (130 mg); ν_{max} (CCl_4) 1672 (enone), 3100, 1642, 894 (vinylidene), 1565, and 1070 cm^{-1} (furan).

Hydrogenation of Dihydrocurzerenone over Platinum in Methanol.—Dihydrocurzerenone (5) (87 mg) was hydrogenated over PtO_2 (13 mg) in methanol (4 ml). Evaporation of the filtrate gave *tetrahydrocurzerenone* (7)* as an oil (61 mg); ν_{max} (CCl_4) 1668 (enone), 1567, and 1068 cm^{-1} (furan).

Hydrogenation of Dihydroepicurzerenone over Platinum in Methanol.—Dihydroepicurzerenone (6) (100 mg) in methanol (4 ml) was hydrogenated over PtO_2 (20 mg). The product was chromatographed over silica gel (5 g). Benzene eluted *tetrahydroepicurzerenone* (8)* as an oil (98 mg); ν_{max} (CCl_4) 1668 (enone), 1566, and 1063 cm^{-1} (furan).

Alkaline Treatment of Curzerenone.—Curzerenone (18 mg) and KOH (100 mg) in methanol (1.5 ml) was kept at room temperature under nitrogen for 2 days. Addition with water and extraction with ether gave a 1:1 mixture of curzerenone and epicurzerenone, identified by the n.m.r. spectrum.

Alkaline Treatment of Epicurzerenone.—Similar treatment of epicurzerenone (15 mg) with KOH (110 mg) in methanol (1 ml) yielded a 1:1 mixture of curzerenone and epicurzerenone.

Pyrolysis of Furanodienone at 200°.—Furanodienone (30 mg) was heated under nitrogen at 195–200° for 10 min to give curzerenone (25 mg), identical with a natural sample by i.r. and n.m.r.

Pyrolysis of Isofuranodienone at 200°.—Isofuranodienone (30 mg) was heated under nitrogen at 195–200° for 90 min to give epicurzerenone (30 mg), identified by comparison of i.r. and n.m.r. spectra.

Reduction of Curzerenone with Lithium Aluminum Hydride in Ether.—Curzerenone (3.25 g) and LiAlH_4 (1.3 g) in anhydrous ether (100 ml) were stirred at room temperature for 3 h. Extraction with ethyl acetate gave a product which was chromatographed over silica gel. Elution with benzene–ethyl acetate (5:1) yielded 4,5,6,7-tetrahydro-5 β -isopropenyl-3,6 β -dimethyl-6-vinylbenzofuran-4-ol (10)* as an oil (2.15 g); ν_{max} (CCl_4) 3525 (OH), 3078, 1638, 993, 914 (vinylidene, vinyl), 1562, and 1004 cm^{-1} (furan).

Successive elution with the same solvent and crystallization from light petroleum gave the epimeric alcohol (11)* as prisms, m.p. 82–84°; ν_{max} (CCl_4) 3550 (OH), 3080, 1641, 991, 915, 900 (vinylidene, vinyl), 1563, and 1001 cm^{-1} (furan).

Chromic Acid Oxidation of the Alcohol (10).—To the alcohol (10) (50 mg) in pyridine (1 ml) was added CrO_3 –pyridine complex (100 mg–2 ml). After standing at room temperature overnight, the mixture was worked up as usual to give curzerenone (43 mg).

Acetylation of the Alcohol (10).—The alcohol (10) (2.00 g) in acetic anhydride (10 ml) and pyridine (20 ml) was set aside at room temperature overnight. Extraction with

[†] For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1973, Index issue.

ethyl acetate afforded a product (2.05 g) which was chromatographed over silica gel (70 g). Elution with benzene gave the acetate (12)* as an oil (1.83 g); ν_{\max} (CCl₄) 1730, 1220 (AcO), 3060, 1642, 998, 910, and 889 cm⁻¹ (vinylidene, vinyl).

