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PHENYLALKYNES FROM *ARTEMISIA CAPILLARIS*

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Key Word Index—*Artemisia capillaris*; Compositae; phenylalkynes; capillaridins A–H.

Abstract—Eight new phenylalkynes, capillaridins A–H, together with three known compounds, capillin, capillene and *O*-methoxycapillene, were isolated and identified from the aerial parts of *Artemisia capillaris*.

INTRODUCTION

Artemisia capillaris is a famous traditional Chinese medicine. It is listed officially in the Chinese Pharmacopoeia and used mainly as a choleretic, anti-inflammatory and diuretic agent in the treatment of epidemic hepatitis [1]. Several compounds, including flavonoids, chromones, phenylalkynes and coumarins have been isolated from this species [2–13]. In continuation of our chemical investigation of alkynes from natural source [14], we were interested in the constituents of the aerial parts of *A. capillaris*. This paper deals with the isolation and structural elucidation of eight new phenylalkynes, capillaridin A (**1**), B (**2**), C (**3**), D (**4**), E (**5**), F (**6**), G (**7**) and H (**8**), together with three known compounds, by means of spectroscopic methods.

RESULTS AND DISCUSSION

Capillaridin A (**1**), yellow needles, had the molecular formula $C_{24}H_{16}O_3$ by HREI mass spectroscopy, $[M]^+$ *m/z* 352.1099. It exhibited the presence of two triple bonds from the IR absorption at 2185 cm^{-1} and ^{13}C NMR signals, two carbonyls from the IR bands at 1633 and 1674 cm^{-1}, two methyls from ^1H NMR signals and two phenyl groups from ^1H NMR signals. Then, four quarternary ^{13}C signals led us to construct a tetrasubstituted furan ring. According to the chemical shift of the furan, the triple bond should be attached to C-2 and C-4 owing to the upfield shift of the absorption by the anisotropic property of the triple bond. The fragment ions at *m/z* 309 $[M-CH_3C{=}O]^+$ and 105 $[PhC{=}O]^+$ suggested the partial structure, 2-benzoylethynyl-4-acetylethynylfuran. The remaining phenyl and methyl would be substituted on C-5 and C-3, respectively, which support by long-range ^1H-^{13}C correlations between the signals of H-2‴ (δ 8.12) and C-5 (δ 160.5).

Capillaridin B (**2**) was obtained as optically active colourless needles with the molecular formula $C_{12}H_{10}O$. A phenyl group was present from the signals in the ^1H NMR spectrum, two triple bonds from the signals in the ^{13}C NMR spectrum, together with alkynyl absorption at 2258 cm^{-1} in the IR spectrum. In the ^{13}C NMR spectrum, an upfield-shifted methyl signal at δ 4.3 suggested that this methyl should be attached at one terminal of the butadiynyl moiety; this was confirmed by the presence of ^2J–^5J long-range ^1H-^{13}C correlation between the methyl (δ 1.95) and C-5, C-4, C-3 and C-2. Combined with the above fragments, a downfield methine singlet at δ 5.48 was located a carbon bearing a phenyl, a pentadiynyl and a hydroxyl (δ 2.34).

Two *trans*- and *cis*- isomers, capillaridin C (**3**) and capillaridin D (**4**), were isolated as yellow oils and gave almost the same UV, IR, ^1H and ^{13}C NMR spectra. The HREI mass spectrum determined the molecular formulas as $C_{12}H_{10}O$. In compound **3**, IR absorptions at 2218 cm^{-1} and two ^{13}C NMR signals indicated that only one triple bond was present. A *trans*-α,β-unsaturated carbonyl unit was confirmed by the presence of mutually coupled olefinic protons in the ^1H NMR spectrum and a carbonyl band at 1632 cm^{-1} in the IR spectrum. A methyl (δ 2.11) showed long-range ^1H-^{13}C correlations with C-5, C-4 and C=O, indicating that a propynyl group was attached to the other side of the carbonyl. Two phenyl protons, H-2′ and H-6′ (δ 7.55), showed long-range correlations with C-1 (δ 148.0), suggesting that the phenyl group was positioned on the double bond. The major difference between compound **4** and **3** was the smaller coupling constant (12.0 Hz) between the two vinyl

