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A BIPHENYL TYPE NEOLIGNAN AND A BIPHENYL ETHER FROM *MAGNOLIA HENRYI*

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Abstract—A new biphenyl type neolignan 5,5′-diallyl-2,2′-dihydroxy-3-methoxybiphenyl and a new related ether 4′,5-diallyl-2-hydroxy-3-methoxybiphenyl ether were isolated from the bark of *Magnolia henryi* in addition to magnolol (5,5′-diallyl-2,2′-dihydroxybiphenyl)

INTRODUCTION

Magnolia species characteristically produce isoquinoline and related alkaloids [1, 2], lignans and neolignans [1–13] and occasionally sesquiterpene lactones and other sesquiterpenes [1, 12, 14–20] We now report isolation of the biphenyl type neolignans magnolol (**1a**) [1, 2, 12] and 5,5′-diallyl-2,2′-dihydroxy-3-methoxybiphenyl (**1c**) from the trunk bark of *Magnolia henryi* Dunn, a species which has not been examined previously Compound **1c** is new The new closely related 4′,5-diallyl-2-hydroxy-3-methoxybiphenyl ether (**2a**) was also found

RESULTS AND DISCUSSION

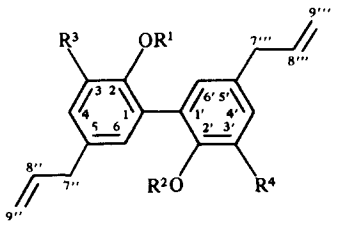
The molecular formula $C_{19}H_{20}O_3$ from the MS of **1c** and its ^{1}H NMR spectrum (see Experimental section) indicated the presence of one methoxyl in addition to the two phenolic hydroxyls and the two allyl radicals present in magnolol (**1a**) and its isomer honokiol (**3**) [2, 3, 12] Of the five aromatic protons, two on ring A were *m*-coupled and the remaining three on ring B were in a 1,2,4 relationship The reasonable assumption that the new *bis*-allylphenyl derivative, like magnolol, acuminatin [4], dehydrodieugenol (**1e**) [21, 22] and its monomethyl ether **1f** [22], was formed by *o,o*-coupling of eugenol, chavicol or, as in the case of honokiol, by *o,p*-coupling of a chavicol or eugenol derivative reduced the number of possible isomers considerably In fact the ^{1}H and ^{13}C NMR signals emanating from the 1,2,4-trisubstituted ring B portion of the molecule corresponded in all respects to the ^{1}H and ^{13}C NMR spectrum of magnolol (see Experimental section and Table 1), thus leading to formula **1c** where only the location of the methoxy group on C-2 or C-3 remained to be fixed Further confirmation for this conclusion was found by comparing the ^{13}C NMR spectrum of **1c** with the ^{13}C NMR spectrum of **3b** which has recently been obtained by synthesis [23]

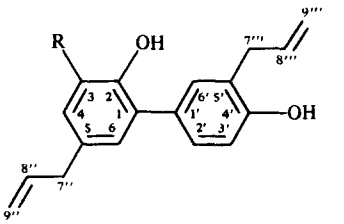
That the methoxyl was attached to C-3 of ring A became clear on comparing the ^{1}H NMR spectra of **1c** and its diacetate **1d**. The only significant paramagnetic shifts which duplicated those observed in the conversion of magnolol **1a** to its diacetate **1b** (see Experimental section) were associated with H-3′ and H-4′ of ring B, hence the hydroxyl of ring A was on C-2 This conclusion emerges as well from a comparison of the ^{1}H and ^{13}C NMR spectra of **1c** with those of synthetic **3b** [23] (see Table 1)

The second new substance from *M henryi* was an isomer of **1c** Like its companion it contained two allyl residues and one methoxyl group but had only one phenolic hydroxyl as evidenced by formation of a monoacetate The ^{1}H NMR spectrum established the presence of one *p*-disubstituted and one 1,2,4,5-tetra-substituted aromatic ring Biogenetic considerations based on alternate coupling modes of chavicol radical A with eugenol then led to **2a** as a plausible structure for the new biphenyl ether Placement of the methoxyl on C-3 was further supported by the absence of paramagnetic shifts in the signals of the aromatic protons on conversion of **2a** to be acetate **2b**

Biphenyl ether **2a** is a methyl ether of obovatol (**2c**) which accompanies magnolol in *Magnolia obovata* [2] and in *M watsonii* [12] A similar ether, isomagnolol (**2d**), accompanies magnolol in *Sassafras randaiense* [24] while ether **2e** is a congener of dehydrodieugenol **1e** and its monomethyl ether **1f** in *Ocotea corymbosa* [22]

