New Benzofuranosesquiterpenes from *Farfugium japonicum*. Farfugin A and Farfugin B[1]

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(Received April 27, 1974)

Two new benzofuranosesquiterpenes, farfugin A and farfugin B, have been isolated from *Farfugium japonicum* (L.) Kitamura, and their structures have been determined as **1** and **2**, respectively.

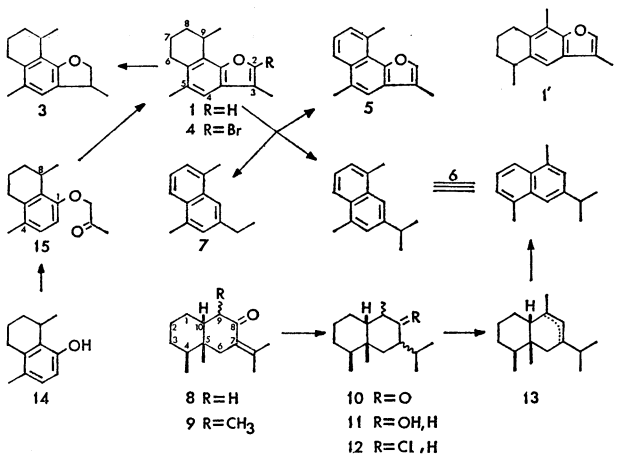
During chemical investigations on plants of the genus *Ligularia* (Compositae) and related plants,[2] two new sesquiterpenes, which we have named farfugin A and farfugin B, have been isolated from *Farfugium japonicum* (L.) Kitamura (=*Ligularia tussilaginea* Makino). We wish to report the structure determination leading to **1** and **2** for farfugin A and farfugin B, respectively.

A benzene extract of the rhizome of the plant was subjected to vacuum distillation and subsequent separation by column chromatography on silica gel to give farfugin A and farfugin B. Farfugin A (**1**) crystallized from methanol as colorless needles, mp 80.5—82.5 °C, $[\alpha]_D$+39°. The molecular formula of **1**, $C_{15}H_{18}O$, was determined by elemental analysis and the appearance of the molecular ion peak at *m/e* 214. Neither carbonyl nor hydroxyl absorption was observed in the IR spectrum. The UV and PMR spectra showed the presence of a β-methyl substituted benzofuran moiety with an α-proton,[3] an aromatic proton, an aromatic methyl, a secondary methyl spin coupled with a benzylic proton, two other benzylic protons, and four aliphatic protons (*Cf.* Experimental).

Hydrogenation of **1** over palladium–charcoal in methanol gave dihydrofurfugin A (**3**), whose PMR spectrum showed signals due to a part [$-OCH_2CH(CH_3)-$] of dihydrofuran moiety. An α-proton on the furan ring of **1** could be replaced by a bromine atom when **1** was treated with bromine in chloroform to afford bromofarfugin A (**4**).

Farfugin A (**1**) was dehydrogenated with palladium–charcoal to give a naphthofuran derivative (**5**) and a mixture of two naphthalene derivatives (**6** and **7**). Although a separation of the mixture failed due to paucity of the material, its UV, IR, and PMR spectra were closely related (*Cf.* Experimental) to those of 1,5-dimethyl-3-isopropylnaphthalene (**6**)[4] prepared from fukinone (**8**).[5] The sole difference between the two PMR spectra was that a *triplet* (J=7.5 Hz, $-CH_2\underline{CH_3}$) at δ 1.35 appeared in the spectrum of the mixture (**6** and **7**), while did not in that of **6** obtained from **8**. Combined glc-mass spectrometry of the mixture (**6** and **7**) revealed that it consisted of **6** [M^+ at *m/e* 198 ($C_{15}H_{18}$)] and **7**[M^+ at *m/e* 184 ($C_{14}H_{16}$)] in a ratio of 1 : 3. These observations showed that the mixture was composed of **6** and 1,5-dimethyl-3-ethylnaphthalene (**7**). The structure of the naphthofuran derivative (**5**) could be derived after completion of the structure determination of **1**.