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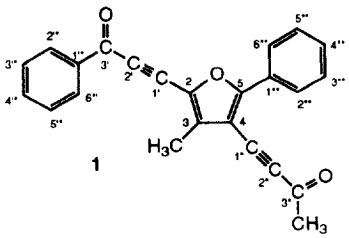

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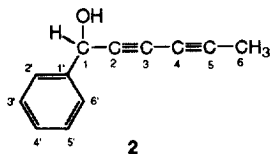

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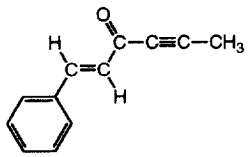

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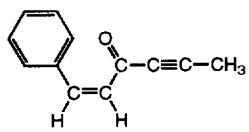

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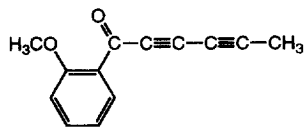

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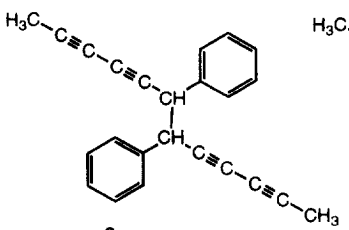

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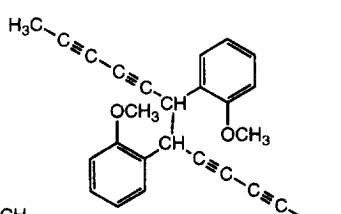

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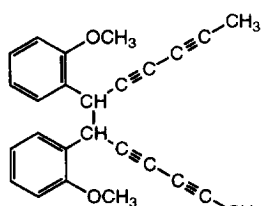

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protons, indicating the *cis*-configuration for the double bond.

Capillaridin E (**5**), a yellow oil, was determined to possess the molecular formula $C_{13}H_{10}O_2$. The presence of an *ortho*-disubstituted benzene ring was supported by the presence of four mutually coupled protons in the ^{1}H NMR spectrum. A pentadiynyl unit was proved by alkynyl absorption at 2285 cm^{-1} in the IR spectrum and four carbon signals along with a methyl carbon in the ^{13}C NMR spectrum. It also supported by long-range correlations between the methyl and C-5, C-4 and C-3. The last signal in the ^{1}H NMR spectrum was a methoxyl which should be one substituent of the benzene ring. Hence, the two groups, a methoxyphenyl and a pentadiynyl linked to a carbonyl group, which showed absorption at 1600 cm^{-1} in the IR spectrum.

Capillaridin F (**6**) was obtained as colourless needles with the molecular formula $C_{24}H_{18}$, $[M]^+$ *m/z* 306.1805. The ^{1}H and ^{13}C NMR spectra and the base fragment in the mass spectrum at *m/z* 153 showed that this compound is a highly symmetrical molecule, possibly a dimer. According to the NMR spectra, it consisted of two pentadiynyl moieties from the observation of four alkynyl carbon signals and one methyl carbon, two phenyl groups and two methine protons at δ 4.05. Comparison between the spectral data of **6** with those of **2** indicated that the two 1-phenyl-2,4-hexadiyn-1-yl units were linked together in **6**, explaining the absence of the hydroxyl group.

Capillaridins G (**7**) and H (**8**) were isolated as yellow oils. Mass spectrometry and other spectroscopic methods (^{1}H, ^{13}C NMR, IR, UV) exhibited almost the same data and showed them to be conformational isomers. The molecular formula for the two isomers was determined as $C_{26}H_{22}O_2$ by the HREI mass spectrometry. This corresponds to two CH_2O units more than that of **6**. Spectral data indicated that two methoxyl groups were present in **7** and **8**. In the aromatic region of the ^{1}H NMR spectra, the methoxyls should be substituted on a benzene proton *ortho* to the side-chain, according to the integration and splitting pattern of the aromatic signals. A slight upfield shift of all ^{1}H NMR signals in **8** indicated that the anisotropic current caused the two benzene rings to lean towards each other. Determination of the absolute configuration of the two chiral centres is still under investigation. Based on the above evidence, capillaridins G and H have been assigned the tentative structures **7** and **8**.

