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OPTICAL RESOLUTION OF (±)-DEHYDRODIISOEUGENOL: STRUCTURE REVISION OF ACUMINATIN

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Key Word Index—*Magnolia kachirachirai*; Magnoliaceae; dehydrodi-isoeugenol; acuminatin; resolution; ^{13}C NMR.

Abstract—The lignan, acuminatin, whose structure was previously reported as **3**, was found to be identical with the methyl ether of (+)-dehydrodi-isoeugenol, and therefore its structure must now be revised to (+)-**2**.

INTRODUCTION

In the course of our investigation of the lignans [1] of the leaves of *Magnolia kachirachirai*, (±)-dehydrodi-isoeugenol [(±)-**1**] and its methyl ether (±)-**2** were prepared and their spectral data compared with those of related compounds. Unexpectedly, the ^1H NMR and IR spectra of (±)-**2** were found to be identical to those of (+)-acuminatin for which structure **3** has been assigned [2]. We hereby report on the revision of the structure of acuminatin to (+)-**2**.

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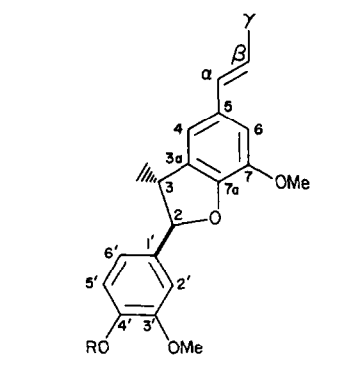
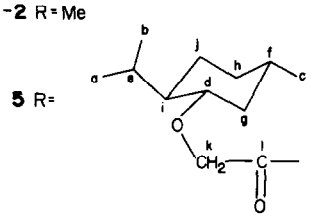
RESULTS AND DISCUSSION

Direct comparison between (+)-acuminatin and (±)-**2** was not possible because of the unavailability of a reference sample. Furthermore, (±)-**2** was found to have a higher mp than that reported for (+)-acuminatin [122–123° vs 77.5°]. Consequently, additional supporting evidence was sought to confirm the revised structure (+)-**2** for acuminatin.



(+)-**1** R = H
(+)-**2** R = Me



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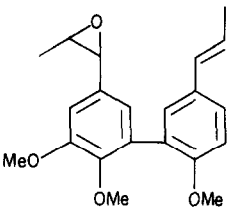

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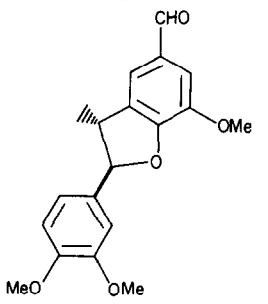

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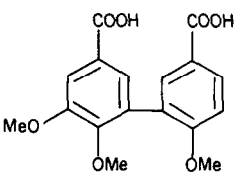

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Table 1. ^{13}C NMR shifts of (+)-acuminatin (2) and related compounds

Carbons	2	4	5†
2	93.6	94.9	93.0
3	45.7	45.0	45.1
3a	133.1*	131.8	133.3*
4	113.6	119.9	113.6
5	135.5*	133.9*	133.3*
6	110.1	112.4	110.2
7	144.3	145.2	144.3
7a	146.9	153.5	146.7
3-Me	17.8	18.0	18.2
OMe	56.0 and 56.1	56.2	56.0 and 56.2
1′	132.4*	132.1*	132.6*
2′	110.0	110.0	110.6
3′	149.5	149.7	151.4
4′	149.5	149.9	139.6
5′	111.5	111.6	122.7
6′	119.2	119.4	118.6
α	131.2	190.4	131.1
β	123.3	—	123.5
γ	18.3	—	18.2

*Assignments bearing the same symbol in the same column may be interchangeable.