The reference compound (**6**) was prepared as follows. Methylation of fukinone (**8**) with methyl iodide in a mixture of potassium *t*-butoxide and *t*-butyl alcohol gave 9-methylfukinone (**9**), which was hydrogenated over palladium–charcoal in ethanol to afford 9-methyldihydrofukinone (**10**). The ketone (**10**) was then reduced with lithium aluminium hydride to yield an alcohol (**11**). Treatment of **11** with phosphorus oxychloride in pyridine gave, besides a chloride (**12**), a mixture of hydrocarbons (**13**), which was subjected to dehydrogenation with palladium–charcoal to afford **6**[4] (Scheme 1).



Scheme 1.

The result of dehydrogenation experiments along with spectral data of farfugin A described as above led to two alternative structures (**1** and **1'**) for farfugin A. The presence of intramolecular nuclear Overhauser effects (NOE)[6] between the aromatic proton (at C–4) and the aromatic methyl (at C–5), and between the same aromatic proton (at C–4) and the methyl (at C–3), observed for bromofarfugin A (**4**), showed that the structure of farfugin A must be represented by **1** rather than by **1'** (Table 1). This was confirmed by the following synthesis.

Treatment of 4,8-dimethyl-1-hydroxy-5,6,7,8-tetrahydronaphthalene (**14**)[7] with chloroacetone, potassium iodide, and potassium carbonate in dry acetone under reflux gave 1-acetonyloxy-4,8-dimethyl-5,6,7,8-tetrahydronaphthalene (**15**). The ether (**15**) was then heated with polyphosphoric acid to afford (±)-**1**, mp 73—73.5 °C, identical with natural (+)-**1** in all respects [IR in Nujol (**1** was soluble in Nujol), UV, PMR, MS, and tlc] except mp and $[\alpha]_D$ data (Scheme 1).

Farfugin B (**2**) was isolated as a colorless oil. A molecular ion peak at *m/e* 214 ($C_{15}H_{18}O$) was observed in the mass spectrum. The presence of an α-proton and a β-methyl on the benzofuran moiety, two aromatic protons, an aromatic methyl, an olefinic methyl, and

Table 1. Nuclear Overhauser effects[a)]

Compounds	Observed protons	Saturated protons	NOE
4	4-H (7.00 s)	3-Me (2.12 s)	7
	4-H	5-Me (2.27 s)	15
	4-H	9-Me (1.38 d J=7 Hz)	nil
16	4-H (6.88 s)	5-Me (2.23 s)	14
	7-H (6.58 s)	5-Me	nil
	4-H	3-H (3.45m)	3
	7-H	3-H	nil
	1'-H (2.52m)	4-H (6.88 s)	nil
	3-Me (1.29 d J=7 Hz)	7-H (6.58 s)	nil
	1'-H	7-H	9
	4-H	1'-H (2.52m)	nil
	7-H	1'-H	19

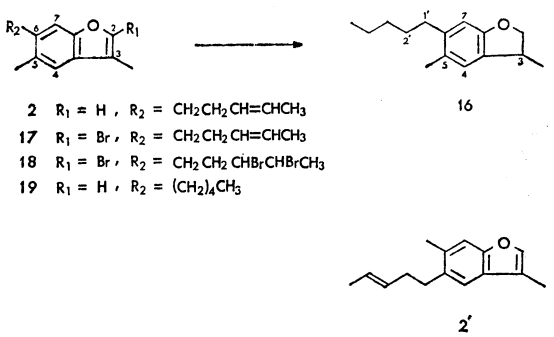
a) The NOE's are expressed as increases in integrated signal intensities in %. The other indications are given in Experimental.

two olefinic protons was shown from its UV and PMR spectral data (*Cf.* Experimental).

Hydrogenation of **2** over palladium–charcoal in ethanol gave tetrahydrofarfugin B (**16**), whose PMR spectrum showed a multiplet as AM part of an AMX system due to a methylene of dihydrofuran moiety, and two *singlets* at δ 6.58 and 6.88 due to two aromatic protons (*Cf.* Experimental).

These observations led to a 3-methylbenzofuran structure with an additional methyl and a C_5H_9 substituent on C–5 and C–6 (that is, either 2 or 2'; each with the side chain replaced by C_5H_9) for farfugin B.

