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CYCLOHEXANE OXIDE DERIVATIVES FROM *KAEMPFERIA ANGUSTIFOLIA* AND *KAEMPFERIA* SPECIES

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Key Word Index—*Kaempferia angustifolia*, *Kaempferia* sp., Zingiberaceae, (−)-pipoxide, oxygenated cyclohexane, (+)-zeylenol.

Abstract—(−)-(3*S*,4*R*,5*S*,7*S*)-5-Benzoyloxymethyl-6-oxadicyclo-[4,1,0]hept-1-ene-3,4-diol 3-benzoate [(−)-pipoxide] and the two (+)-zeylenol related substances, (−)-(1*R*,2*S*,3*R*,4*S*)-2-benzoyloxymethylcyclohex-5-ene-1,2,3,4-tetrol 1,4-dibenzoate, and (1*R*,2*S*,3*R*,4*S*)-2-hydroxymethylcyclohex-5-ene-1,2,3,4-tetrol 1,4-dibenzoate, together with 2′-hydroxy-4,4′,6′-trimethoxychalcone, were isolated from the rhizomes of *Kaempferia angustifolia*, in addition to crotepoxide, boesenboxide and (+)-zeylenol The rhizomes of an unnamed *Kaempferia* species have also been found to contain the zeylenol derivatives

INTRODUCTION

Recently, we have reported the isolation and characterization of crotepoxide **1** [1] and the new substances, boesenboxide (**2**) and (+)-zeylenol (**3**) [2] from the rhizomes of *Kaempferia* sp (local name krachaikao). Further examination of the rhizomes of krachaikao has now yielded two additional new oxygenated cyclohexane derivatives, (−)-(1*R*,2*S*,3*R*,4*S*)-2-benzoyloxymethylcyclohex-5-ene-1,2,3,4-tetrol 1,4-dibenzoate (**11**)§ and (1*R*,2*S*,3*R*,4*S*)-2-hydroxymethylcyclohex-5-ene-1,2,3,4-tetrol 1,4-dibenzoate (**16**). *Kaempferia angustifolia* (local name: townanghang) was found to contain (−)-(3*S*,4*R*,5*S*,7*S*)-5-benzoyloxymethyl-6-oxadicyclo [4, 1, 0] hept-1-ene-3,4-diol 3-benzoate [(−)-pipoxide] (**5**), as well as compounds **11**, **16**, crotepoxide (**1**), boesenboxide (**2**), (+)-zeylenol (**3**) and 2′-hydroxy-4,4′,6′-trimethoxychalcone This paper is concerned with the identification of the structures of the three new oxygenated cyclohexane derivatives

RESULTS AND DISCUSSION

Pipoxide (**6**) has previously been found in *Piper hookeri* [3] and *Uvaria purpuria* [4], in the (+)-optical form ($[\alpha]_D^{23}$ +53°). Physical properties of compound **5**, especially the 400 MHz ^{1}H NMR data, are identical to those reported for (+)-pipoxide (**6**) with the exception of the optical rotation ($[\alpha]_D^{23}$ −54°)

Treatment of (+)-pipoxide with dilute sulphuric acid gave (−)-zeylenol (**4**) ($[\alpha]_D^{25}$ −107.5°), by opening of the epoxide ring, and similarly (−)-pipoxide gave (+)-zeylenol ($[\alpha]_D^{25}$ +121.6°). The products had identical physical properties apart from the optical rotations. It has been claimed [5] that treatment of (+)-pipoxide with 97% sulphuric acid in dichloromethane at −20° gave (−)-zeylenol (30%) and another product (50%) assigned the enantiomeric structure to **16** but no further details have been published.

Epoxidation of (−)-pipoxide gave the *trans*-diepoxide **7** ($[\alpha]_D^{25}$ +15°) and acetylation yielded the derivative **8** ($[\alpha]_D^{25}$ +57°). Compounds **7** and **8** are enantiomeric with the compounds we have already prepared from (+)-pipoxide [2] in a similar sequence of reactions, i.e. **9** ($[\alpha]_D^{25}$ −24°) and **10** ($[\alpha]_D^{25}$ −53°).