Reduction of the Acetate (12) with Lithium-Ammonia.—The acetate (12) (1.8 g) in ether (30 ml) was added with stirring to lithium (5 g) in liquid ammonia (0.3 l). Stirring was continued for 1 h and the reaction stopped by addition of NH₄Cl (15 g). Dilution with water and extraction with ethyl acetate yielded a product (1.4 g) which was chromatographed on silica gel. Light petroleum eluted isofuranogermacrene (curzerene) as an oil (47 mg), identical with the natural material by t.l.c., g.l.c., i.r., and n.m.r. spectra.

Reduction of the Isofuranogermacrene over Platinum in Methanol.—The foregoing isofuranogermacrene (35 mg) was hydrogenated over PtO₂ (5 mg) in methanol (10 ml) at room temperature overnight. Evaporation of the filtrate gave the tetrahydro-derivative (13) as an oil (33 mg), identical with the tetrahydro-derivative of the natural curzerenone by g.l.c.—mass spectrometry; m/e 220 (M^+) and 108 (100%).

Reduction of Furanodienone with Lithium Aluminum Hydride.—A mixture of furanodienone (17 mg) and LiAlH₄ (6 mg) in anhydrous ether (2.5 ml) was stirred at room temperature for 90 min. The customary work-up gave a product (17 mg) which was subjected to preparative t.l.c. and crystallized from ether—light petroleum to furnish the racemic 8,12-epoxygermacra-1(10),4,7,11-tetraen-6-ol (14) as needles (12 mg), m.p. 94—96°; ν_{\max} (Nujol) 3410 (OH), 1669, 1618, 971, 928, 891, 866 (ethylene bond), 1545, and 1138 cm⁻¹ (furan).

Pyrolysis of the Germacratetraenol.—The alcohol (14) (12 mg) in propan-1-ol (5 ml) was heated under reflux for 3 h. The product, after evaporation of the solvent, was submitted to preparative t.l.c. and crystallization from light petroleum to give the racemic benzofuranol (11) as prisms (1 mg), m.p. 82—84°, identical with the benzofuranol obtained by LiAlH₄ reduction of curzerenone by t.l.c., g.l.c., and i.r. spectra.

Hydrogenation of Pyrocurzerenone over Platinum in Methanol.—Pyrocurzerenone (43 mg) was hydrogenated over PtO₂ (10 mg) in methanol (10 ml) at room temperature overnight. The filtrate afforded a product which on crystallization from light petroleum gave dihydropyrocurzerenone (16)* as needles (28 mg), m.p. 72—73°; λ_{\max} (EtOH) 216 (log ϵ 4.47), 248 (4.23), 254 (4.25), 262 (3.76), 281 (3.76), and 291 nm (3.64); ν_{\max} (KBr) 1615, 1570, 1535, 1100, 840, and 755 cm⁻¹ (benzofuran).

Pyrolysis of Curzerenone at 250—270°.—Curzerenone (127 mg) was heated under nitrogen at 250—270° for 6 h. Silica gel chromatography of the product (light petroleum elution) followed by crystallization from light petroleum gave pyrocurzerenone as needles (43 mg), m.p. 76.4—77.5°.

Pyrolysis of Epicurzerenone at 250—270°.—Epicurzerenone (40 mg) was heated under nitrogen at 250—270° for 6 h, and the product was chromatographed over silica gel. Elution with light petroleum and crystallization from light petroleum afforded pyrocurzerenone as needles (12 mg), m.p. 76.5—77.5°.

Pyrolysis of Curzerenone at 350°.—Curzerenone (300 mg) was heated under nitrogen at 350° for 30 min and the product was chromatographed over silica gel (5 g). Elution with light petroleum and crystallization from light petroleum gave furanocadalene (1,5,8-trimethylnaphtho[2,1-b]furan)

(17)* as plates (74 mg), m.p. 98—100°; λ_{\max} (EtOH) 223 (log ϵ 4.53), 248 (4.56), 301 (3.94), 313 (3.82), and 327 nm (3.53); ν_{\max} (KBr) 1621, 1597, 1518, 1102, 857, 813, 794, and 770 cm⁻¹ (naphthofuran) (Found: C, 86.05; H, 6.8. C₁₈H₁₄O requires C, 85.7; H, 6.7%).