EXPERIMENTAL

UV were run in MeOH, IR in $CHCl_3$, except where noted. ^{1}H NMR were measured at 400 MHz or 200 MHz in $CDCl_3$ using TMS as int. standard. MS were obtained at 70 eV using a direct inlet system. Mps: uncorr.

Plant material

Artemisia capillaris Thunb was collected from Chiayi Hsien, Taiwan in September 1992 and ident-

ified by Prof. C. S. Kuoh. A voucher specimen is deposited in the herbarium of the National Cheng Kung University, Tainan, Taiwan.

Extraction and isolation

A hot MeOH extract of aerial parts (12.5 kg) was concd under red. pres. and the crude syrup was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was subjected to CC on silica gel eluted with $CHCl_3$–Me_2CO to give 7 frs. Fr. 1 was rechromatographed on a silica gel column and eluted with benzene–Me_2CO (25:1) to give **9** (1.98 g), **10** (0.15 g), **11** (43.3 mg), **1** (17.6 mg), **2** (0.35 g), **3** (50.9 mg), **4** (1.0 mg), **5** (4 mg), **6** (5.7 mg), **7** (2.5 mg) and **8** (1.7 mg), successively.

Capillaridin A (**1**). Yellow needles ($CHCl_3$), mp 148–149°. HREIMS: calcd for $C_{24}H_{16}O_3$, *m/z* 352.1098 $[M]^+$, found 352.1099. UV λ_{max} (MeOH) nm: 227, 273, 286 (sh), 355. IR ν_{max} cm^{-1}: 2185, 1674, 1633, 1595. EI-MS *m/z* (rel. int.): 352 ($[M]^+$, 100), 337 (17), 309 (8), 105 (28). ^1H NMR ($CDCl_3$): δ 2.34 (3H, *s*, 3-Me), 2.47 (3H, *s*, H-4″), 7.06 (1H, *t*, *J* = 8.0 Hz, H-4‴), 7.66 (1H, *tt*, *J* = 8.4, 1.2 Hz, H-4‴), 7.48 (2H, *t*, *J* = 8.0 Hz, H-3‴, 5‴), 7.55 (2H, *t*, *J* = 8.4 Hz, H-3‴, 5‴), 8.12 (2H, *d*, *J* = 8.0 Hz, H-2‴, 6‴), 8.18 (2H, *dd*, *J* = 8.4, 1.2 Hz, H-2‴, 6‴). ^{13}C NMR ($CDCl_3$): δ 10.1 (3-Me), 32.6 (C-4″), 81.8 (C-1″), 81.9 (C-1′), 95.5 (C-2″), 96.3 (C-2′), 103.6 (C-4), 126.0 (C-2‴, 6‴), 128.4 (C-1‴), 128.7 (C-3‴, 5‴), 129.0 (C-3‴, 5‴), 129.4 (C-2‴, 6‴), 130.6 (C-4‴), 131.7 (C-3), 134.3 (C-4‴), 136.5 (C-1‴), 137.2 (C-2), 160.5 (C-5), 176.8 (C-3′), 183.5 (C-3″).

Capillaridin B (**2**). Colourless needles ($CHCl_3$), mp 83–84°. $[\alpha]_D$ −57.4° (*c* 0.012, $CHCl_3$). CD (*c* 0.00072, MeOH) nm: $[\theta]_{222}$ + 1403, $[\theta]_{205}$ + 166. HREIMS: calcd for $C_{12}H_{10}O$, *m/z* 170.0732 $[M]^+$, found 170.0731. UV λ_{max} (MeOH) nm: 214, 241, 254. IR ν_{max} cm^{-1}: 3410, 2258. EIMS *m/z* (rel. int.): 170 ($[M]^+$, 38), 152 (30), 142 (100), 77 (39). ^1H NMR ($CDCl_3$): δ 1.95 (3H, *s*, H-6) 2.34 (1H, *br s*, OH), 5.48 (1H, *s*, H-1), 7.3–7.5 (5H, *m*, H-2′–6′). ^{13}C NMR ($CDCl_3$): δ 4.3 (C-6), 63.6 (C-5), 64.9 (C-1), 71.7 (C-3), 74.2 (C-2), 78.2 (C-4), 126.6 (C-2′, 6′), 128.5 (C-4′), 128.6 (C-3′, 5′), 139.9 (C-1′).