A nature of the C_5H_9 group was shown to be *trans-n*-3-pentenyl from the following evidences. Bromination of **2** yielded bromofarfugin B (**17**) and tribromofarfugin **B** (**18**). A doublet (J=7.5 Hz, $C\underline{H}_3CH\underline{B}r$–) appeared at δ 1.86 in the PMR spectrum of **18**, in place of the olefinic methyl signal at δ 1.65 in that of **2**. The PMR spectrum of dihydrofarfugin B (**19**), obtained by hydrogenation of **2** over platinum catalyst in methanol, showed signals at δ 0.91 due to a primary methyl. An IR absorption band at 965 cm^{-1} due to *trans*-olefinic linkage was absent in the IR spectra of **16**, **18**, and **19** (Scheme 2).



Scheme 2.

Two alternative structures of **2** and **2'** could thus be shown for farfugin B. The presence of NOE's between the aromatic proton (at C–4) and the aromatic methyl (at C–5), and between the other aromatic proton (at C–7) and the benzylic protons (at C–1'), observed for tetrahydrofarfugin B (**16**), favored the structure **2** over **2'** for farfugin B (Table 1). The structure of farfugin B should therefore be represented by 3,5-dimethyl-6-(*trans-n*-3-pentenyl)benzofuran (**2**). This received support from a recent synthesis of dihydrofarfugin B (**19**) from 1-methyl-2-bromo-4-methoxybenzene described elsewhere.[8)]

Experimental

IR, UV, and mass spectra were measured using a Hitachi EPI-G2, a Hitachi EPS-3, and a Hitachi RMU-6-Tokugata spectrometers, respectively. A gas chromatograph, Hitachi K53, was equipped with this mass spectrometer for measurements by combined glc-mass spectrometry. Optical rotations, $[\alpha]_D$, were measured with a YANACO OR-50 spectrometer. PMR spectra were taken on a JEOL 4H-100 (100 MHz), a JEOL PS-100 (100 MHz), and a Hitachi R-20 (60 MHz) spectrometers. For the measurement of NOE's, the PMR spectra were taken with a Varian HA-100 spectrometer operating at 100 MHz in the frequency-swept and internal TMS-locked mode, for *ca.* 5% (w/v) degassed solution in $CDCl_3$. NOE experiments were performed with sweep rates of 0.4 Hz per sec for integration and 0.2 Hz per sec for signals on the spectrometer with a Hewlett-Packard HP-200ABR audio-oscillator and an HP-5212A electronic counter. Accuracies for NOE values are about ±2%. Chemical shifts are expressed in δ (TMS as internal standard), and coupling constants in Hz. All melting points were determined on a hot block and reported uncorrected. Merck Kieselgel G and Kieselgel 60 PF_{254} were used for analytical and preparative tlc, respectively. For column chromatography silica gel (Wakogel C–200) and neutral alumina (Showa Chemical Co.) were used.

*Isolation of Farfugin A (**1**) and Farfugin B (**2**).* The rhizomes of *Farfugium japonicum* (L.) Kitamura were extracted with hot benzene. The residue obtained (24 g) after evaporation of the solvent was subjected to distillation at 150 °C under 0.3 mmHg to give a brown oil (4 g), which, by repeated distillation, afforded a yellow oil(2.7 g). The oil was chromatographed on silica gel (150 g) using light petroleum as eluent (each 150 ml). The eluted fractions were collected and examined by tlc.

Fractions 6—8 were combined and the solvent was removed to give crude **1** (153 mg), which was further chromatographed on silica gel. Fractions eluted with light petroleum, on evaporation of the solvent, gave a residue, which afforded after crystallization from ethanol *farfugin A* (**1**; 102 mg), mp 80.5—82.5 °C, $[\alpha]_D^{20}$ +39° (c 0.34, in EtOH); UV (cyclohexane): λ_{max} 252.5 nm (ε 14500), 281 (2800), and 291 (3200); IR (Nujol): 1590 and 1540 cm^{-1}; PMR ($CDCl_3$): δ 1.37 (3H, d, J=7.5 Hz, $C_{(9)}$–CH_3), 2.16 (3H, d, J=1.2 Hz; $C_{(3)}$–CH_3), 2.27 (3H, s; $C_{(5)}$—CH_3), 2.63 (2H, m; $C_{(6)}$–H), 3.35 (1H, m; $C_{(9)}$–H), 7.05(1H, s; $C_{(4)}$–H), 7.20 (1H, m; $C_{(2)}$–H), and 1.5—2.0 (4H; $C_{(7)}$–H and $C_{(8)}$–H); MS: *m/e* 214 (relative intensity 79%, $M^+(C_{15}H_{18}O)$) and 199 (100%, $[M-CH_3]^+$). Found: C, 83.67; H, 8.24%. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47%.