Compound **11**, $C_{28}H_{24}O_8$, $[\alpha]_D^{25}$ −59°, was identified as (+)-zeylenol monobenzoate from its spectroscopic properties. The ^{1}H NMR spectrum of **11** showed the presence of three benzoate groups (δ 7.04–8.03). In addition, an AB quartet at δ 4.67 and 5.05, a triplet at δ 4.38 and multiplets at δ 5.94, 5.69, 5.85 and 6.00 could be assigned through the coupling constants and by specific double irradiation experiments, to H_2-7, H-2, H-3, H-4, H-5 and H-6, respectively Compound **11** had similar ^{1}H NMR spectral data to those reported for (+)-zeylenol [2]. However, compound **11** contained three benzoate groups while (+)-zeylenol had only two. Benzoylation of (+)-zeylenol gave compound **11**.

Several other derivatives of **11** were prepared to provide further characterization, namely the mono- and diacetate derivatives **12** and **13**, and the benzoate **14** and dibenzoate **15** which were also obtained from the benzoylation of (+)-zeylenol. Benzoylation of (−)-zeylenol

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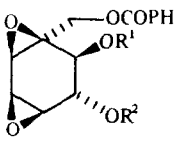
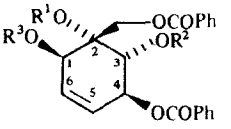
Part 12 in the series 'Constituents of the Zingiberaceae'; for Part 11 see ref [2]

The plant was previously described as *Boesenbergia* species [2], it is now identified as *Kaempferia* species by Miss Puanpen Sirirugsa, Department of Biology, Faculty of Science, Prince of Songkla University, Hat Yai, Thailand

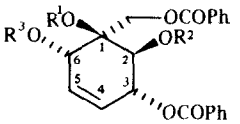
§Systematic numbering is shown in **3** and **5**, to retain consistency with the literature, the conventional cyclohexane numbering shown in **4** is used hereafter All structures show absolute stereochemistry



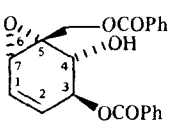
	R^1	R^2
1	Ac	Ac
2	Ac	COPh



	R^1	R^2	R^3
3	H	H	H
11	H	H	COPh
12	H	Ac	COPh
13	Ac	Ac	COPh
14	H	COPh	H
15	H	COPh	COPh



	R^1	R^2	R^3
4	H	H	H
19	H	H	COPh
20	H	COPh	H
21	H	COPh	COPh



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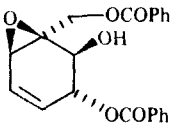

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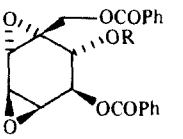

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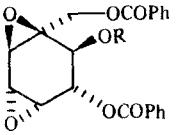
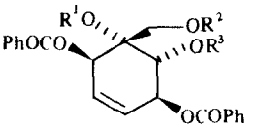
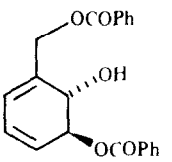
8 R = Ac



9 R = H
10 R = Ac



	R^1	R^2	R^3
16	H	H	H
17	H	Ac	Ac
18	Ac	Ac	Ac



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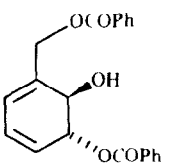

23

(**4**) gave the corresponding three enantiomers **19**, **20** and **21**. The physical properties of the enantiomeric pairs **11** and **19**, **14** and **20** and **15** and **21** are identical with the exception that their optical rotations are opposite in sign. ^{1}H NMR data of the derivatives **12**–**15** are shown in Table 1.

Compound **16** was an oil The ^{1}H NMR spectrum of **16** indicated the presence of two benzoate groups (δ7 47–8.10) An AB quartet at δ3.72 and 4 23 (J = 12 0 Hz), two doublets at δ4 23 (J = 7.5 Hz) and 5 40 (J = 4 3 Hz), two doublet of doublets at δ5 84 and 5.94 and a multiplet at δ5 99 were assigned to H_2-7, H-2, H-6, H-3, H-4 and H-5, respectively The AB quartet (δ3 72 and 4 23) for CH_2 was seen at higher field than that of (+)-zeylenol (δ4 72 and 4 87) Also the signal of H-6 in **16** appeared at δ5 40 while that of (+)-zeylenol was δ4.35 Therefore, it appeared that the two benzoate groups of **16** were attached to C-3 and C-6 Upon standing in solution at room temperature **16** transformed to (+)-zeylenol through ester interchange Acetylation of **16** gave the diacetate **17** and the triacetate **18** ^{1}H NMR spectral data for **16**–**18** are shown in Table 1.

