Phytochemistry, Vol 23, No 11, pp 2643–2645, 1984
Printed in Great Britain

0031–9422/84 $3 00 + 0 00

NEOLIGNANS FROM *MAGNOLIA KACHIRACHIRAI*

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(*Received* 20 *February* 1984)

Key Word Index—*Magnolia kachirachirai*, Magnoliaceae, neolignan, benzofuranoid, kachirachirol-A, kachirachirol-B, licarin-A, eupomatenoid

Abstract—Two new neolignans named kachirachirol-A and B were isolated from the leaves of *Magnolia kachirachirai* and their chemical structures determined to be 2-(*p*-hydroxyphenyl)-7-methoxy-3-methyl-5-*trans*-propenylbenzofuran and *rel*-(2*S*,3*S*)-2-catechyl-2,3-dihydro-7-methoxy-3-methyl-5-*trans*-propenylbenzofuran

INTRODUCTION

Previously, Li and El-Feraly [1] reported the isolation of three benzofuranoid neolignans eupomatenoid-7 (**2**), (±)-licarin-B (**4**) and (±)-licarin-A (**5**) and a tetrahydrofuranoid lignan (+)-galbacin (**9**) from the leaves of *Magnolia kachirachirai* (Chinese name Heng-chun mulan), the indigeneous magnoliaceous plant in Taiwan In the course of the reinvestigation of the dried leaves of this plant, eight neolignans (**1**–**8**) were isolated, two of them (**3** and **7**) were new compounds We now report on the structure elucidation of these new neolignans named kachirachirol-A and B

RESULTS AND DISCUSSION

The first compound kachirachirol-A (**3**), $C_{19}H_{18}O_3$, ($[M]^+$ *m/z* 294), colourless prisms, gave a bluish colour with ferric chloride–ethanol The IR spectrum ($CHCl_3$) showed the presence of a hydroxyl at 3530 cm^{-1} and phenyl groups at 1605, 1510 cm^{-1} The ^1H NMR spectrum showed the following signals δ1 91 (3H, *d*, *J* = 6 Hz, =CH–C<u>H</u>$_3$), 2 40 (3H, *s*, =C(Ar)–CH$_3$), 3 98 (3H, *s*, Ar–OMe), 5 74 (1H, *s*, OH), 6 19 (1H, *dq*, *J* = 6, 16 Hz, –CH=C<u>H</u>–CH$_3$), 6 53 (1H, *d*, *J* = 16 Hz, Ar–C<u>H</u>=CH–), 6 98 (2H, *d*, *J* = 9 Hz, Ar–H), 7 30, 7 32 (2H, each *d*, *J* = 1 5 Hz, Ar–H) and 7 37 (2H, *d*, *J* = 9 Hz, Ar–H) The spin–spin coupling constants (*J* = 9 Hz and *J* = 1 5 Hz) in the aromatic region were due to *meta* (δ7 30 and 7 32) and *ortho* (δ6 98 and 7 37) coupling These spectral data of **3** are very similar to those reported for eupomatenoid-1 (**1**) [2, 3] except for the aromatic region in the ^1H NMR spectrum On acetylation with acetic anhydride in pyridine, **3** gave a monoacetyl derivative These results suggested that the structure of **3** must be 2-(*p*-hydroxyphenyl)-7-methoxy-3-methyl-5-*trans*-propenylbenzofuran