Fractions 11—14 gave a residue (57 mg), which was chromatographed on silica gel. Fractions eluted with light petroleum were collected. Evaporation of the solvent gave

farfugin B (**2**; 49 mg), colorless liquid; UV (EtOH): λ_{max} 251.5 nm (ε 10500), 281.5 (3500), and 291.5 (3900); IR (liquid): 3020, 1575, and 965 cm^{-1}; PMR ($CDCl_3$): δ 1.65(3H, *m*; $-CH=CHC\underline{H}_3$), 2.19(3H, d, J=1.2 Hz; $C_{(3)}-C\underline{H}_3$), 2.37 (3H, s; $C_{(5)}-C\underline{H}_3$), 5.45 (2H, m; $-C\underline{H}=C\underline{H}-$), and 7.20 (3H, m; $C_{(2)}$-H, $C_{(4)}$-H, and $C_{(7)}$-H), and 2.5—3.0 (4H; $C_{(1')}$-H and $C_{(2')}$-H); MS: *m/e* 214 (37%, M^+ ($C_{15}H_{18}O$)) and 159 (100%).

*Hydrogenation of Farfugin A (**1**) over Palladium-Charcoal.* A solution of **1** (39 mg) in methanol (10 ml) was stirred with 10% palladium-charcoal (30 mg) in an atmosphere of hydrogen for 6 hr. Filtration of the catalyst and evaporation of the solvent under reduced pressure gave a crystalline product (32 mg), which was recrystallized from ethanol to give *dihydrofarfugin A* (**3**), mp 51—52 °C, UV (cyclohexane): λ_{max} 285 nm (ε 3200) and 292.5 (3500); IR (Nujol): 1610 and 1590 cm^{-1}; PMR ($CDCl_3$): δ 1.24 (3H, d, J=7 Hz; $C_{(9)}-CH_3$), 1.2 7(3H, d, J=6.5 Hz, $C_{(3)}-CH_3$), 2.15 (1H, s; $C_{(5)}-CH_3$), 2.55(2H, m; $C_{(6)}$-H), 3.00 (1H, m; $C_{(9)}$-H), 3.45 (1H, m; $C_{(3)}$-H), 4.03 (1H, dd, J=8 Hz and 7 Hz; $C_{(2)}$-H), 4.63 (1H, t, J=8 Hz; the other $C_{(2)}$-H), and 6.80 (1H, s; $C_{(4)}$-H); MS: *m/e* 216 (55%, M^+ ($C_{15}H_{20}O$)) and 201 (100%, $[M-CH_3]^+$).

*Bromination of Farfugin A (**1**).* A solution of bromine (23 mg) in chloroform (2 ml) was added dropwise to a solution of **1** (30 mg) in chloroform (5 ml) with stirring. The color of the solution disappeared immediately. Evaporation of the solvent gave a crystalline residue (40 mg), which was passed through a column of silica gel using light peroleum as eluent to afford *bromofarfugin A* (**4**; 38 mg), mp 99.5—100 °C (recrystallized from EtOH); IR (Nujol): 1590 cm^{-1}; PMR ($CDCl_3$): δ 1.38 (3H, d, J=7 Hz; $C_{(9)}-CH_3$), 2.12 (3H, s; $C_{(3)}-CH_3$), 2.27 (3H, s; $C_{(5)}-CH_3$), 2.63 (2H, m; $C_{(6)}$-H), 3.37 (1H, m; $C_{(9)}$-H), and 7.00 (1H, s; $C_{(4)}$-H); MS: *m/e* 294 (100%, M^+ ($C_{15}H_{17}OBr$)), 292 (100%, M^+), 279 (89%, $[M-CH_3]^+$), and 277 (90%, $[M-CH_3]^+$). Found: C, 61.66; H, 5.83%. Calcd for $C_{15}H_{17}OBr$: C, 61.44; H, 5.84%.