The isolation of (−)-pipoxide (**5**) is significant since the substance was postulated [2] as an intermediate in the formation of (+)-zeylenol (**3**) That is, (−)-pipoxide (**5**) arises by epoxidation on the α-face of the diene **22**, whereas (+)-pipoxide (**6**), and thus (−)-zeylenol (**4**), crotepoxide (**1**), boesenboxide (**2**) etc., arise by epoxidation on the β-face of the enantiomeric diene **23** The latter process has to date been the most commonly observed one, the present results provide further examples of the former pathway, to give substances enantiomeric with those previously isolated. As before [2] one stereochemical pathway is not operating exclusively Recently (−)-pipoxide has been isolated from *Uvaria pandensis* (Annonaceae), along with (+)-pandoxide and (+)-senepoxide, providing a further example of these processes [7]

Table 1 ^{1}H NMR chemical shifts and coupling constants, (in Hz), for oxygenated cyclohexane derivatives

	5	7	8	11 (in C_6H_6)	12	13	14	15	16	17	18
H-2	4 33, *dd* (5.4, 8 1)	4.43, *d* (8 1)	5 97, *d* (8 4)	4 38, *t* (6.3)	5 86, *d* (7.3)	6 16, *d* (7 8)	5 99, *d* (5 0)	6 07, *d* (7 0)	4 23, *d* (7 5)	5 74, *d* (7.2)	6 05, *d* (8 0)
H-3	5 57, *ddd* (1 8, 2 7, 8 1)	5 51, *dd* (8.1, 1 2)	5 56, *dd* (8 4, 1 1)	5 94, *dddd* (6 3, 2 6, 1.7, 0.9)	5 95, *ddd* (7.3, 1 8, 1 0)	5 96, *dd* (7.8, 1 3)	6 14, *ddd* (5 0, 2 5, 1 5)	6.13, *ddd* (7 0, 2 5, 1 0)	5 84, *dd* (7 5, 2 0)	5.92, *dd* (7 2, 1.8)	5 91, *dddd* (8.0, 2 2, 1 8, 0 8)
H-4	5.92, *dt* (1 8, 9.9)	3 48, *ddd* (4.4, 1 2, 0 5)	3 59, *ddd* (4 4, 1.1, 0 5)	5 69, *ddd* (10 0, 2.6, 0.5)	6 082, *d* (1.8)	6 112, *d* (1.3)	5 97, *dd* (10.0, 2.5)	6.12, *dd* (10 0, 2 5)	5 94, *dd* (10 0, 2 0)	6 04, *dd* (10 0, 1 8)	6.09, *dd* (10 0, 2 2)
H-5	6 12, *ddd* (2.7, 3 9, 9 9)	3 62, *dd* (4.4, 2 5)	3 68, *dd* (4 4, 2 5)	5 85, *ddd* (10.0, 4 1, 1 7)	6.08, *dd* (3 5, 1.0)	6 11, *d* (2 3)	6.06, *ddd* (10.0, 4.0, 1 5)	6.15, *ddd* (10.0, 3 5, 1 0)	5 99, *ddd* (10 0, 4 3, 1.8)	6.11, *dd* (10.0, 2 4)	6 04, *ddd* (10.0, 4 3, 1 8)
H-6	3.65, *dd* (1 8, 3 9)	3 77, *dd* (2.5, 0.5)	3.82, *dd* (2 5, 0 5)	6.00, *ddd* (4 1, 0 9, 0.5)	5 78, *d* (3 5)	6 45, *d* (2.3)	4.42, *t* (4 0)	5 82, *d* (3 5)	5 40, *d* (4.3)	5.65, *dd* (2 4, 0 8)	6 41, *dd* (4.3, 0.8)
H-7A, B	4 48, *d*, 5.02, *d* (11 7)	4 33, *d*, 4 88, *d* (12.2)	4.26, *d*, 4 55, *d* (12 1)	4 67, *d*, 5 03, *d* (12 0)	4 52, *d*, 4.78, *d* (12 0)	4 90, *d*, 5.15, *d* (12 0)	4 61, *d*, 4.86, *d* (12.0)	4 63, *d*, 4.83, *d* (12.0)	3 72, *d*, 4.23, *d* (12.0)	4.37, *d*, 4 42, *d* (12.0)	4 72, *d*, 4 84, *d*, (12 0)
OAc	—	—	2 01, *s*	—	2.11, *s*	1.98, *s*, 2 16, *s*	—	—	—	1.98, *s*, 2 12, *s*	1 89, *s*, 2.05, *s*, 2 14 *s*
m-ArH	7 46, *m*	7 45, *m*	7 45, *m*, 7.47, *m*	7 04, *m*	7.40, *m*	7.30, *td*, 7 39, *td*, 7.44, *td* (8 0, 1.5)	7 34, *m*	7 33, *td*, 7 35, *td*, 7 41, *td*, 7.47, *td* (7 5, 1 5)	7.47, *m*	7.48, *m*	7.48, *m*
p-ArH	7 59, *m*	7 56, *m*	7 58, *m*, 7.60, *m*		7.57, *m*	7 50, *tt*, 7 54, *tt*, 7.57, *tt* (8 0, 1.5)	7 49, *m*	7.48, *tt*, 7 50, *tt*, 7.55, *tt*, 7 61, *tt* (7.5, 1 5)	7.66, *m*	7 61, *m*	7.61, *m*
o-ArH	8.05, *m*	8 03, *m*, 8 15, *m*	8 03, *m*	8 03, *m*	7 93, *dd*, 8.01, *dd*, 8 07, *dd* (8 0, 1.5)	7 95, *dt*, 8.00, *dt*, 8 05, *dt* (8.0, 1 5)	7.92, *m*, 8 02, *m*	7.86, *dt*, 7 96, *dt*, 8.06, *dt*, 8.11, *dt* (7 5, 1 5)	8.04, *m*, 8 10, *m*	8 06, *m*	8 09, *m*
OH	3 09, *d* (5.4)	3.4, *br*	—	3.30, *d* (6.3) 3.67, *s*	3 26, *s*	—	3.06, *d* (4.0) 3 23, *s*	—	3.02, *br*, 3.60, *br*, 3 70, *br*		