Capillaridin C (**3**). Yellow oil. HREIMS: calcd for $C_{12}H_{10}O$, *m/z* 170.0732 $[M]^+$, found 170.0731. UV λ_{max} (MeOH) nm: 229, 306. IR ν_{max} cm^{-1}: 2218, 1632, 1610. EI-MS *m/z* (rel. int.): 170 ($[M]^+$, 58), 169 (100), 141 (77), 155 (28), 77 (33). ^1H NMR ($CDCl_3$): δ 2.11 (3H, H-6), 6.74 (1H, *d*, *J* = 16.0, H-2), 7.40 (3H, *m*, H-3′, H-4′, 5′), 7.55 (2H, *m*, H-2′, 6′), 7.70 (1H, *d*, *J* = 16.0 Hz, H-1). ^{13}C NMR ($CDCl_3$): δ 4.1 (C-6), 78.5 (C-4), 90.7 (C-5), 128.4 (C-3′, 5′), 128.5 (C-4′), 128.9 (C-2′, 6′), 130.9 (C-2), 134.0 (C-1′), 148.0 (C-1), 178.4 (C-3).

Capillaridin D (**4**). Yellow oil. HREIMS: calcd for $C_{12}H_{10}O$, *m/z* 170.0732 $[M]^+$, found 170.0731. UV λ_{max} (MeOH) nm: 229, 306. IR ν_{max} cm^{-1}: 2218, 1632, 1610. EIMS *m/z* (rel. int.): 170 ($[M]^+$, 58), 169 (100), 141 (80), 155 (25), 77 (38). ^1H NMR ($CDCl_3$): δ 1.78 (3H, H-6), 6.24 (1H, *d*, *J* = 12.0, H-2), 7.05 (1H, *d*, *J* = 12.0 Hz, H-1), 7.36 (3H, *m*, H-3′, H-4′, 5′), 7.56 (2H, *m*, H-2′, 6′).

Capillaridin E (**5**). Yellow oil. HREIMS: calcd for $C_{13}H_{10}O_2$, *m/z* 198.0732 $[M]^+$, found 198.0731. UV λ_{max} (MeOH) nm: 269 (sh), 280, 294 (sh), 337. IR ν_{max} cm^{-1}: 2285, 1654, 1600. EIMS *m/z* (rel. int.): 198 ($[M]^+$, 44), 169 (100), 141 (55), 91 (50), 77 (50). ^1H NMR ($CDCl_3$): δ 2.06 (3H, *s*, H-6), 3.93 (3H, *s*, 2′-OMe), 6.98 (1H, *dd*, *J* = 8.4, 2.0 Hz, H-3′), 7.04 (1H, *td*, *J* = 8.4, 2.0 Hz, H-5′), 7.53 (1H, *td*, *J* = 8.4, 2.0 Hz, H-4′), 7.98 (1H, *dd*, *J* = 8.4, 2.0 Hz, H-6′). ^{13}C NMR ($CDCl_3$): δ 4.9 (C-6), 55.9 (2′-OMe), 63.7 (C-4), 72.7 (C-2), 77.3 (C-5), 86.1 (C-3), 112.2 (C-3′), 120.3 (C-5′), 126.3 (C-1′), 132.6 (C-4′), 135.3 (C-6′), 160.0 (C-1′), 175.6 (C-1).