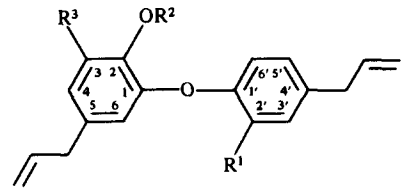
A





1a R^1, R^2, R^3, R^4 = H
1b R^1, R^2 = Ac, R^3, R^4 = H
1c R^1, R^2 = H, R^3 = OMe, R^4 = H
1d R^1, R^2 = Ac, R^3 = OMe, R^4 = H
1e R^1, R^2 = H, R^3, R^4 = OMe
1f R^1 = Me, R^2 = H, R^3, R^4 = OMe

3a R = H
3b R = OMe



2a R^1 = H, R^2 = H, R^3 = OMe
2b R^1 = H, R^2 = Ac, R^3 = OMe
2c R^1 = H, R^2 = H, R^3 = OH
2d R^1, R^2, R^3 = H
2e R^1, R^3 = OMe, R^2 = H

Table 1. ^{13}C NMR spectra of compounds **1a** and **1c**

C	1a*	1c†	3b‡
1		125 29 *s*	127 22 *s*
1′	124 5 *s*	124 22 *s*	130 39 *s*
2′		140 05 *s*	140 84 *s*
2′	151 0 *s*	151.84 *s*	128 58 *d*
3		146 63 *s*	146.78 *s*
3′	116.8 *d*	117 64 *d*	115 60 *d*
4		110 51 *d*	109 79 *s*
4′	129 8 *d*	129 38 *s*	153 29 *s*
5		132 46 *s*	133 33 *s*
5′	133 3 *s*	132 80 *s*	125 23 *s*
6		123 52 *d*	122 35 *s*
6′	131 4 *d*	130 91 *d*	131.10 *d*
7″		39 58 *t*	39 98 *t*
7‴	39 4 *t*	39 98 *t*	35 44 *t*
8″		137 38 *d*	137 73 *d*
8‴	137 6 *d*	137.79 *d*	136 44 *d*
9″		115 63 *t*	115 60 *t*
9‴	115 8 *t*	115.82 *t*	116 36 *t*
OMe		56 16 q	56.19 q

*Taken from ref [2]
†Run at 67.89 MHz in $CDCl_3$.
‡Taken from ref [23]

EXPERIMENTAL

Isolation of M henryi *constituents* Ground trunk bark of *Magnolia henryi* Dunn (8 kg), collected in Karnchanabory Province, Thailand, in January 1987, was thoroughly extracted with MeOH. Evaporation of the MeOH gave a residue (452 g) which was stirred with $CHCl_3$ and filtered Evaporation of the $CHCl_3$ extract furnished 15 g of residue which was chromatographed over silica gel ($CHCl_3$–hexane 4.1, 200 ml fractions). Frs 1 and 2 gave non-polar material which was not examined further Frs 3 and 4 were combined and evapd, purification of the residue by TLC (Silica gel, $CHCl_3$–hexane 9 1) furnished 60 mg of **2a**. Frs 5–7 were combined and evaporated Purification of the residue (0.50 g) by TLC (silica gel, $CHCl_3$–Me_2CO 24 1) gave 0.35 g of **1c** as a reddish gum. Fractions 8–15 were combined. Purification of the residue by TLC (silica gel, $CHCl_3$–hexane 9 1) gave 0 78 g of **1a** whose physical constants (see below) corresponded to those in the literature [2]

5,5′-Diallyl-2,2′-dihydroxy-3-methoxybiphenyl (**1c**) Gum, MS(*m/z*, rel int): 296 $[M]^+$ (100), 267 (13), 223 (16), 214 (11), 149 (12), 134 (11), IR ν_{max} cm^{-1} 3600–3300 (OH), 3080, 3010, 2980, 2940, 1640 (C=C), 1600, 1520, 1500, 1480, 1430, 1380, 1280, 1230, 1110, 1060, 1000, 930, ^1H NMR (270 MHz, $CDCl_3$): δ3 38 (*d*, *J* = 7 Hz, $2CH_2$), 3 92 (*s*, –OMe), *m*, 4H, –CH=CH_2), 5 88–6.08 (*m*, 2H, CH=CH_2), 6 74 and 6 77 (both *d*, *J* = 2 Hz, H-4 and H-6), 6 98 (*d*, *J* = 8.6 Hz, H-3′), 7 10 (*d*, *J* = 2 Hz, H-6′), 7 12 (*dd*, *J* = 8.6, 2 Hz, H-4′)