Circular dichroism studies

The presence of dibenzoate and/or allylic benzoate moieties in the series of compounds in hand offered the opportunity to study their interactions as coupled oscillators in circular dichroism and thus obtain information concerning absolute configuration We have already reported [2] that boesenboxide (**2**) shows a positive, split Cotton effect (λ_{ext} 235, 217 nm), as does the diepoxide **10** derived from (−)-pipoxide (λ_{ext} 236, 220 nm) As pointed out it would be difficult to predict *a priori* of the 1,3-dibenzoate substituents, but it is evidently such as to produce the *positive* split due to exciton coupling, and the results led to the absolute configuration shown, based on the known configuration [5] of (−)-pipoxide Consistent with these observations, the diepoxide **8** derived from (+)-pipoxide gives a negative, split Cotton effect, essentially the mirror image of that of **10**, thereby confirming the opposite absolute configuration of both this compound, and (+)-pipoxide

As previously reported (−)-zeylenol **4** exhibits an apparently plain, negative Cotton effect (λ_{ext} 232 nm) (and (+)-zeylenol a *positive* Cotton effect of similar shape)

These curves arise from the exciton chirality between the C-3 benzoate and Δ^4-double bond chromophores (allylic benzoate system) and lead to the assigned absolute configurations. In these cases it seems that there is negligible interaction between the C-3 and C-7 benzoate chromophores, as the curves would be expected to show more complex character from additive effects In contrast, we observe that (+)-pipoxide gives an apparently normal, positive, split Cotton effect (λ_{ext} 235, 211 nm) typical of the dibenzoate exciton coupling as observed in **2** and **9**. Apparently, the flattening of the cyclohexene ring caused by the 1,6-oxide ring suppresses the allylic benzoate coupling and favours the dibenzoate coupling. (−)-Pipoxide gives a mirror image, negative split Cotton effect, each curve has an extra extremum at 209 nm It is interesting to note that Schulte and Ganem [5] in their application of the exciton chirality method did not attempt to measure the CD spectrum of (+)-pipoxide, but instead studied transesterification products with the benzoate groups in 1,2- and 1,3-relationships, presumably in order to favour the dibenzoate chirality effect