*Dehydrogenation of Farfugin A (**1**) over Palladium-Charcoal.* A mixture of **1** (51 mg) and 10% palladium-charcoal (53 mg) in a sealed tube under a nitrogen atmosphere was heated at 300 °C for 5 min. The reaction mixture was extracted with ether and evaporation of the solvent gave an oil (30 mg), which was submitted to separation by preparative tlc (silica gel impregnated with 1,3,5-trinitrobenzene, 10%; solvent: light petroleum). A silica gel layer (R_f 0.2) containing naphthofuran-trinitrobenzene adduct and that (R_f 0.4) containing naphthalene-trinitrobenzene adduct were collected respectively, and each of them was placed on the top of a column of alumina. Elution with benzene gave 3,5,9-trimethyl-naphtho[1,2-*b*]-furan (**5**; 7 mg), and a mixture (7 mg) of 1,5-dimethyl-3-isopropylnaphthalene (**6**) and 1,5-dimethyl-3-ethylnaphthalene (**7**), respectively. *3,5,9-trimethylnaphtho-[1,2-b]furan* (**5**): mp 64.5—65.5 °C (recrystallized from EtOH); UV (MeOH): λ_{max} 248.5 nm (ε 49000), 253 (48000), 282.5 (5300, shoulder), 291 (5800), 302 (4300, shoulder), 324 (1800), and 339 (1500); IR (Nujol): 1570 cm^{-1}; MS: *m/e* 210 (100%, M^+($C_{15}H_{14}O$)), 209 (38%, $[M-H]^+$), and 195 (38%, $[M-CH_3]^+$).

Spectral data of the mixture of *naphthalene derivatives* (mixture of **6** and **7**) was as follows; UV (MeOH): λ_{max} 226 nm (ε 51700), 231 (72000), 278 (5100), 287 (5700), 293 (4800), and 324 (100) (ε was calculated based on assumption of molecular weight 198); IR (liquid): 1620, 1598, 865, 795, and 745 cm^{-1}; PMR ($CDCl_3$): δ 1.35 (t, J=7.5 Hz; $-CH_2C\underline{H}_3$), 1.37 (d, J=7.5 Hz; $-CH(C\underline{H}_3)_2$, 2.68 (s; aromatic $C\underline{H}_3$), and 7.2—8.0 (m, aromatic protons); glc (retention time): (i) 8.3 and 6.8 min (Diasolid H523 (2%), 1.5 m column, 160 °C, N_2 gas flow 80 ml/min); (ii) 17.0 min (Polydiethylene glycosuccinate on Chromosorb W (20%), 2 m column, 180 °C, N_2 gas flow 60 ml/min).

*Methylation of Fukinone (**8**).* To a solution of potassium *t*-butoxide in *t*-butanol, prepared from potassium (600 mg) and *t*-butanol (40 ml), a solution of fukinone[5] (**8**; 995 mg) in *t*-butanol (10 ml) and methyl iodide (6 g) were added dropwise under a nitrogen atmosphere. The reaction mixture was set aside for 5 hr at 25 °C. After neutralization with aqueous acetic acid (AcOH, 5 ml, and H_2O, 20 ml), the mixture was condensed under reduced pressure and extracted with ether. The extract was treated as usual and the resulting residue (1.97 g) was chromatographed on silica gel (150 g). Elution with light petroleum-ether (200 : 3; each fraction, 150 ml) gave an oil, 9-methylfukinone (**9**; 559 mg; from frs 15—19) and **8** (248 mg; from frs 22—25). *9-Methylfukinone* (**9**); UV (EtOH): λ_{max} 250 nm (ε 6500); IR (liquid): 1690 and 1630 cm^{-1}; PMR ($CDCl_3$): δ 0.81 (3H, d, J=7 Hz; $C_{(4)}-CH_3$), 0.94 (3H, s; $C_{(5)}-CH_3$). 1.07 (3H, d, J=7 Hz; $C_{(9)}-CH_3$), 1.80 (3H, s; $C=CCH_3$), and 1.91 (3H, s; $C=CCH_3$); MS: *m/e* 234 (30%, M^+ ($C_{16}H_{26}O$)), 219 (3%, $[M-CH_3]^+$), 187 (42%), 163 (39%), and 109 (100%).