Acetylation of 30 mg of **1c** with 3 ml Ac_2O and 0.4 ml pyridine at room temp for 15 hr followed by the usual work-up and purification by TLC (silica gel, $CHCl_3$–hexane 1:1) gave 28 mg of the diacetate **1d**, gum, MS (*m/z*, rel. int.) 380 $[M]^+$ (3), 338 (45), 296 (100), 239 (9), 223 (10), 165 (9), 149 (8), 115 (5), 91 (5), IR ν_{max} cm^{-1} 3040, 3010, 2970, 2840, 1760 (C=O), 1640 (C=C), 1600, 1500, 1470, 1430, 1380, 1350, 1280, 1200, 1150, 1120, 1000, 920, ^1H NMR (270 MHz, $CDCl_3$) δ 2.05 (*s*, OAc), 2.07 (*s*, -OAc), 3.39 (*d*, $J = 7$ Hz, 2-CH_2-), 3.83 (*s*, -OMe), 5.15 (*m*, 4H, -CH=CH_2), 5.92 (*m*, 2H, -CH=CH_2), 6.70 and 6.80 (both *d*, $J = 2$ Hz, H-4 and H-6), 7.07 (*d*, $J = 8.6$ Hz, H-3'), 7.10 (*d*, $J = 2$ Hz, H-6'), 7.19 (*dd*, $J = 8.6$, 2 Hz, H-4').

4'5-Diallyl-2-hydroxy-3-methoxybiphenyl ether (**2a**) Gum, MS (*m/z*, rel. int.) 296 $[M]^+$ (100), 240 (3), 131 (6), 117 (13), 91 (7), IR ν_{max} cm^{-1} 3500–3400 (-OH), 3080, 3010, 2920, 2830, 1640 (C=C), 1600, 1510, 1460, 1440, 1320, 1230, 1090, 920. ^1H NMR (270 MHz, $CDCl_3$) δ 3.01 (*d*, $J = 7$ Hz, -CH_2-), 3.10 (*d*, $J = 7$ Hz, -CH_2-), 3.71 (*s*, -OMe), 5.06 (*m*, 4H, -CH=CH_2), 5.92 (*m*, 2H, -CH=CH_2), 6.43 and 6.53 (both *s*, H-4 and H-6), 6.90 (*d*, $J = 8.6$ Hz, H-3'5'), 7.10 (*d*, $J = 8.6$ Hz, H-2', 6')

Acetylation of 20 mg of **2a** in the manner described for **2a** and purification by TLC (silica gel, $CHCl_3$–hexane 1:1) gave 15 mg of the monoacetate **2b** as a gum, MS (*m/z*, rel. int.) 338 $[M]^+$ (9), 296 (100), 254 (8), 117 (14), 91 (10), IR ν_{max} cm^{-1} 3090, 3020, 2950, 1730 (C=O), 1640 (C=C), 1600, 1500, 1480, 1430, 1370, 1290, 1240, 1190, 1100, ^1H NMR (270 MHz, $CDCl_3$) δ 2.88 (*s*, OAc) 3.29 (*d*, $J = 7$ Hz, -CH_2-), 3.35 (*d*, $J = 7$ Hz, -CH_2-), 5.08 (*m*, 4H, -CH=CH_2), 5.93 (*m*, 2H, -CH=CH_2), 6.41 and 6.55 (both *d*, $J = 1.7$ Hz, H-4 and H-6), 6.92 (*d*, $J = 8.6$ Hz, H-3', 5'), 7.11 (*d*, $J = 8.6$ Hz, H-2', 6')

Magnolol (*5,5'-diallyl-2,2'-dihydroxybiphenyl* (**1a**) Mp 100–102°, MS (*m/z*, rel. int.) 266 $[M]^+$ (100), 247 (9), 237 (31), 206 (19), 197 (34), 184 (31), 178 (11), 165 (13), 152 (11), 128 (9), 105 (5), ^1H NMR (270 MHz, $CDCl_3$) δ 3.37 (*d*, $J = 7$ Hz, H-1''), 5.07 (*dd*, $J = 10.2$ Hz, H-3''a), 5.10 (*dd*, $J = 16.2$, H-3''b), 5.98 (*m*, $J = 16.10$, 7 Hz, H-2''), 6.95 (*d*, $J = 8.6$ Hz, H-3), 7.08 (*d*, $J = 2$ Hz, H-6), 7.14 (*dd*, $J = 8.6$, 2 Hz, H-4)

Acetylation of 43 mg of **1a** in the usual manner and purification of the crude product by TLC gave 25 mg of the diacetate as a gum, ^1H NMR (270 MHz, $CDCl_3$) δ 2.05 (*s*, 2 Ac), 3.41 (*d*, $J = 7$ Hz, H-1''), 5.11 (*m*, H-3''a, b), 5.98 (*m*, H-2''), 7.07 (*d*, $J = 8$ Hz, H-3), 7.12 (*d*, $J = 2$ Hz, H-6), 7.21 (*dd*, $J = 8$, 2 Hz, H-4)

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