EXPERIMENTAL

Unless otherwise stated, analyses were carried out by Scientific and Technological Research Equipment Center, Chulalongkorn University, Bangkok, Thailand UV ethanolic solns Optical rotations $CHCl_3$ solns Circular dichroism measurements MeOH solns TLC prep TLC were on silica gel PF254 Silica gel 70–230 mesh (Merck) or Lichroprep RP-18 25–40 μm (Merck) was used for CC

Extraction of Kaempferia *sp rhizomes* The milled rhizomes (2 kg) were extracted with $CHCl_3$ at room temp Removal of $CHCl_3$ *in vacuo* gave a dark brown oil (154 6 g) A portion (50 3 g) of the oil was chromatographed on a column of silica gel (1 3 kg) and gradiently eluted with hexane–EtOAc Successive fractions obtained were combined on the basis of their behaviour on TLC and evapd to give 18 fractions (10 7, 0 40, 3 82, 2 23, 0 95, 2 86, 4 60, 2 00, 1 33, 1 06, 1 46, 0 67, 2 46, 2 95, 0 80, 7 63, 0 23 and 0 89 g, respectively).

(−)-(1R,2S,3R,4S)-2-*Benzoyloxymethyl*-*cyclohex*-5-*ene*-1,2,3,4-*tetrol* 1,4-*dibenzoate* (**11**) Fraction 13 (2 46 g) was dissolved in MeOH Crude boesenboxide (**2**) (344 mg) was separated and collected by filtration The filtrate was evapd to give a residue which was chromatographed on prep TLC using hexane–EtOAc (4 1) to give **11** Compound **11** was obtained as a colourless solid (73 mg) which crystallized from Me_2CO–hexane as colourless needles, mp 138–138 5° (Found C, 68 9, H, 5 0 $C_{28}H_{24}O_8$ requires C, 68 9, H, 4 9%) $[\alpha]_D^{25}$ −59 7° (*c*, 0 39) $\nu_{max}^{CHCl_3}$ cm^{-1} 3450, 1720, 1601, 1260, 1110, 701 UV λ_{max}^{EtOH} nm (log ε) 282 (3 43), 274 (3 58), 230 (4 70)

(1R,2S,3R,4S)-2-*Hydroxymethyl*-*cyclohex*-5-*ene*-1,2,3,4-*tetrol* 1,4-*dibenzoate* (**16**) A portion of fraction 16 (1 1 g) was separated on prep TLC using benzene–EtOAc (4 1) as the mobile phase to give a mixture of (+)-zeylenol (**3**) and **16** as a pale yellow solid (600 mg) The mixture was purified on a column of silanized (RP-18) silica gel using MeOH–H_2O (4 1) as the eluant to give (+)-zeylenol (**3**) as a colourless solid (251 mg) and compound **16** as a gum (36 mg) Upon standing in soln at room temp, the triol **16** changed to (+)-zeylenol (**3**) to give a mixture of **16** and **3** Compound **16** was acetylated with Ac_2O-pyridine to yield the diacetate **17** and triacetate **18**

Synthesis of compound **11** To a soln of (+)-zeylenol (**3**) (104 mg) in dry CH_2Cl_2 (3 ml) and dry pyridine (0 5 ml), benzoyl chloride (0 03 ml) was added The mixture was stirred at 15° for 1 hr and poured into crushed ice and extracted with CH_2Cl_2 The organic layer was washed with 20% aq HCl and H_2O, dried over Na_2SO_4 and evapd to dryness The crude product obtained was purified by prep TLC using hexane-Me_2CO (3 1) as the mobile phase and the chromatograms were developed twice to give compounds **15**, **11** and **14**