*Hydrogenation of 9-Methylfukinone (**9**) over Palladium-Charcoal.* The methylated product (**9**; 559 mg) was hydrogenated with 10% palladium-charcoal (65 mg) in ethanol at room temperature. Filtration of the catalyst and evaporation of the solvent gave a residue (506 mg), which was passed through a column of silica gel (100 g) using light petroleum-ether (200 : 3) as eluent. The eluate was evaporated under reduced pressure to give oily *9-methyldihydrofukinone* (**10**; 402 mg), IR(liquid): 1710 cm^{-1}; MS: *m/e* 236 (31%, M^+ ($C_{16}H_{28}O$)), 221 (14%, $[M-CH_3]^+$), 194 (40%), 97 (52%), 84 (74%), 81 (51%). 69 (73%), 67 (55%), and 55 (100%).

*Reduction of **10** with Lithium Aluminium Hydride.* To a suspension of lithium aluminium hydride (464 mg) in dry ether (30 ml), a solution of **10** (403 mg) in dry ether was added and stirred for 4 hr at room tmeperature. The excess reagent was decomposed with water and the reaction mixture was extracted with ether. The extract was treated as usual to give an oily *9-methyldihydrofukinol* (**11**; 408 mg), IR (liquid): 3450 cm^{-1}; MS: *m/e* 220 (6%, $[M-H_2O]^+$), 205 (24%, $[M-H_2O-CH_3]^+$) 177 (59%), 136 (75%), 109 (79%), 107 (66%), 95 (65%), 81 (56%), 67 (69%) and 55 (100%). A molecular ion peak at *m/e* 238 ($C_{16}H_{30}O$) was not observed.

*Dehydration of **11** with Phosphorus Oxychloride.* A solution of **11** (408 mg) and phosphorus oxychloride (2 ml) in pyridine (20 ml) was allowed to stand overnight at room temperature. The reaction mixture was poured into ice-water and extracted with ether. The extract was treated as usual to give a residue (341 mg), which was chromatographed on silica gel (100 g) using light petroleum as eluent (each fraction 20 ml). Fractions 10—12 gave a mixture of dehydrated products (**13**; 171 mg). Fractions 13—14 gave a residue, which was subjected to repeated chromatography on silica gel using light petroleum as eluent to afford the mixture of dehydrated products (**13**; 15 mg) and a chloride (**12**; 82 mg). The mixture of *9-methyleremophilenes* (**13**): colorless liquid, IR (liquid): 1650 cm^{-1}; PMR ($CDCl_3$): δ 5.16 (m, olefinic protons); MS: *m/e* 220 (5%, M^+ ($C_{16}H_{28}$)), 205 (4%, $[M-CH_3]^+$), 177 (70%), 109 (43%), 107 (44%), 97 (49%), 95 (100%), and 81 (71%). *Chloride* (**12**): colorless liquid, PMR ($CDCl_3$): δ 4.25 (m, $-CHCl-$); MS: *m/e* 258 (1.5%, M^+ ($C_{16}H_{29}OCl$)), 256 (2.5%, M^+), 221 (28%, $[M-Cl^+]$), 177 (57%), 109 (65%), 107 (96%), 81 (73%), 69 (65%), 67

(65%), and 55 (100%).

Dehydrogenation of ***13*** *over Palladium-Charcoal.* Dehydrated product (**13**; 60 mg) was heated with 10% palladium-charcoal (70 mg) at 300 °C for 5 min in a sealed tube under a nitrogen atmosphere. Another 60 mg of **13** was dehydrogenated described as above. The reaction mixtures were combined and extracted with ether. Evaporation of the solvent gave a residue (89 mg), which was submitted to preparative tlc. A diluted solution of 1,3,5-trinitrobenzene in methanol was sprayed on the plate. A zone developing a yellow color was collected and placed on the top of a column of alumina. The column was eluted with benzene to give oil 1,5-dimethyl-3-isopropylnaphthalene[4] (**6**; 24 mg). Picrate, orange needles, mp 110—113 °C (recrystallized from EtOH); trinitrobenzene-adduct, yellow needles, mp 139—141 °C (recrystallized from EtOH).

