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A PHENOLIC AMIDE FROM *ACTINODAPHNE LONGIFOLIA*

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Key Word Index—*Actinodaphne longifolia*; Lauraceae; *N-trans*-feruloyl 3-methyldopamine; *N-trans*-feruloyl tyramine; phenolic amide.

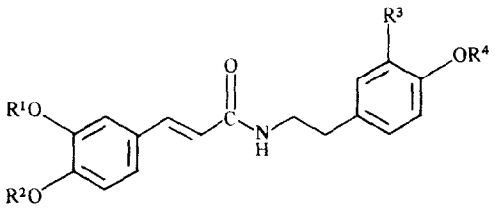
Abstract—Further examination of *Actinodaphne longifolia* has led to the isolation of a new phenolic amide, *N-trans*-feruloyl 3-methyldopamine, along with *N-trans*-feruloyl tyramine. The structure of this compound was elucidated by spectroscopic and chemical means.

INTRODUCTION

Previously, we have isolated a new lignan, actifolin [1], and two new ester compounds, secoisolancifolide [2] and secoisoobtusilactione [2], from the leaves of *Actinodaphne longifolia* (Blume) Nakai (Lauraceae). In the course of our further investigation of the wood of this plant, two phenolic amides were isolated and one of them was a new compound. We now wish to report the isolation and characterization of this phenolic amide (**1**).

RESULTS AND DISCUSSION

The new compound **1**, colourless oil, gave a brown colour with ethanolic ferric chloride and exhibited absorption bands for hydroxyl group (3400 cm^{-1}), amide group (1650 cm^{-1}), and benzene ring (1590 and 1510 cm^{-1}) in the IR spectrum. The molecular formula of **1** was determined to be $C_{19}H_{21}NO_5$ by the high-resolution mass spectrum (*m/z* 343.1423). Treatment of **1** with acetic anhydride in pyridine gave a diacetyl derivative (**1a**). In the ^1H NMR spectrum of **1**, signals of two methylene groups (δ 2.76, *t*, $J = 7.1$ Hz; 3.51, *q*, $J = 7.1$ Hz), two methoxyl groups (δ 3.83 and 3.88), *trans*-olefine group (δ 6.50 and 7.45, each *d*, $J = 15.8$ Hz), and six aromatic protons (δ 6.66–7.16, *m*) were observed. The ^{13}C NMR spectrum indicated the presence of 19 carbons, and all the signals of **1** was very similar to those of **2** except for the signals of aromatic carbons in phenethylamine portion (Table 1). The mass spectrum of **1** showed a molecular ion peak at *m/z* 343, and a base peak at *m/z* 177 which corresponded to a feruloyl moiety [3]. These data suggested that this compound consist of feruloyl moiety and 4-hydroxy-3-methoxyphenetylamine segment. Condensation of ferulic acid and 4-hydroxy-3-methoxyphenetylamine in the presence of *N,N'*-dicyclohexylcarbodiimide (DCC) afforded *N-trans*-feruloyl 3-methyldopamine which was identical with **1** in all respects. Other regioisomers (**3**–**5**) of this compound were also synthesized, but were not identical with the natural product. Comparing the ^{13}C NMR spectra of these compounds, the chemical shifts of two 3-methoxy-4-hydroxyphenyl groups of **1** were in good agreement with those of the corresponding segments of these isomers.



1 R^1 = Me, R^2 = R^4 = H, R^3 = OMe
1a R^1 = Me, R^2 = R^4 = Ac, R^3 = OMe
2 R^1 = Me, R^2 = R^3 = R^4 = H
3 R^1 = R^4 = Me, R^2 = H, R^3 = OH
4 R^1 = R^4 = H, R^2 = Me, R^3 = OMe
5 R^1 = H, R^2 = R^4 = Me, R^3 = OH

Thus, the structure of *N-trans*-feruloyl 3-methyldopamine was represented by the formula **1**. This is the first naturally occurring amide which has a 4-hydroxy-3-methoxyphenethylamine moiety as an amine unit.

In addition to the new compound discussed above, a known amide, *N-trans*-feruloyl tyramine (**2**) [4], was isolated and identified from this plant. These phenolic amides were so far isolated from several families (Solanaceae [3], Liliaceae [4], Rutaceae [5], and Menispermaceae [6]) of plants, but this is the first example to isolate these amides from *Lauraceae*.

EXPERIMENTAL

MS were recorded on Hitachi M-52 and HRMS on M-80 spectrometers. UV spectra were recorded on a double beam spectrophotometer. ^1H NMR spectra were measured at 270 MHz, and ^{13}C NMR spectra at 25.0 MHz with TMS as an int. standard. CC was run on Merck silica gel (230–400 mesh). TLC and prep. TLC were carried out on silica gel. The spots were detected by spraying with 2% ceric sulphate in 1M H_2SO_4 and by UV light.