Capillaridin F (**6**). Colourless needles ($CHCl_3$), mp 150–151°. HREIMS: calcd for $C_{24}H_{18}$, *m/z* 306.1411 $[M]^+$, found 306.1409. UV λ_{max} (MeOH) nm: 220, 238 (sh), 263 (sh). IR ν_{max} cm^{-1}: 2256, 1498. EIMS *m/z* (rel. int.): 306 ($[M]^+$, 6), 153 (100), 127 (11), 77 (6). ^1H NMR ($CDCl_3$): δ 1.92 (6H, *s*, 2 × Me), 4.05 (2H, *s*, H-1, 1′), 7.12 (4H, *m*, H-2″, 2‴, H-6″, 6‴), 7.24 (6H, *m*, H-3″, 3‴, H-4″, 4‴, H-5″, 5‴). ^{13}C NMR ($CDCl_3$): δ 4.3 (C-6, 6′), 45.9 (C-1, 1′), 64.3 (C-4, 4′), 70.2 (C-3, 3′), 74.6 (C-2, 2′), 75.3 (C-5, 5′), 127.5 (C-4″, 4‴), 128.0 (C-3″, 3‴, C-5″, 5‴), 128.7 (C-2″, 2‴, C-6″, 6‴), 137.3 (C-1″, 1‴).

Capillaridin G (**7**). Yellow oil. HREIMS: calcd for $C_{26}H_{22}O_2$, *m/z* 366.1620 $[M]^+$, found 366.1620. UV λ_{max} (MeOH) nm: 219, 274, 280 (sh). IR ν_{max} cm^{-1}: 2256, 1600, 1492. EIMS *m/z* (rel. int.): 366 ($[M]^+$, 6), 183 (100), 139 (12), 77 (45). ^1H NMR ($CDCl_3$): δ 1.91 (6H, *s*, 2 × Me), 3.82 (6H, *s*, 2″, 2″-OMe), 4.62 (2H, *s*, H-1, 1′), 6.80 (2H, *dd*, *J* = 7.8, 1.5 Hz, H-3″, 3‴), 6.98 (2H, *td*, *J* = 7.8, 1.5 Hz, H-5″, 5‴), 7.23 (2H, *td*, *J* = 7.8, 1.5 Hz, H-4″, 4‴), 7.70 (2H, *dd*, *J* = 7.8, 1.5 Hz, H-6″, 6‴). ^{13}C NMR ($CDCl_3$): δ 4.2 (C-6, 6′), 37.4 (C-1, 1′), 55.4 (2″, 2‴-OMe), 64.8 (C-4, 4′), 69.2 (C-3, 3′), 73.8 (C-2, 2′), 75.3 (C-5, 5′), 110.1 (C-3″, 3‴), 120.3 (C-5″, 5‴), 127.1 (C-1″, 1‴), 128.4 (C-6″, 6‴), 130.2 (C-4″, 4‴), 156.1 (C-2″, 2‴).

Capillaridin H (**8**). Yellow oil. HREIMS: calcd for $C_{26}H_{22}O_2$, *m/z* 366.1620 $[M]^+$, found 366.1617. UV λ_{max} (MeOH) nm: 223, 274, 282 (sh). IR ν_{max} cm^{-1}: 2256, 1599, 1492. EIMS *m/z* (rel. int.): 366 ($[M]^+$, 5), 183 (100), 139 (15), 77 (40). ^1H NMR ($CDCl_3$): δ 1.93 (6H, *s*, 2 × Me), 3.50 (6H, *s*, 2″, 2‴-OMe), 4.78 (2H, *s*, H-1, 1′), 6.66 (2H, *dd*, *J* = 7.7, 1.5 Hz, H-3″, 3‴), 6.81 (2H, *td*, *J* = 7.7, 1.5 Hz, H-5″, 5‴), 7.14 (2H, *td*, *J* = 7.7, 1.5 Hz, H-4″, 4‴), 7.24 (2H, *dd*, *J* = 7.7, 1.5 Hz, H-6″, 6‴). ^{13}C NMR ($CDCl_3$): δ 4.3 (C-6, 6′), 36.3 (C-1, 1′), 55.1 (2″, 2‴-OMe), 68.3 (C-4, 4′), 74.1 (C-3, 3′), 76.0 (C-2, 2′), 76.7 (C-5, 5′), 109.4 (C-3″, 3‴), 119.9 (C-5″, 5‴), 125.7 (C-1″, 1‴), 128.3 (C-6″, 6‴), 129.8 (C-4″, 4‴), 156.2 (C-2″, 2‴).

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