Spectral data of *1,5-dimethyl-3-isopropylnaphthalene* (**6**) were as follows; UV (EtOH): λ_{max} 225.5 nm (ε 49000), 231 (81000), 277.5 (4800), 287 (5700), 292.5 (4700), 318 (100), and 323 (100); IR (liquid): 1620, 1600, 865, 795, and 745 cm^{-1}; PMR ($CDCl_3$): δ 1.35 (6H, d, J=7.5 Hz; $-CH(C\underline{H}_3)_2$), 2.69 (6H, s, aromatic CH_3), and 7.2—8.0 (5H, m; aromatic protons); glc (retention time): (i) 8.3 min (Diasolid H523 (2%), 1.5 m column, 160 °C, N_2 gas flow 80 ml/min); (ii) 16.8 min (Polydiethylene glycosuccinate on Chromosorb W (20%), 2 m column, 180 °C, N_2 gas flow 60 ml/min).

*1-Acetonyloxy-4,8-dimethyl-5,6,7,8-tetrahydronaphthalene (****15****).* A solution of 1-hydroxy-4,8-dimethyl-5,6,7,8-tetrahydronaphtharene[7] (**14**; 896 mg) in dry acetone was refluxed with chloroacetone (964 mg), potassium iodide (314 mg), and potassium carbonate (2.50 g) for 6 hr. After the solvent was distilled off the residue was extracted with ether. The extract was washed, dried, and evaporated to afford a viscous oil (1.48 g), which was chromatographed on silica gel (75 g). Fraction eluted with benzene-light petroleum (2 : 1) gave *1-acetonyloxy-4,8-dimethyl-5,6,7,8-tetrahydronaphthalene* (**15**; 1.01 g), mp 50—51 °C (recrystallized from light petroleum); IR (Nujol): 1728, 1600, 1583, and 795 cm^{-1}; PMR ($CDCl_3$): δ 1.25 (3H, d, J=7 Hz; $C_{(8)}$-CH_3), 2.11 (3H, s; $C_{(4)}$-CH_3), 2.23 (3H, s; $-COCH_3$), 4.32 (2H, s; $-OCH_2CO-$), 6.32 (1H, d, J=9 Hz; $C_{(2)}$-H or $C_{(3)}$-H), and 6.78 (1H, d, J=9 Hz; $C_{(3)}$-H or $C_{(2)}$-H); MS: *m/e* 232 (20%, $M^+(C_{15}H_{20}O_2)$), 217 (10%, $[M-CH_3]^+$), 189 (20%, $[M-CH_3CO]^+$), 174 (100%), and 159 (88%). Found: C, 77.55; H, 8.64%. Calcd for $C_{15}H_{20}O_2$: C, 77.77; H, 8.77%.

*Cyclization of the Ether (****15****).* The ether (**15**; 971 mg) was heated with polyphosphoric acid (10 g) at 100 °C for 35 min under a nitrogen atmosphere. Ice-water was added and the reaction mixture was extracted with ether. The extract was washed with aqueous solution of sodium bicarbonate and then with water. After the solution was dried over anhydrous sodium sulfate, the solvent was removed to give a residue (860 mg), which was chromatographed on silica gel. Fractions eluted with light petroleum afforded a crystalline product, *(±)-farfugin A* (**±1**; 344 mg), mp 73—73.5 °C (recrystallized from EtOH); UV (cyclohexane): λ_{max} 253 nm (ε 13500), 281 (2800), and 290.5 (3000); IR (Nujol): 1590 and 1540 cm^{-1}; PMR ($CDCl_3$): δ 1.40 (3H, d, J=7 Hz; $C_{(9)}$-CH_3), 2.19 (3H, d, J=1 Hz; $C_{(3)}$-CH_3), 2.30 (3H, s; $C_{(5)}$-CH_3), 2.65 (2H, m; $C_{(6)}$-H), 3.37 (1H, m; $C_{(9)}$-H), 7.13 (1H, s; $C_{(4)}$-H), and 7.29 (1H, m; $C_{(2)}$-H); MS: *m/e* 214 (47%, $M^+(C_{15}H_{18}O)$), and 199 (100%, $[M-CH_3]^+$). Found: C, 84.02; H, 8.42%. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47%.