Extraction and separation of compounds. Actinodaphne longifolia (Blume) Nakai (Lauraceae) was collected in Kagoshima prefecture, Japan in August 1987. The wood (3.0 kg) of the plant material was extracted with EtOH. The EtOH extract was

Table 1. ^{13}C NMR spectral data (acetone-d_6) of compounds 1–5.

C	1	2	3	4	5
Feruloyl					
1	166.6	166.7	166.7	166.4	166.6
2	120.0	120.0	119.9	120.6	120.5
3	140.5	140.4	140.5	140.2	140.3
1′	128.2	128.3	128.2	129.5	129.4
2′	111.3	111.3	111.3	112.4	112.4
3′	149.1	149.1	149.1	149.8	149.8
4′	148.6	148.6	148.6	147.7	147.7
5′	116.1	116.1	116.1	114.1	114.1
6′	122.6	122.6	122.6	121.4	121.4
MeO	56.2	56.3	56.2*	56.3	56.3
Amine					
1	41.9	41.9	41.8	41.9	41.8
2	36.2	35.7	35.9	36.2	35.9
1′	131.7	131.1	133.4	131.7	133.4
2′	113.1	130.5	112.6	113.1	112.6
3′	148.2	116.1	147.4	148.2	147.4
4′	145.8	156.7	146.9	145.8	146.8
5′	115.7	116.1	116.5	115.7	116.4
6′	122.0	130.5	120.5	122.0	120.5
MeO	56.2	—	56.3*	56.3	56.3

*Assignments may be interchanged.

divided into *n*-hexane soluble (26.8 g) and $CHCl_3$ soluble fractions (12.3 g). From the *n*-hexane soluble fraction, sesquirosefuran (110 mg), longifolin (200 mg), 8-[2′-(3′-methyl)furanyl]-2,6-dimethyl-2,6-octadiene-4-one (63 mg), isolancifolide (29 mg), and isoobtusilactone (4 mg) were isolated [2]. The $CHCl_3$ soluble fraction was chromatographed on silica gel, and elution with $CHCl_3$–Me_2CO (19:1) afforded an oil (5.0 g). A portion 2.4 g) of the oil was chromatographed on silica gel with $CHCl_3$–Me_2CO (2:1), and subsequently with *n*-hexane–Me_2CO (1:1) to afford *N-trans*-feruloyl tyramine (**2**) (18 mg) and *N-trans*-feruloyl 3-methyldopamine (**1**) (12 mg).

N-*trans*-Feruloyl tyramine (**2**) was identified by direct comparison with an authentic sample prepared by condensation of *trans*-ferulic acid and tyramine, according to the same procedure as described in the synthesis of **1**.

N-trans-*Feruloyl 3-methyldopamine* **1**. Colourless oil. MS *m/z*: 343 (M^+), 194, 193, 192, 177, 150. HRMS *m/z*: 343.1423 (M^+, calcd for $C_{19}H_{21}NO_5$: 343.1418). IR ν_{max}^{KBr} cm^{-1}: 3400, 1650, 1590, 1515. UV λ_{max}^{EtOH} nm: 218, 231, 287, 319. ^1H NMR (Me_2CO-d_6): δ 2.76 (2H, *t*, J = 7.1 Hz, $-CH_2$–Ar), 3.51 (2H, *q*, J = 7.1 Hz, –NH–CH_2–), 3.83, 3.88 (6H, 2 × *s*, 2 × OMe), 6.50 (1H, *d*, J × 15.8 Hz, –CH=C<u>H</u>–CO–), 6.66–7.16 (6H, *m*, arom H), 7.45 (1H, *d*, J × 15.8 Hz, Ar–C<u>H</u>=CH–). ^{13}C NMR: see Table 1.

Acetylation of **1**. A mixture of **1** (2.0 mg) in Ac_2O (0.2 ml) and pyridine (0.2 ml) was stirred overnight at room temp. The reaction mixture was diluted with H_2O and extracted with EtOAc. The EtOAc layer was washed with H_2O, dried over Na_2SO_4 and evapd to give **1a** as colourless oil (2.3 mg, 93%). MS *m/z*: 427 (M^+), 385, 343, 194, 193, 192, 177, 150. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3450, 1765, 1670, 1630, 1605, 1510. UV λ_{max}^{EtOH} nm: 216, 278, 307. ^1H NMR ($CDCl_3$): δ 2.32 (6H, *s*, 2 × OAc), 2.88 (2H, *t*, J = 6.4 Hz, $-CH_2$–Ar), 3.66 (2H, *q*, J = 6.4 Hz, –NH–CH_2–), 3.81, 3.85 (6H, 2 × *s*, 2 × OMe), 5.72 (1H. *t*, J = 6.4 Hz, NH), 6.29 (1H, *d*, J = 15.8 Hz, –CH=C<u>H</u>–CO–), 6.77–7.11 (6H, *m*, arom H), 7.58 (1H, *d*, J = 15.8 Hz, Ar–C<u>H</u>=CH–).