Compound **15** was obtained as a colourless solid (53 mg) which was crystallized from MeOH as colourless needles, mp 170–172 (Found C, 70 5, H, 4 7 $C_{35}H_{28}O_9$ requires C, 70 9, H, 4 8%) $[\alpha]_D^{25}$ −43 6° (*c*, 0 21) $\nu_{max}^{CHCl_3}$ cm^{-1} 3450, 1720, 1601, 1262, 1105, 700 UV λ_{max}^{EtOH} nm (log ε) 282 (3 93), 275 (4 00), 227 (5 16)

Compound **11** (27 mg) crystallized from hexane–Me_2CO as colourless needles, mp 128 5–130 $[\alpha]_D^{25}$ −67 5° (*c*, 0 04) Its ^{1}H NMR, IR and UV spectra were identical with those of the natural product

Compound **14** was obtained as a colourless gum (26 mg) (Found C, 68 7, H, 5 0 $C_{28}H_{24}O_8$ requires C, 68 9, H, 4 9%) $[\alpha]_D^{25}$ +131 4 (*c*, 0 16) $\nu_{max}^{CHCl_3}$ cm^{-1} 3420, 1720, 1601, 1262, 1112, 700 UV λ_{max}^{EtOH} nm (log ε) 282 (3 16), 274 (3 26), 230 (4 37)

Benzoylation of (−)-*zeylenol* (**4**) (−)-Zeylenol (**4**) (107 mg) was benzoylated with benzoyl chloride (0 03 ml) and dry pyridine (0 5 ml) in dry CH_2Cl_2 (4 0 ml) at 15° for 1 hr After the usual work-up, the crude product obtained was separated on prep TLC using hexane-Me_2CO (3 1) as the mobile phase and the chromatograms were developed twice to give compounds **21**, **19** and **20**

Compound **21** was obtained as a colourless solid (58 mg) which was crystallized from MeOH as colourless needles, mp 171–172° (Found C, 71 3, H, 4 8 $C_{35}H_{28}O_9$ requires C, 70 9, H, 4 8%) $[\alpha]_D^{25}$ +54 6° (*c*, 0 15) Compound **19** was obtained as a colourless oil (29 mg) which was crystallized from hexane–Me_2CO as colourless needles, mp 134–136° (Found C, 68 9, H, 5 0 $C_{28}H_{24}O_8$ requires C, 68 9, H, 4 9%) $[\alpha]_D^{25}$ +48 8 (*c*, 0 17) Compound **20** was obtained as a colourless oil (28 mg) (Found C, 68 6, H, 5 0 $C_{28}H_{24}O_8$ requires C, 68 9, H, 4 9%) $[\alpha]_D^{25}$ −115 4 (*c*, 0 19) ^{1}H NMR, IR and UV spectra of **19**–**21** were identical to those of their enantiomers **11**, **14** and **15**, respectively, but their optical rotations were opposite in sign

Acetylation of compound **11**. Ac_2O (0 5 ml) was added to a soln of compound **11** (81 mg) in dry pyridine (2 ml) The mixture was stirred at room temp overnight and was worked-up as usual to give a pale yellow residue The residue was purified by prep TLC

with CH_2Cl_2–MeOH (49 1) to give the acetate **12** (45 mg) as a colourless oil, (Found C, 67 8, H, 5 3. $C_{30}H_{26}O_9$ requires C, 67 9; H, 4 9%). $[\alpha]_D^{25}$ −39.7° (*c*, 0.21) $\nu_{max}^{CHCl_3}$ cm^{-1} 3440, 1750, 1720, 1601, 1260, 1102, 701 UV λ_{max}^{EtOH} nm (log ε): 283 (3 07), 274 (3 18), 230 (4.29).