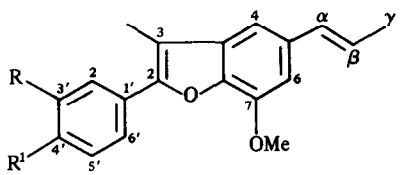
The second substance kachirachirol-B (**7**), $C_{19}H_{20}O_4$ ($[M]^+$ *m/z* 312), colorless needles, gave a bluish color with ferric chloride–ethanol and a brown color with titanium trichloride in methanol–pyridine [4] These color tests suggest that **7** possesses a catecholic character The IR spectrum ($CHCl_3$) of **7** showed the presence of a hydroxyl at 3550 cm^{-1} and phenyl groups at 1610, 1520 and 1495 cm^{-1} The UV spectrum (MeOH) showed absorption at λ_{max} 268 and 272 nm indicating the presence of a conjugated benzenoid system The ^1H NMR spectrum showed the following signals δ1 34 (3H, *d*, *J* = 7 Hz, –CH(Ar)–C<u>H</u>$_3$), 1 85 (3H, *d*, *J* = 6 Hz, =CH–C<u>H</u>$_3$), 3 2–3 5 (1H, *m*, –CH(Ar)–C<u>H</u>(OAr)–CH$_3$), 3 84 (3H, *s*, Ar–OMe), 5 03 (1H, *d*, *J* = 9 Hz, Ar–C<u>H</u>(OAr)–CH–), 5 2–5 7 (2H, *br s*, OH), 6 05 (1H, *dq*, *J* = 6, 16 Hz, –CH=C<u>H</u>–CH$_3$), 6 36 (1H, *d*, *J* = 16 Hz, Ar–C<u>H</u>=CH–) and 6 74–6 90 (5H, *m*, Ar–H) The spin–spin coupling constant (*J* = 9 Hz) between the two methine protons to be assigned for H-2 and H-3 (δ5 03 and 3 2–3 5) indicates the *trans* vicinal coupling of the dihydrofuran ring These spectral data of **7** also resembled closely those reported for (±)-licarin-B (**4**) except for the absence of a methylenedioxy group On methylenation with dichloromethane and sodium hydroxide in DMSO, **7** gave a methylenedioxy derivative which was identical with (−)-licarin-B (**4**) *O*-Methylation with potassium carbonate and methyl iodide in acetone, **7** gave an *O*,*O*-dimethyl ether which was identical with (−)-acuminatin (**6**) derived from (−)-licarin-A (**5**), and not (−)- but (+)-acuminatin as described in ref [5] These results established that the structure of **7** is *rel*-(2*S*,3*S*)-2-catechyl-2,3-dihydro-7-methoxy-3-methyl-5-*trans*-propenylbenzofuran

In addition to the two new compounds above, six known neolignans eupomatenoid-1 (**1**), eupomatenoid-7 (**2**), (−)-licarin-B (**4**), (−)-licarin-A (**5**), (−)-acuminatin (**6**) and (+)-guaiacin (**8**) [6] and a sesquiterpene caryophyllene epoxide [7, 8] were isolated and characterized from this plant

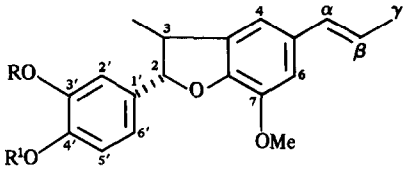
EXPERIMENTAL

Mps are uncorr IR spectra were measured in $CHCl_3$ and UV spectra in MeOH ^1H NMR spectra were recorded at 100 MHz using $CDCl_3$ as solvent and TMS as int standard, chemical shifts are reported in δ (ppm) values

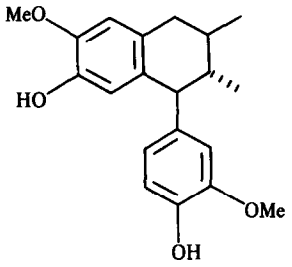
Extraction and separation of compounds The MeOH extract of dried leaves (3 27 kg) of *M kachirachirai* Dandy collected in June 1982 in Kending Tropical Botanical Garden, Republic of China was divided into *n*-hexane (112 g) and $CHCl_3$ soluble



1 R,R¹ = $-OCH_2O-$
2 R = OMe, R¹ = OH
3 R = H, R¹ = OH
3a R = H, R¹ = OAc



4 R,R¹ = $-CH_2-$
5 R = Me, R¹ = H
6 R = R¹ = Me
7 R = R¹ = H



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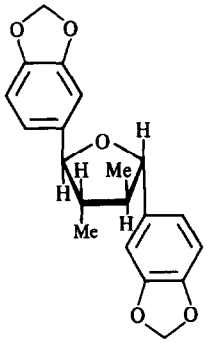

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fractions (80 g) The former fraction gave eupomatenoid-1 (**1**, 2 3 g),(−)-hicarin-B (**4**, 30 mg) and caryophyllene epoxide (44 mg) The latter fraction was chromatographed on a column of silica gel (600 g) using C_6H_6 with gradually increasing proportions of EtOAc as eluent and further purified by prep TLC The first fraction (C_6H_6) gave eupomatenoid-1 (**1**, 23 mg), eupomatenoid-7 (**2**, 2 16 g), kachirachirol-A (**3**, 5 mg), (−)-hicarin-B (**4**, 33 mg), (−)-hicarin-A (**5**, 413 mg), (−)-acuminatin (**6**, 16 mg) and (+)-guaiacin (**8**, 508 mg) The second fraction (C_6H_6–EtOAc, 20 1) gave kachirachirol-B (**7**, 217 mg)

