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LAUREBIPHENYL, A DIMERIC SESQUITERPENE OF THE CYCLOLAURANE-TYPE FROM THE RED ALGA *LAURENCIA NIDIFICA*

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Key Word Index—*Laurencia nidifica*; Rhodomelaceae; red alga; dimeric sesquiterpene of cyclolaurane-type; laurebiphenyl.

Abstract—Laurebiphenyl, a new, dimeric sesquiterpene of the cyclolaurane-type, was isolated from the red alga *Laurencia nidifica*. Its structure was determined by spectral and chemical means.

INTRODUCTION

The marine red alga *Laurencia nidifica* has proved to be a source of various halogenated and non-halogenated sesquiterpenes and halogenated C_{15} non-terpenoid compounds [1–3]. We have recently isolated and characterized a cyclolaurane sesquiterpene, laurequinone, from *L. nidifica* [4]. In our continuing investigation of this alga, we have now isolated a new, dimeric sesquiterpene of the cyclolaurane-type, laurebiphenyl (**1**), the structure elucidation of which is described in this paper. So far, two dimeric sesquiterpenes of the cyclolaurane-type possessing the biphenyl skeleton have been isolated from *L. decidua* [3, 5].

RESULTS AND DISCUSSION

The fresh alga was extracted with acetone and the acetone extract was further extracted with ethyl acetate. The oily extract was repeatedly separated by CC and TLC to give a new compound, laurebiphenyl (**1**).

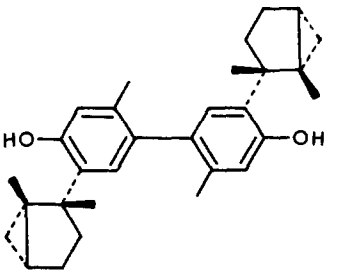
Laurebiphenyl (**1**), $C_{30}H_{38}O_2$, mp 232–232.5°, $[\alpha]_D^{25}$ + 15.2° ($CHCl_3$; *c* 0.092). From the spectral (UV, IR and NMR) data of **1**, the presence of the following groups was indicated: a 2,4,5-trisubstituted phenol group [UV λ_{max} nm: 208, 241 (sh) and 284; IR ν_{max} cm^{-1}: 3600, 3480, 1610, 1565, 1495 and 1155; ^1H NMR (measured at 60°): δ7.25 (*s*) and 6.63 (*s*); ^{13}C NMR: δ152.7 (*s*), 134.8 (*s*), 133.5 (*s*), 131.1 (*s*), 130.9 (*d*) and 117.8 (*d*)], an aromatic methyl group [^1H NMR (measured at 60°): δ2.01 (*s*); ^{13}C NMR (measured at 60°): δ24.0 (*q*)], two tertiary methyl groups [^1H NMR: δ1.45 (*s*) and 1.28 (*s*); ^{13}C NMR: δ19.5 (*q*) and 18.9 (*q*)] and a cyclopropane ring [^1H NMR: δ0.53 (*m*); ^{13}C NMR: δ16.4 (*t*)]. The ^1H NMR spectrum of **1** was similar to that of laurinterol [6–9]. Based on these spectral data and the molecular formula, the structure of laurebiphenyl was shown to be **1**. It is interesting to note that in the ^1H NMR spectrum of **1** two singlets, due to the aromatic methyls (δ2.02 and 2.00), were observed at room temperature owing to the prevention of the free rotation of phenyl rings with respect to each other, whereas there appeared only one singlet, corresponding to the aromatic methyls (δ2.01) at 60°: the same phenomenon was observed on the signal arising from one of the aromatic protons [two singlets (δ7.27 and 7.23) at room temperature and one singlet (δ7.25) at 60°]. Structure **1** for laurebiphenyl was confirmed by transformation of debromolaurinterol [6, 7] into laurebiphenyl via oxidative coupling with manganese dioxide.

The structure of laurebiphenyl (**1**) is distinguished by the fact that it is biogenetically formed by oxidative coupling of two molecules of debromolaurinterol at the *para* position of the phenol groups, while the two dimeric cyclolauranes previously reported [3, 5] are biogenetically derived by *ortho* coupling of the phenolic parts of two molecules of a cyclolaurane sesquiterpene (laurinterol or debromolaurinterol).

EXPERIMENTAL

Mps are uncorr. ^1H NMR (90 MHz) and ^{13}C NMR (22.5 MHz): $CDCl_3$, TMS as int. standard; MS (70 eV): direct inlet system; CC: silica gel BW-80 (Fuji-Davison); prep. TLC: silica gel 60 PF_{254} (Merck). The isolated yield is based on the wt of the fresh alga.