Ac_2O (0.5 ml) was added into a soln of compound **11** (85 mg) and 4-dimethylaminopyridine (22 mg) in dry pyridine (3 ml) The mixture was stirred at room temp. overnight. After the usual work-up, the crude product obtained was purified by prep TLC with CH_2Cl_2 to give the diacetate derivative **13** as a colourless solid (63 mg) which was crystallized from MeOH as colourless rhombics, mp 152–153°. (Found· C, 67.1, H, 5 0 $C_{32}H_{28}O_{10}$ requires C, 67 1, H, 4 9%). $[\alpha]_D^{25}$ −9 7° (*c*, 0 19) ν_{max}^{Nujol} cm^{-1} 1752, 1720, 1601, 1450, 1377, 1268, 1212, 1100, 710 UV λ_{max}^{EtOH} nm (log ε) 282 (3 54), 275 (3 62), 230 (4 70)

Acetylation of compound **16** To a soln of compound **16** (201 mg) in triethylamine (3 ml), Ac_2O (1 ml) was added and the mixture stirred at room temp for 3 days. After the usual work-up, the crude product obtained was purified on prep TLC using hexane–Me_2CO (3:1) as the mobile phase to give the triacetate **18** and the diacetate **17** Compound **18** was obtained as a pale yellow oil. (Found· C, 63 6, H, 5 2. $C_{27}H_{26}O_{10}$ requires C, 63 5, H, 5.1%). $[\alpha]_D^{25}$ +7 1° (*c*, 0 3) ν_{max}^{Nujol} cm^{-1} 1728, 1600, 1450, 1375, 1260, 1088, 710 UV λ_{max}^{EtOH} nm (log ε)· 283 (3 13), 275 (3 14), 231 (4 17) The diacetate **17** (211 mg) crystallized from MeOH as colourless needles, mp 174–175°, (Found C, 64.2, H, 5.1 $C_{25}H_{24}O_9$ requires C, 64 1, H, 5 2%) $[\alpha]_D^{25}$ −18 8° (*c*, 0.27) ν_{max}^{Nujol} cm^{-1} 3450, 1745, 1700, 1600, 1445, 1271, 1230, 1070, 708 UV λ_{max}^{EtOH} nm (log ε) 282 (2.26), 274 (2.32), 231 (3 57)

Extraction of Kaempferia angustifolia *rhizomes* The milled fresh rhizomes (7 0 kg) were extracted with $CHCl_3$ at room temp On removal of $CHCl_3$, a pale yellow solid (1.96 g) was collected by filtration. Evaporation of the filtrate gave a brown oil (45.8 g) A portion of the solid (0 3 g) chromatographed on prep. TLC with $CHCl_3$ gave (−)-pipoxide (**5**) as a colourless solid (0 1 g).

The brown oil (45 8 g) was chromatographed on a column of silica gel (1.3 kg) with gradient elution with hexane–EtOAc Successive fractions were combined on the basis of their TLC behaviour to give 2′-hydroxy-4,4′,6′-trimethoxychalcone (348 mg), boesenboxide (**2**) (2.8 g), compound **11** (1 1 g), crotepoxide (**1**) (3 4 g) and a mixture of (+)-zeylenol (**3**) and compound **16** (9 9 g)

The ^1H NMR, IR and UV spectra of the chalcone, compounds **1–3**, **5**, **11** and **16** are identical with those of the authentic specimens

(−)-*Pipoxide* (**5**). Compound **5** was crystallized from $CHCl_3$–hexane as colourless needles, mp 153–154° (Found: C, 67.8, H, 5.0 $C_{20}H_{18}O_6$ requires C, 67.8; H, 5 1%) $[\alpha]_D^{25}$ −54° (*c*, 0.26). ν_{max}^{KBr} cm^{-1}· 3440, 1720, 1680, 1600, 1278, 1265, 1122. UV λ_{max}^{EtOH} nm (log ε): 282 (3.20), 274 (3 35), 228 (4 51) CD λ_{ext} 235, 221, 209 nm, Δε −4 99, +2 83, −2 94. [(+)-pipoxide, CD· λ_{ext} 235, 221, 209 nm, Δε +4.81, −2 55, +2 40]

2′-*Hydroxy*-4,4′,6′-*trimethoxychalcone*. The chalcone derivative was purified by prep TLC with hexane–EtOAc (4 1) as the mobile phase and crystallized from MeOH as yellow rhombics, mp 115° (lit [6] 114–115°)

Boesenboxide (**2**). Compound **2** was purified by prep TLC using hexane–EtOAc (7·3) as the mobile phase and crystallized from MeOH as colourless needles, mp 171–172° $[\alpha]_D^{25}$ +35° (*c*, 0 14)

Crotepoxide (**1**). Compound **1** was crystallized from MeOH as colourless needles, mp 152–153° $[\alpha]_D^{25}$ +64° (*c*, 1 7).