Kachirachirol-A [2-(p-*hydroxyphenyl*)-7-*methoxy*-3-*methyl*-5-trans-*propenylbenzofuran*] (**3**) Colourless prisms ($CHCl_3$), mp 103–104° IR ν_{max} cm^{-1} 3530, 1605, 1510 MS *m/z* 294 $[M]^+$ ($C_{19}H_{18}O_3$), 279, 251, 234 ^1H NMR δ1 91 (3H, *d*, *J* = 6 Hz, propenyl Me), 2 40 (3H, *s*, Me-3), 3 98 (3H, *s*, OMe-7), 5 74 (1H, *s*, OH), 6 19 (1H, *dq*, *J* = 6, 16 Hz, propenyl β-H), 6 53 (1H, *d*, *J* = 16 Hz, propenyl α-H), 6 98 (2H, *d*, *J* = 9 Hz, H-3', H-5'), 7 30, 7 32 (2H, each *d*, *J* = 1 5 Hz, H-4, H-6), 7 37 (2H, *d*, *J* = 9 Hz, H-2', H-6')

Kachirachirol-B [rel-(2S, 3S)-2-*catechyl*-2,3-*dihydro*-7-*methoxy*-3-*methyl*-5-trans-*propenylbenzofuran*] (**7**) Colourless needles (C_6H_6), mp 64–66° $[\alpha]_D$ −60 0° ($CHCl_3$, *c* 0 65) IR ν_{max} cm^{-1} 3550, 1610, 1520, 1495 UV λ_{max} nm 212, 268, 272 MS *m/z* 312 $[M]^+$ ($C_{19}H_{20}O_4$), 297, 279, 269, 256 ^1H NMR δ1 34 (3H, *d*, *J* = 7 Hz, Me-3), 1 85 (3H, *d*, *J* = 6 Hz, propenyl Me), 3 2–3 5 (1H, *m*, H-3), 3 84 (3H, *s*, OMe-7), 5 03 (1H, *d*, *J* = 9 Hz, H-2), 5 2–5 7 (2H, *br s*, OH), 6 05 (1H, *dq*, *J* = 6, 16 Hz, propenyl β-H), 6 36 (1H, *d*, *J* = 16 Hz, propenyl α-H), 6 74–6 90 (5H, *m*, Ar–H)

Kachirachirol-A monoacetate (**3a**) A mixture of kachirachirol-A (5 mg), Ac_2O (1 ml) and pyridine (1 ml) was allowed to stand overnight at room temp A few pieces of crushed ice were added and the soln extracted with $CHCl_3$ The $CHCl_3$ extract was washed with H_2O and dried (Na_2SO_4) Concn of this soln gave a colourless oil (2 mg) IR ν_{max} cm^{-1} 1760, 1600, 1590, 1510 MS *m/z* 336 $[M]^+$ ($C_{21}H_{20}O_4$), 294, 279, 251 ^1H NMR δ1 90 (3H, *d*, *J* = 6 Hz, propenyl Me), 2 32 (3H, *s*, OCOMe-4'), 2 44 (3H *s*, Me-3), 3 92 (3H, *s*, OMe-7), 6 22 (1H, *dq*, *J* = 6, 16 Hz, propenyl β-H), 6 54 (1H, *d*, *J* = 16 Hz, propenyl α-H), 7 12 (2H, *d*, *J* = 8 Hz, H-3', H-5'), 7 32, 7 41 (2H, each *d*, *J* = 2 Hz, H-4, H-6), 7 40 (2H, *d*, *J* = 8 Hz, H-2', H-6')

Methylenation of kachirachirol-B (**7**) NaOH powder (10 mg) and CH_2Cl_2 (1 ml) were added to a soln of kachirachirol-B (**7**) (20 mg) in DMSO (2 ml) and the mixture heated at 110° for 3 hr under a N_2 atmosphere After cooling and dilution with H_2O, the reaction mixture was extracted with $CHCl_3$ and the $CHCl_3$ extract washed with H_2O, then dried (Na_2SO_4) Removal of solvent gave a residue, which was dissolved in $CHCl_3$ The soln was filtered through a short silica gel column and evapd to dryness to give a colourless oil (10 mg), $[\alpha]_D$-15 3° ($CHCl_3$, *c* 1 65) The IR and ^1H NMR spectra of this compound were superimposable on those of (−)-hicarin-B (**4**)

O-Methylenation of kachirachirol-B (**7**) MeI (33 mg) and anhydrous K_2CO_3 (16 mg) were added to a soln of kachirachirol-B (**7**) (9 mg) in Me_2CO (5 ml) and the mixture refluxed overnight The reaction mixture was filtered and concd, the residue dissolved in $CHCl_3$ and the soln washed with H_2O then dried (Na_2SO_4) Concn of this soln gave colourless plates (6 mg), mp

107–108 5°, $[\alpha]_D$-38 3° ($CHCl_3$, *c* 0 30) The IR and ^1H NMR spectra of this compound were indistinguishable from those of (−)-acuminatin (**6**)

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