Extraction and isolation. The alga (*L. nidifica*) was collected in July at Goza, Mie Prefecture, Japan. The fresh alga (8.8 kg) was extracted with Me_2CO (2 × 12 l.) at room temp. Removal of the solvent under red. pres. yielded an aq. phase, which was extracted with EtOAc (2 × 6 l.). Evaporation of the EtOAc extract gave an



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oily residue (44.5 g), a part of which (30.5 g) was chromatographed on silica gel (760 g) with hexane (13 l.) and C_6H_6 (9 l.) successively. The middle fractions of the C_6H_6 eluate (480 mg) were further chromatographed on silica gel (25 g) with hexane–EtOAc (43:7). From the later fractions an amorphous solid (12 mg) was obtained, which was separated by prep. TLC with hexane–Et_2O (3:1) to give crude **1** (6.9 mg). Purification of crude **1** by prep. TLC with C_6H_6 provided crystalline **1** (2.3 mg, 0.000038%).

Laurebiphenyl (**1**). Mp 232–232.5° (from C_6H_6–hexane), $[\alpha]_D^{25}$ +15.2° ($CHCl_3$; *c* 0.092); UV λ_{max}^{MeOH} nm (ε): 208 (34300), 241 (8600, sh), 284 (5200); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3480, 1610, 1565, 1495, 1155; ^1H NMR (measured at 20°): δ7.27 and 7.23 (each 1H, *s*), 6.63 (2H, *s*), 5.10 (2H, *br s*, disappeared on addition of D_2O), 2.02 and 2.00 (each 3H, *s*), 1.45 (6H, *s*), 1.28 (6H, *s*), 0.53 (4H, *m*), 0.9–2.3 (10H, *m*); ^{13}C NMR (measured at 20°): δ152.7 (*s*), 134.8 (*s*), 133.5 (*s*), 131.1 (*s*), 130.9 (*d*), 117.8 (*d*), 48.1 (*s*), 36.4 (*t*), 29.7 (*s*), 25.4 (*t*), 24.5 (*d*), 24.1 (*q*), 23.9 (*q*), 19.5 (*q*), 18.9 (*q*), 16.4 (*t*) [two signals at δ24.1 and 23.9 at 20° collapsed into one signal (δ24.0) at 60°]; MS *m/z* (rel. int.): 430 $[M]^+$ (100), 415 (36), 401 (4), 387 (4), 373 (10), 362 (10), 347 (6); HRMS *m/z* 430.2843 $[M]^+$, calc. for $C_{30}H_{38}O_2$, 430.2869.

Conversion of debromolaurinterol into **1**. A mixture of debromolaurinterol (49.0 mg) and MnO_2 (49.0 mg) in CH_2Cl_2 (2.5 ml) was stirred at room temp. for 5 min. The mixture was filtered under red. pres. Concentration of the filtrate afforded a residue, which was separated by prep. TLC with C_6H_6 to give **1** (10.8 mg, 21%) and unreacted debromolaurinterol (35.2 mg, 72%). Recrystallization from C_6H_6–hexane yielded **1** as colourless crystals, mp 233–233.5°; $[\alpha]_D^{25}$ +16.6° ($CHCl_3$; *c* 1.43). The synthetic **1** was proved to be identical with natural **1** by comparison of the spectral (UV, IR, ^1H NMR, ^{13}C NMR and MS) data and chromatographic behaviour.

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TERPENOIDS FROM *SALVIA PALAESTINA*

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Key Word Index—*Salvia palaestina*; Labiatae; terpenoids; sclareol; antibacterial activity.

Abstract—Six known terpenoids: vergatic acid, ursolic acid, crataegolic acid, lupane-3β-,11α,20-triol, sclareol and sitosteryl 3β-glucoside were isolated from the leaves of *Salvia palaestina* and were identified by spectral data. Among the compounds, sclareol showed high activity against *Staphylococcus aureus*, *S. epidermis*, *Escherichia coli*, *Proteus vulgaris* and *Pseudomonas aeruginosa*, while the triterpenoids were not tested due to solubility problems.

In a previous study with the benzene extract of *Salvia palaestina* Bentham we described the identification of 16 flavonoids and antibacterial activity of cirsimaritin [1]. A further investigation of the same extract has led to the isolation of terpenic compounds, vergatic acid [2], ursolic acid [3], crataegolic acid [4], sclareol [5], sitosteryl 3β-glucoside [6] and lupane-3β,11,20-triol [7]. One of the terpenoids, sclareol, showed a high antibacterial activity against standard test strains of *Staphylococcus aureus*, *S. epidermis*, *Escherichia coli*, *Proteus vulgaris* and