Synthesis of **1**. To a mixture of ferulic acid (96 mg and 4-hydroxy-3-methoxyphenethylamine (110 mg) in THF (20 ml), a soln of DCC (164 mg) in THF (5 ml) was added, and the reaction mixture stirred overninght at room temp. After removal of the solvent, the reaction mixture was diluted with a large vol of H_2O, and extracted with EtOAc. The EtOAc layer was dried over Na_2SO_4, and evapd to dryness to give viscous oil, which was purified by a column of silica gel ($CHCl_3$–Me_2CO, 2:1) to afford **1** as colourless oil (93 mg, 55%). This compound was identical with **1** by direct comparison (MS, IR, UV, ^1H NMR, and co-TLC).

Synthesis of **3**. To a mixture of ferulic acid (160 mg) and 3-hydroxy-4-methoxyphenethylamine (180 mg) in THF (30 ml), a soln of DCC (270 mg) in THF (5 ml) was added, and the reaction mixture was stirred overnight at room temp. The reaction mixture was treated as previously described for **1**. Purification by a column of silica gel ($CHCl_3$–Me_2CO, 2:1) afforded **3** as colourless oil (122 mg, 38%). MS *m/z*: 343 [M^+], 194, 193, 192, 177, 150. IR ν_{max}^{KBr} cm^{-1}: 3400, 1650, 1590, 1515. UV λ_{max}^{EtOH} nm: 219, 231, 289, 319. ^1H NMR (acetone-d_6): δ 2.74 (2H, *t*, J = 7.4 Hz, $-CH_2$–Ar), 3.51 (2H, *q*, J = 7.4 Hz, –NH–CH_2–), 3.80, 3,87 (6H, 2 × *s*, 2 × OMe), 6.52 (1H, *d*, J = 15.8 Hz, –CH=C<u>H</u>–CO–), 6.64–7.16 (6H, *m*, arom H), 7.47 (1H, *d*, J = 15.8 Hz, Ar–C<u>H</u>=CH–). ^{13}C NMR: see Table 1.

Synthesis of **4**. To a mixture of isoferulic acid (87 mg) and 4-hydroxy-3-methoxyphenethylamine (100 mg) in THF (30 ml), a soln of DCC (150 mg) in THF (5 ml) was added, and the reaction mixture was stirred overnight at room temp. The reaction mixture was treated as already described for **1**. Purification by a column of silica gel ($CHCl_3$–Me_2CO, 2:1) afforded **4** as colourless prisms (90 mg, 59%). Mp 176–178° (from Me_2CO). MS *m/z*: 343 (M^+), 194, 193, 192, 177, 150. IR ν_{max}^{KBr} cm^{-1}: 3400, 1645, 1585, 1535, 1510. UV λ_{max}^{EtOH} nm: 219, 232, 288, 319. ^1H NMR (acetone-d_6): δ 2.76 (2H, *t*, J = 7.4 Hz, $-CH_2$–Ar), 3.47–3.53 (2H, *m*, –NH–CH_2–), 3.82, 3,87 (6H, 2 × *s*, 2 × OMe), 6.49 (1H, *d*, J = 15.8 Hz, –CH=C<u>H</u>–CO–), 6.65–7.08 (6H, *m*, arom H), 7.43 (1H, *d*, J = 15.8 Hz, Ar–C<u>H</u>=CH–). ^{13}C NMR: see Table 1.

Synthesis of **5**. To a mixture of isoferulic acid (113 mg) and 3-hydroxy-4-methoxyphenethylamine (130 mg) in THF (30 ml), a soln of DCC (193 mg) in THF (5 ml) was added, and the reaction mixture was stirred overnight at room temp. The reaction mixture was treated as already described for **1**. Purification by a column of silica gel ($CHCl_3$–Me_2CO, 2:1) afforded **5** as colourless prisms (182 mg, 95%). Mp 169–171° (from Me_2CO). MS *m/z*: 343 (M^+), 194, 193, 192, 177, 150. IR ν_{max}^{KBr} cm^{-1}: 3400, 1650, 1610, 1505. UV λ_{max}^{EtOH} nm: 219, 230, 288, 319. ^1H NMR (Me_2CO-d_6): δ 2.73 (2H, *t*, J = 7.4 Hz, $-CH_2$–Ar), 3.46–3.52 (2H, *m*, –NH–CH_2–), 3.80, 3.86 (6H, 2 × *s*, 2 × OMe), 6.49 (1H, *d*, J = 15.8 Hz, –CH=C<u>H</u>–CO–), 6.65–7.08 (6H, *m*, arom H), 7.43 (1H, *d*, J = 15.8 Hz, Ar–C<u>H</u>=CH–). ^{13}C NMR: see Table 1.

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