†In addition to the signals listed in this column, the ^{13}C NMR spectrum showed 12 additional signals due to the menthoxyacetyl moiety at δ 20.9(a), 16.4(b), 22.3(c), 80.7(d), 25.6(e), 31.6(f), 40.2(g), 34.6(h), 48.4(i), 23.6(j), 65.8(k) and 169.0(l). These assignments were made by comparison with those reported [4] for menthol.

Thus, (+)-2 was oxidized to the aldehyde (+)-4 whose ^1H NMR, IR and mass spectra were identical to those of (+)-4 obtained from acuminatin. In addition, the ^{13}C NMR spectra of (±)-2 and (±)-4 (Table 1) did not fit their reported structures.

An unambiguous evidence for the new structure for acuminatin was obtained when (±)-1 was resolved by esterification with (−)-menthoxyacetic acid. The mixture of diastereomeric esters yielded, upon fractional crystallization from methanol, pure (−)-menthoxyacetyl-(+)-1 (5).* Hydrolysis of the latter, provided (+)-1 [(+)-licarin-A], which upon methylation with dimethylsulfate yielded a product identical in all aspects with (+)-acuminatin. Therefore, the structure of (+)-acuminatin should now be revised from 3 to (+)-2.

It is interesting to note that the oxidation of (±)-2 to the aldehyde (±)-4 proceeded in much greater yield than the similar transformation reported [2] for (+)-acuminatin. In addition we found no trace of a dicarboxylic acid by-product with the reported structure of 6, on which the synthesis of the original structure of (+)-acuminatin was based. Thus it appears that the key degradation product 6 may have been produced from an improperly purified sample of (+)-acuminatin.

Besides (+)-acuminatin, there have been two other reports of the natural occurrence of the methyl ethers of dehydrodi-isoeugenol. One such report [5] described the occurrence in an *Aniba* species of an oily compound with spectral properties identical to those of (+)-acuminatin. The second report [6] described a similar compound from *Virola carinata* but unfortunately its stereochemistry was not defined.

EXPERIMENTAL

Mps are uncorr. IR spectra were measured in KBr discs or as an 8% soln in $CHCl_3$ and UV spectra in MeOH. ^1H NMR spectra were recorded at 60 MHz using $CDCl_3$ as solvent and TMS as int. standard; chemical shifts are reported in δ (ppm) units. ^{13}C NMR spectra were measured at 15.03 MHz with chemical shifts also reported in δ (ppm) units.

(±)-Dehydrodi-isoeugenol (racemic licarin-A) [(±)-1]. The material used in this study was initially isolated [1] from the leaves of *M. kachirachirai*, but later on it was more conveniently obtained by $FeCl_3$ oxidation of isoeugenol as previously reported [7].

Menthoxyacetylation of (±)-dehydrodi-isoeugenol [(±)-1]. (±)-Dehydrodi-isoeugenol (3 g), (−)-menthoxyacetic acid (2.166 g), dicyclohexylcarbodiimide (2.08 g) and pyrrolidinopyridine [8] (0.136 g) were stirred under N_2 in C_6H_6 soln for 4 hr, filtered and evaporated at red. pres. Repeated crystallization of the residue (4.85 g) from MeOH gave 633 mg 5, mp 87–88°; $[\alpha]-21°$ ($CHCl_3$; *c* 0.24); IR $\nu_{max}^{CHCl_3}$ exhibited a C=O band at 1777 cm^{-1}; ^1H NMR ($CDCl_3$) same pattern as (±)-1 with additional signals at δ 0.88 (9 H, *m*, 3 Me) and δ 4.40 (2 H, *s*, $-CH_2-\overset{\overset{O}{\|}}{C}-$); ^{13}C NMR spectrum Table 1; MS *m/z*: 522 $[M]^+$ (65%) (Found: C, 73.51; H, 8.33. $C_{32}H_{42}O_6$ (522) requires: C, 73.52; H, 8.10%.)