Successive elution with the same solvent and crystallization from light petroleum afforded pyrocurzerenone (15) as prisms (25 mg), m.p. 76.5—77.5°.

Pyrolysis of Curzerenone at 240°.—Curzerenone (43 mg) was heated under nitrogen at 235—240° for 3 h to give a 3 : 1 mixture of curzerenone and epicurzerenone, identified by the n.m.r. spectrum.

Pyrolysis of Epicurzerenone at 240°.—Epicurzerenone (30 mg) was heated under nitrogen at 230—240° for 3 h to afford a 1 : 3 mixture of curzerenone and epicurzerenone.

Pyrolysis of Dihydrocurzerenone at 250°.—Dihydrocurzerenone (5) (40 mg) was heated under nitrogen at 230—250° for 4 h to yield a 4 : 1 mixture of dihydrocurzerenone (5) and dihydroepicurzerenone (6), identified by the n.m.r. spectrum.

Pyrolysis of Dihydroepicurzerenone at 250°.—Dihydroepicurzerenone (6) (40 mg) was heated under nitrogen at 230—250° for 4 h to give a 1 : 4 mixture of dihydrocurzerenone (5) and dihydroepicurzerenone (6).

Deuteration of a Mixture of Curzerenone and Epicurzerenone.—Deuterium exchange was effected by treating a 1 : 1 mixture of curzerenone and epicurzerenone (100 mg) with 2*N*-NaOD (0.5 ml) and dioxan (1 ml) at room temperature for 5 h. The solvent was distilled off under reduced pressure, and the same sequence was repeated four times. Addition of dilute HCl, extraction with ether, and distillation under diminished pressure furnished a 1 : 1 mixture* of [5-²H]-curzerenone and -epicurzerenone.

Pyrolysis of the Mixture of 5-Deuterio-curzerenone and -epicurzerenone.—The 1 : 1 mixture of 5-deuterio-curzerenone and -epicurzerenone (80 mg) was heated under nitrogen at 350° for 20 min. The product was chromatographed over AgNO₃-impregnated silica gel (10%; 10 g). Elution with light petroleum gave deuteriated pyrocurzerenone* (12 mg) followed by deuteriated furanocadalene* (25 mg).

Pyrolysis of Pyrocurzerenone at 350°.—Pyrocurzerenone (72 mg) was heated under nitrogen (38 mmHg) at 350° for 1 h in a sealed tube. The gas in the tube was analysed by mass spectrometry; m/e 28 (N₂) and 2 (H₂). The solid was chromatographed over AgNO₃-impregnated silica gel (10%; 10 g). Elution with light petroleum and crystallization from light petroleum furnished dihydropyrocurzerenone (16) as needles (2 mg), m.p. 71—73°, identical with the product of hydrogenation of pyrocurzerenone by t.l.c. and i.r. spectra.

Successive elution with the same solvent and crystallization from light petroleum afforded pyrocurzerenone as needles (18 mg), m.p. 76.5—77.5°. Further elution with the same solvent and crystallization from light petroleum gave furanocadalene as needles (40 mg), m.p. 98—100°.

We are grateful to Professor N. Tamiya, Tohoku University, for the determination of hydrogen. Thanks are also due to the Research Laboratory, Yoshitomi Pharmaceutical Co., Ltd., for mass spectra, to the Department of Chemistry, Tohoku University, for some of the n.m.r. spectra, and to the Analytical Laboratories, Pharmaceutical Institute, Tohoku University, for some of the n.m.r. spectra and elemental analyses.