Compound **11**. Compound **11** (1 1 g) was separated on prep TLC using benzene–EtOAc (9 1) as the developing solvent and the chromatograms were developed × 4 to give compound **11** as a colourless solid (0.5 g) which was crystallized from Me_2CO–hexane as colourless needles, mp 138–138.5°. $[\alpha]_D^{25}$ −59 7° (*c*, 0.39)

(+)-*Zeylenol* (**3**) *and compound* **16**. A portion of the mixture of **3** and **16** (508 mg) was separated on a column of reverse phase RP-18 silica gel with MeOH–H_2O (8.2) as the mobile phase to give (+)-zeylenol **3** as a colourless solid (241 mg) and **16** as a colourless oil (30 mg)

(+)-Zeylenol (**3**) was crystallized from EtOAc as colourless needles, mp 130–131° $[\alpha]_D^{25}$ +113 5° (*c*, 0 24) Compound **16** was isolated as a colourless oil Compound **16** changed to (+)-zeylenol (**3**) readily, **16** was therefore acetylated with Ac_2O–pyridine to yield the acetate derivatives **17** and **18** as described above

Preparation of (+)-*zeylenol* **3** *from* (−)-*pipoxide* (**5**). A mixture of (−)-pipoxide (**5**) (54 mg), dioxane (10 ml) and 2 M H_2SO_4 (1 ml) was stirred at room temp for 2 hr The soln was poured into cold H_2O, and extracted with $CHCl_3$ The organic layer was washed with H_2O, dried over Na_2SO_4 and evapd to dryness. The residue obtained was purified by prep. TLC with $CHCl_3$–MeOH (19·1) to give **3**, colourless needles from MeOH–H_2O, mp 125–126° $[\alpha]_D^{25}$ +121 6° (*c*, 0 05) The ^1H NMR, IR and UV spectra are identical with those of the natural (+)-zeylenol [2].

Preparation of (−)-*zeylenol* **4** *from* (+)-*pipoxide* (**6**). Compound **4** was prepared by the procedure used for **3** except (+)-pipoxide (**6**) (63 mg) was used instead of (−)-pipoxide (**5**) After the work-up and purification, **4** was obtained as colourless needles from MeOH–H_2O, mp 131–132° $[\alpha]_D^{25}$ −107 5° (*c*, 0.12). ^1H NMR, IR and UV spectra were identical with those of natural (−)-zeylenol

Synthesis of (+)-(1R,2S,4S,5R,6R,7R)-4-*benzoyloxymethyl*-3,8-*dioxatricyclo*[5,1,0,$0^{2,4}$]*octane*-5,6-*diol* 6-*benzoate* (**7**) A mixture of (−)-pipoxide (**5**) (67 mg) and *m*-CPBA (38 mg) in CH_2Cl_2 (5 ml) was refluxed under N_2 for 6 hr. The mixture was evaporated to dryness and the residue obtained was purified by prep TLC with hexane–Me_2CO (2.1) to give compound **7** as a colourless oil (75 mg) $[\alpha]_D^{25}$ +15° (*c*, 0 15)

Synthesis of (+)-(1R,2S,4S,5R,6R,7R)-4-*benzoyloxymethyl*-3,8-*dioxatricyclo*[5,1,0,$0^{2,4}$]*octane*-5,6-*diol* 5-*acetate* 6-*benzoate* (**8**). Compound **7** (53 mg) was treated with Ac_2O (0.5 ml) and pyridine (2 ml) at room temp overnight. After the usual work-up, the residue obtained was purified by prep TLC to give the acetate **8** (25 mg) crystallized from MeOH as colourless needles, mp 109–110° (Found C, 65.3, H, 4 7 $C_{23}H_{20}O_8$ requires C, 65.1, H, 4 8%) $[\alpha]_D^{25}$ +57° (*c*, 0.34). CD. λ_{ext} 236, 219 nm, Δε −5 15, +2.61 ^1H NMR, IR and UV spectra of compounds **7** and **8** were identical with those of their enantiomers **9** and **10**, respectively [2]

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