Hydrolysis of (−)-menthoxyacetyldehydrodi-isoeugenol (5) to (+)-1. Diastereoisomer 5 (623 mg) was stirred with 18 ml dioxane and 6 ml 2.5 N NaOH for 3 hr. Usual work-up provided 372 mg residue that crystallized from hexane to give 147 mg needles of (+)-licarin-A [(+)-1]; mp 118–119°; $[\alpha]_D+66°$ ($CHCl_3$; *c* 0.37) [lit. values for (−)-licarin-A† are 114–116° and 59° respectively]; CD (MeOH; *c* 0.0015): $[\theta]_{273}+9128$ and $[\theta]_{233}-5868$; the IR ($CHCl_3$), ^1H NMR ($CDCl_3$) and MS were indistinguishable from those of (±)-1.

Methylation of (±)-dehydrodi-isoeugenol [(±)-1] and (+)-licarin-A [(+)-1]. (±)-Dehydrodi-isoeugenol (1 g) was dissolved in 50 ml 95% EtOH and the soln stirred with 10 ml $MeSO_4$ in alkaline medium (4 N NaOH) for 2 hr. After usual work-up 1.2 g oily residue was crystallized from *iso*-propyl ether to give colourless needles (1.1 g), mp 122–123° (lit. [9] mp 125°), and with IR and ^1H NMR spectra indistinguishable from those of (+)-acuminatin isolated [2] from *M. acuminata*. The assignments of the carbon signals of the ^{13}C NMR spectrum (Table 1) were accomplished by comparison with the reported [10] values for (−)-licarin-A and by studying the coupled spectra as well as PND, SFORD and LSPD [11] spectra; MS *m/z*: 326 $[M]^+$ (100%) (Found: C, 73.59; H, 6.80. $C_{20}H_{22}O_4$ (522) requires: C, 73.71; H, 6.93%).

(+)-Licarin-A [(+)-1] (150 mg) obtained from the hydrolysis of 5 was similarly methylated to give 113 mg of oil that crystallized from *iso*-propyl ether to give needles, mp 75–

*This compound can be also named (−)-menthoxyacetyl-(+)-licarin-A as the name licarin-A is used to describe naturally occurring pure optical antipodes of (±)-dehydrodi-isoeugenol [3].

†(−)-Licarin-A is the only optical antipode described in the lit. [3]. The (+)-antipode hitherto, has not been obtained in an optically pure form.

76°; $[\alpha]_D + 44°$ (MeOH; *c* 0.3). Lit. values [2] for (+)-acuminatin are 77.5° and 43.3° respectively. The ^1H NMR, IR, ^{13}C NMR and MS were identical to those of the racemic material obtained above.

Oxidation of (±)-*acuminatin* [(±)-**2**] *to the aldehyde* (±)-**4**. (±)-Acuminatin (372 mg) was oxidized with $KMnO_4$–$NaIO_4$ as previously reported [2] to give 249 mg crystalline residue that yielded pure (±)-**4** upon crystallization from Et_2O, mp 119–120°; IR $\nu_{max}^{CHCl_3}$: 1678 cm^{-1} (CHO); ^1H NMR ($CDCl_3$): δ 1.46 (3 H, *d*, $J = 7.2$ Hz, Me-3), δ 3.60 (1 H, *m*, H-3), δ 3.96 (3 H, *s*, –OMe), δ 3.89 (6 H, *s*, 2-OMe), δ 5.28 (1 H, *d*, $J = 9.6$ Hz, C_2-H), δ 6.91–7.38 (5 H, aromatic Hs) and δ 9.86 (1 H, *s*, –CHO); ^{13}C NMR ($CDCl_3$) signals see Table 1; MS: *m/z* 328 (100%) $[M]^+$. (Found: C, 69.50; H, 6.14. $C_{19}H_{20}O_5$ (328) requires: C, 69.47; H, 6.32%.)

The Na_2CO_3 soln after removal of aldehyde **4** was analysed for the dimethyl ester of **6** as previously reported [2], but there was no trace of such a compound.

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