*Hydrogenation of Farfugin B (****2****) over Palladium-Charcoal.* A solution of **2** (29 mg) in ethanol was stirred with 10% palladium-charcoal (28 mg) for 5.5 hr under an atmosphere of hydrogen. Filtration of the catalyst and evaporation of the solvent gave a residue (22 mg), which was passed through a column of silica gel using light petroleum as eluent to afford oily *tetrahydrofarfugin B* (**16**; 19 mg); IR (liquid): 3020, 1618, and 1580 cm^{-1}; PMR ($CDCl_3$): δ 0.89 (3H, m; terminal CH_3 on the side chain), 1.29 (3H, d; J=7 Hz; $C_{(3)}$-CH_3), 2.23 (3H, s; $C_{(5)}$-CH_3), 2.52 (2H, m; benzyl) protons), 3.45 (1H, m; $C_{(3)}$-H), 4.01 (1H, dd, J=8 Hz and 7 Hz; $C_{(2)}$-H, 4.63 (1H, t, J=8 Hz; the other $C_{(2)}$-H), 6.58 (1H, s; $C_{(7)}$-H), and 6.88 (1H, s; $C_{(4)}$-H); MS: *m/e* 218 (100%, M^+ ($C_{15}H_{22}O$)), 203 (49%, $[M-CH_3]^+$), 162 (59%), and 161 (64%).

*Bromination of Farfugin B (****2****).* To a solution of **2** (36 mg) in carbon tetrachloride (5 ml), a solution of bromine (40 mg) in carbon tetrachloride (2 ml) was added dropwise with stirring and the resulting solution was allowed to stand at room temperature for 30 min. The products were examined by tlc. Evaporation of the solvent gave a residue (60 mg), which was chromatographed on silica gel using light petroleum as eluent to afford bromofarfugin B (**17**; 18 mg) and tribromofarfugin B (**18**; 36 mg). *Bromofarfugin B* (**17**): mp 36—37 °C (recrystallized from EtOH); IR (liquid): 3070, 3020, 1635, 1595, 1575, and 965 cm^{-1}; PMR ($CDCl_3$): δ 1.65 (3H, m; terminal CH_3), 2.12 (3H, s; $C_{(3)}$-CH_3), 2.34 (3H, s; $C_{(5)}$-CH_3), 5.45 (2H, m; $-C\underline{H}$=$C\underline{H}-$), and 7.13 (2H, s; $C_{(4)}$-H and $C_{(7)}$-H); MS: *m/e* 294 (71%, M^+ ($C_{15}H_{17}OBr$)), 292 (71%, M^+), 239 (100%), and 237 (100%). *Tribromofarfugin B* (**18**): mp 74—74.5 °C (recrystallized from EtOH); IR (Nujol): 1590, 1575, and 870 cm^{-1}; PMR ($CDCl_3$): δ 1.86 (3H, d, J=7.5 Hz; $-CHBr-C\underline{H}_3$), 2.13 (3H, s; $C_{(3)}$-CH_3), 2.40 (3H, s; $C_{(5)}$-CH_3), 4.20 (2H, m; $-C\underline{H}Br-C\underline{H}Br-$), 7.17 (1H, s; $C_{(4)}$-H or $C_{(7)}$-H), and 7.19 (1H, s; $C_{(7)}$-H or $C_{(4)}$-H); MS: *m/e* 456 (15%, $M^+(C_{15}H_{17}OBr_3)$), 454 (44%, M^+), 452 (44%, M^+), 450 (16%, M^+), 239 (100%), and 237 (100%). Found: C, 39.93; H, 3.77%. Calcd for $C_{15}H_{17}OBr_3$: C, 39.77; H, 3.78%.

*Hydrogenation of Farfugin B (****2****) over Paltinum Oxide.* Hydrogenation of **2** (8 mg) was effected over platinum oxide (8 mg) in methanol (2 ml) with stirring for 14 hr at 30 °C. Filtration of the catalyst and evaporation of the solvent gave oily *dihydrofarfugin B* (**19**; 8 mg), IR (liquid): 1575, 860, and 775 cm^{-1}; PMR ($CDCl_3$): δ 0.91 (3H, m; terminal CH_3), 2.23 (3H, d, J=1 Hz; $C_{(3)}$-CH_3), 2.42 (3H, s; $C_{(5)}$-CH_3), and 7.30 (3H, m; $C_{(2)}$-H, $C_{(4)}$-H, and $C_{(7)}$-H); MS: *m/e* 216 (19%, M^+ ($C_{15}H_{20}O$)) and 159 (100%).

The authors wish to thank Dr. M. Fukuyama and Mr. K. Sato, Sagami Chemical Research Center, Sagamihara-shi, for the measurements of NOE's.

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